# Fluoride and Cardiovascular Disease: 2013

*Implications for Public Health in Ireland and other Fluoridated Communities*

By: Declan Waugh BSc. CEnv. MCIWEM. MIEMA. MCIWM.

## Abstract

Cardiovascular disease (CVD) is Ireland's greatest killer with almost 10,000 people dying every year from conditions such as coronary heart disease and congestive cardiac failure (heart failure); cerebral (brain) conditions such as stroke; and peripheral (limb) conditions such as peripheral vascular disease. The main base cause of heart disease is atherosclerosis whereby blood vessels narrow or become completely blocked. Mortality rates from CVD increased sharply after commencement of water fluoridation in Ireland and peaked when all major urban areas and the majority of the population were fluoridated in the mid 1970's. Today Ireland continues to have the highest rate of premature deaths from ischaemic heart disease (<65yrs) in the European Union and life expectancy for both men and women ranks below the EU 15 average life expectancy. Research has demonstrated that fluoride is a risk factor in cardiovascular disease, as well as other major diseases including hypothyroidism, diabetes and obesity. Fluoride interferes with heart function, incorporates into the aorta and atherosclerotic plaque in coronary arteries as well as impairs homocysteine, insulin and glycogen synthesis in addition to mitochondria respiration all of which are known contributors to heart disease. Research has demonstrated that oxidative stress and inflammation are important pathophysiological mechanisms involved during ischaemic stroke. Fluoride is recognized to contribute to oxidative stress and inflammation as well as respiratory disease. Coronary heart disease has been found to be strongly associated with dental fluorosis (a biomarker for chronic overexposure to fluoride). Ireland has the highest prevalence of dental fluorosis in the EU and is also the only EU Member State to support mass intoxication of its population with fluoride and silicofluorides through public water supplies. The recent epidemic of respiratory disease diabetes and obesity in Ireland and their future contribution to cardiovascular illhealth will place further enormous social and economic burdens on the Irish state. In light of these findings it is critical that risk factors such as fluoride exposure are urgently reassessed and mass medication without informed consent of populations through artificial fluoridation of water is ended to protect public health.

**Keywords:** Cardiovascular disease, ischaemic heart disease, diabetes, obesity, respiratory disease, water fluoridation, risk factors.

## Introduction

Cardiovascular disease remains the most common cause of death in Ireland, currently accounting for one-third of all deaths and one in five premature deaths.

Vascular diseases, of which cardiovascular disease is the most common, account for over 40% of all deaths and 37% of deaths under 65 years in Ireland. Approximately 10,000 people die each year in Ireland from cardiovascular disease (CVD) - including coronary heart disease (CHD), stroke and other circulatory disease. The largest number of these deaths relate to CHD - mainly heart attack - at 5,000, with approximately 22% of premature deaths (under age 65) due to CVD. According to figures from the cardiac rehabilitation unit at Wexford General Hospital, the number of deaths from Coronary Artery Disease in Ireland is 60,7 per 100,000, almost twice the EU average of 32.6.[1]

Ireland has the highest rate of premature deaths from ischaemic heart disease (<65yrs) in the European Union[2] and life expectancy still ranks below the EU15 average for both men and women.[3]

This article reviews the available information examining how fluoride interferes with heart function, incorporates to the aorta and atherosclerotic plague in coronary arteries, and contributes to cardiovascular disease in general.

Data provided in this document will show how mortality rates from cardiovascular disease increased sharply in Ireland post commencement of water fluoridation. While mortality rates in the past decade have reduced significantly this could not have occurred without the documented four-fold increase in prescribed medication for cardiovascular disease and increased expenditure in healthcare and intervention. Without such, it can be presumed mortality rates in Ireland would be much higher than they currently are. Apart from the human cost, the cost of cardiovascular disease to the Irish economy – which includes the costs of healthcare, loss in productivity and informal care – is a significant burden.

Given the scientific information currently available demonstrating that fluoride is a risk factor in cardiovascular disease, as well as diabetes, thyroid disorders, mental depression, skin disorders, obesity and gastrointestinal disorders, in addition to its potential contribution to increased cancer prevalence in Ireland, and observing that the prevalence of many of these conditions in Ireland is significantly above the EU average; it is therefore of the upmost priority that the Government of Ireland take appropriate action and comply with the 'precautionary principle' in ending fluoridation of drinking water and mass fluoride intoxication of the population of Ireland immediately.

The few mainland European Member States that did previously fluoridate water supplies have all long since ceased to support such a policy. Where fluoridation was stopped, it was shown to have no negative impacts on the populations dental health and was observed to benefit public health in their communities.[4,5,6,7]

The current health behaviour of the Irish population demonstrates that mass fluoride intoxication of the population with untested industrial chemicals is dangerous and is contributing to the enormous health burden of disease now prevalent in Ireland today.

To add to the current crisis the Department of Health recently warned that *"there is a potential epidemic of heart failure in Ireland over the next 10 years"*[8] It is of paramount importance therefore that every precaution must be taken to reduce the exposure of Irish citizens to any unnecessary risk factors, such as fluoridation of drinking water, that is clearly contributing to increasing disease burdens in society.

This paper presents some of the information currently available which clearly demonstrates that fluoride exposure is a contributor to cardiovascular disease. Much of this data has already been provided to the Government of Ireland by this author, however, this paper includes new evidence to support previous communications to the Government that highlighting the health risks associated with water fluoridation using silicofluoride chemicals.

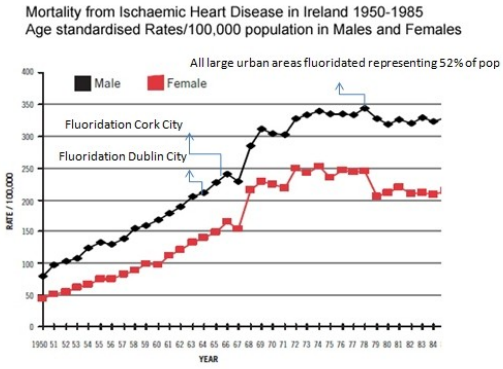
We are also approaching the 100th anniversary of the 1916 Rising, a pivotal historic period that led to the establishment of the Irish Republic. At the current time Ireland holds the presidency of the Council of the European Union.

It is lamentable therefore that in 2013 the Government of Ireland continues to enforce the mass medication of its population, mandated by national legislation, using untested industrial chemicals; a policy that every other mainland European country has independently decided, through risk assessment, is unjustifiable, unethical, uneconomical, unsafe and environmentally unsustainable.

## History of Water Fluoridation and Ischaemic Heart Disease in Ireland

In 1962, prior to commencement of water fluoridation in Ireland, mortality for males from ischaemic heart disease was a rate of 190 deaths per 100,000 and 140 per 100,000 for females. In 1964, more than 25 per cent of the population of the State were receiving water from fluoridated piped water supplies. This included the greater Dublin area and the adjacent areas on the east coast. Fluoridation commenced in the second largest urban area Cork City and County in 1965 and over the following seven to eight years all the major urban communities throughout the country were fluoridated.[9]

In 1969, just a few years after commencement of fluoridation the rate of mortality from ischaemic heart disease had dramatically increased to 315 deaths per 100,000 for males and 235 deaths per 100,000 for females, representing an increase of 65% in mortality for this disease in both males and females respectively. By 1979, it had reached a peak of 350 deaths per 100,000 for males and 250 deaths per 100,000 for females representing an 84% increase in mortality for this disease in less than a decade after commencement of water fluoridation as illustrated below.




Source: 50 years of Heart Disease in Ireland Mortality, Morbidity and Health Services Implications, Irish Heart Foundation, Feb 2001

As is evident in the graph, a sharp increase in mortality occurred in 1967 and continued to rise significantly above European averages until 1978, when levels reached plateaued out and from where they eventually started to decline. This dramatic increase in mortality rates occurred in Ireland at a time when age adjusted mortality rates were falling internationally by 2% per annum in the 1970's and 1980's.[10]

While deaths rates have declined since for the period 2000-2004 Ireland had on average 144 deaths from CHD per 100,000 population,which was higher than EU 15 of 92 deaths per 100,000 and higher than the EU 27 of 113 deaths per 100,000. [11]

In comparison, the age adjusted mortality rate in the United States, (where approximately 65% of the population consume fluoridated water, compared to 75% in Ireland) is 135.0 deaths per 100,000. The rate for males was 41.6% higher than for females (176.5 versus 103.1 per 100,000 population, respectively).[12]

Similarly the age adjusted mortality rates for fluoridated Australia at 123 per 100,000 are also above the European average. As with fluoridated America and Ireland, the mortality rate in Australia for males at 169 per 100,000 is significant.[13]

The major decline In Ireland has occurred in the last decade, brought about largely by increased clinical intervention, medication and behavioral change. It has been estimated that half of the decrease in death rates can be attributed to treatments and interventions.[14] If it were not for fluoridation, it is most likely that mortality rates would have levelled off earlier and not have risen to the record levels attained in the 1970's, at a time in stark contrast when significant decreases in mortality were being observed in other countries.

## Current Status

It is well known that life expectancy in Ireland compares poorly with that in other developed countries. Remarkably life expectancy for Irish men at age 60 in 1985-1987 (16.0 years) had changed little from that for 1925-1927 (15.8 years).[15] Ireland ranks below the EU15 average for life expectancy for both men and women.[16]

Any gains in life expectancy through lower death rates from infectious diseases such as pneumonia and tuberculosis were cancelled out by increased death rates from cardiovascular disease (CVD).[17]

Ireland currently has the highest rate of premature deaths from ischaemic heart disease (<65yrs) in the European Union[18].

In 2010 it was estimated that more than 79,000 (2.4%) adults aged 18+ years in RoI have been told by a doctor in the previous 12 months that they have CHD (clinically diagnosed CHD). This excludes undiagnosed CHD and is likely to be an underestimate of the number of people with the condition.[19]

In 2007 nearly 131,000 adults had ever had a Coronary Heart Disease (CHD, angina and heart attack). By 2020 this is expected to rise to over 195,000 people - an additional 65,000 people (a 50% increase in less than 15 years).

In 2007 almost 59,000 adults have ever had a stroke. By 2020 this is expected to rise to almost 87,000 people – an additional 28,000 adults (an increase of 48% in less than 15 years).[20]

These figures do not include individuals who have undiagnosed cardiovascular disease. International research has shown that 50% of men and 64% of women who have had a fatal heart attack or stroke never knew they had the disease.[21]

From 2000 to 2004 Ireland had on average 144 deaths from CHD per 100,000 population, which was higher than EU 15 of 92 deaths per 100,000 and higher than the EU 27 of 113 deaths per 100,000.[22]

The Department of Health, National Cardiovascular Health Policy Report[23] published in 2010 compares cardiovascular health data for Ireland with other EU Member States from the years 2003 to 2007 across all ages.

During this time Ireland had a reduction on the years 2000-2004 to on average 118 (age-standardised) deaths from ischaemic heart disease per 100,000 population annually.

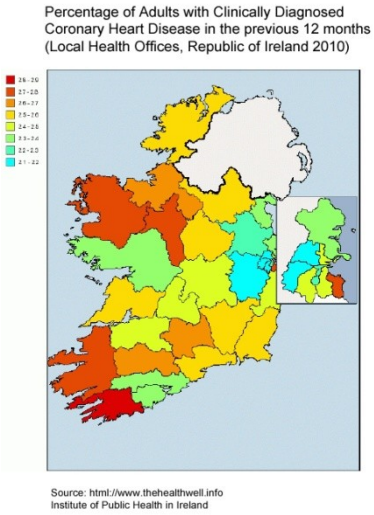
Mortality was however higher than the EU15[1] rate of 80 deaths per 100,000 and higher than the EU27[2] rate of 101 deaths per 100,000.

The Department of Health reported that in regard to premature deaths, ischaemic heart disease death rates annually in Ireland averaged 25 per 100,000, compared to 18 deaths in the EU 15 and 24 in the EU 27.

The Department of Health further observed that this could not have been achieved without the increasing workload in health services in the hospital, primary care including a four-fold increase in the use of prescribed cardiovascular medication.

## *Geographic Variation in CHD*

There is a wide geographic variation in mortality rates from cardiovascular disease in Ireland. This is illustrated in Figure 3 below. The incidence rates do not include undiagnosed CHD.




The geographic spread for CHD largely mirrors that for other major diseases in Ireland such as diabetes, cancer and neurological illness. The areas with the highest prevalence of disease burdens are largely those where drinking water is both soft (low in calcium) and fluoridated.[24]

It is interesting to note that the most Southerly part of Ireland has the highest incidence of CHD. Drinking water in large parts of South and South East Ireland including West Cork located in the southern tip of (the area identify as red on the map above) Ireland, are extremely soft with less than 20mg/L calcium. Similarly soft drinking water is found in large parts of geographic areas such as Mayo, Donegal, Kerry, Wexford, Waterford and Roscommon. All of these counties have elevated CHD significantly above the National and European average.

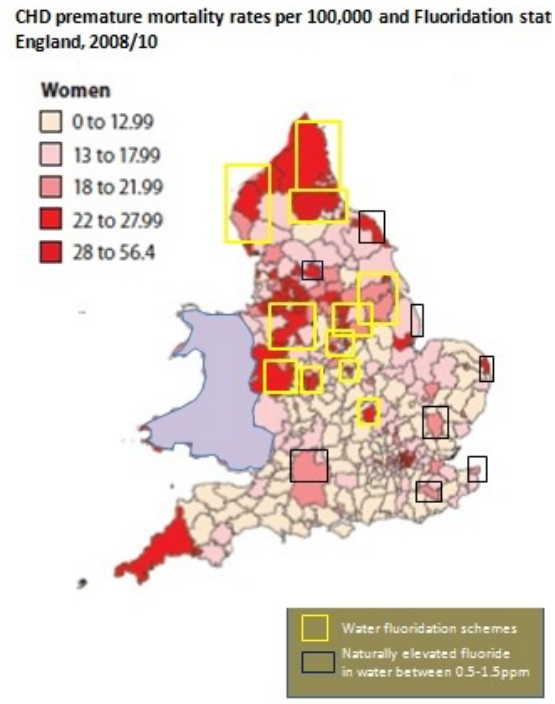
## *Comparison with England*

In comparison, the highest deaths through CHD in England are in the North West of England with a death rate of 93.2 per 100,000. The figure for the South West of England is 67.4 per 100,000. CHD rates in England are lower than in the rest of the UK. Over 5% lower for men and 20% lower for women in England than in Northern Ireland. 20% lower for men and 50% lower for women in England than in Scotland. The data from England is remarkable as mortality rates for CHD are geographically located in areas where water fluoridation programmes are currently in use. It is to be noted that these areas also largely reflect those with greatest social inequality in England.

The exception being Cornwall in the South West of England, however it is known that drinking water in this region has low calcium and is defined as soft water. This would explain the high incidence of CHD in this region.[25]

[1] EU15 data refers to 9 countries in 2007 and 12 in 2006 who had reported mortality data.
[2] EU27 data refers to 19 countries in 2007 and 23 in 2006 who had reported mortality data.

Nevertheless the correlation between fluoridation of public water supplies programmes, fluoride content in drinking water and CHD is significant, as illustrated below.




Source: England CHD Statistics Factsheet 2012 .
The extent of water fluoridation in UK, British Fluoridation Society

## *Comparison with Northern Ireland and Europe*

According to figures from the cardiac rehabilitation unit, Wexford General Hospital, the number of deaths from Coronary Artery Disease in Ireland is 60,7 per 100,000, almost twice the EU average of 32.6.[26] In comparison the age standardized death rate from CHD in Northern Ireland is 60.44 for men and women 21.01.

However it must be noted that poverty, stress and social conflict play a major role in heart disease and this is reflected for the data for NI. Significantly higher CHD prevalence is noted in the geographic areas with the highest social inequality, poverty and unemployment. These same areas not only represent those that are the most socially deprived but also where conflict and trauma were most prevalent during the *'Troubles'* in Northern Ireland. For example significantly higher CHD rates for males are to be found in Derry (80.09), Belfast.(89.05) and Ballymena (115.45) compared to more rural areas such as Castlereagh (30.08) Antrim (24.9) and Moyle (33.48).[27]

What is also remarkable about the data for Northern Ireland is that the only two locations in Northern Ireland where fluoridation was introduced and continued for approximately 30 years, in Tandragee Co. Armagh and Hollywood, County Down, both had significantly higher rates of premature mortaility compared to the their adjoining local authority districts.[28]

In comparing CHD in Ireland with Europe the Age-standardized Disability-adjusted life years (DALYs) per 100,000 for CHD, stroke and other CVD, provides further insights to the impact of CHD and the gap between Ireland and other European Member States. The DALYS for CHD for Ireland is calculated at 671 compared to the UK (657), Iceland (470), Norway (503), for Sweden (506), Denmark (478),.Germany (574), France (259). Spain (367) and the Netherlands (460). A similar pattern is provided for CVS.[29]

## Confounding Factors:

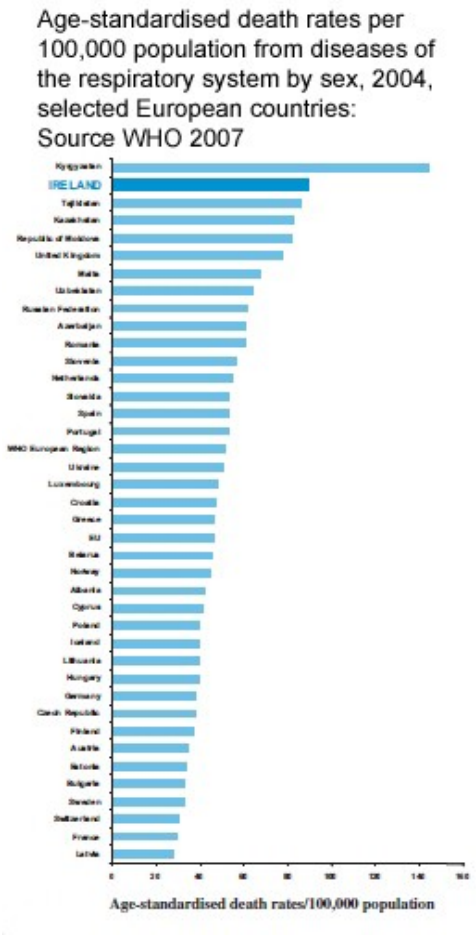
There are many compounding factors in CHD, some of these are discussed in the following section with comparisons where appropriate between Ireland with other EU Member States.

## *Influence of Smoking*

Tobacco, like tea is a significant source of fluoride and is a major source of dietary fluoride intake. In Europe, about 20% of deaths from CVD in men and about 3% of deaths from CVD in women are due to smoking. The equivalent figures for the 25 countries that made up the EU in 2006 (EU-25) are 16% and 5% respectively. For the period 1995-99 Ireland had one of the lowest prevalence of smoking for adults in EU at 32.4 percent, compared to France (35%), Germany (43%), Denmark (35.4%), Italy (33.8%), Norway (33.4%), the Netherlands (38.9%),Spain (42.8%) and Switzerland (39%).[30]

It is obvious that one would expect countries with higher smoking prevalence's than Ireland to have higher CHD mortality rates. The difference between CHD mortality rates for Ireland and other European countries should be considerable less than they currently are as historically higher smoking prevalence in other European Member States should have seen a marked increase in CHD mortality rates from smoking compared to Ireland. Yet this is not the case.

What is extraordinary however is that in 2008, Ireland had the highest death rate from respiratory disease in EU, almost twice the EU average.[31] In the entire league of European countries only Kyrgyzstan (formerly part of the Soviet Union) has a death rate from respiratory disease higher than Ireland.[32] Remarkably approximately 69% of the population in Kyrgyzstan has dental fluorosis with up to 16% suffering from skeletal fluorosis.[33] This clearly demonstrates that the population is chronically over-exposed to fluoride and that fluoride is a significant contributor to disease burdens.




It is not surprising to find that according to the latest WHO data published in April 2011 Coronary Heart Disease Deaths in Kyrgyzstan reached 12,884 or 30.19% of total deaths. The age adjusted Death Rate is 349.39 per 100,000 of population ranking Kyrgyzstan third in the world for Cardiovascular disease.[34]

It is significant therefore the two countries in Europe with the highest exposures to fluoride have by far the highest mortality from both cardiovascular and respiratory diseases. High mortality rates both these diseases are also recorded for the United States of America where the majority of the population are also exposed to fluoridated water.[35]

The ability of fluoride to impair the bodies immune system[36] may explain

help explain this anomaly, reducing the ability of the body to fight disease.

In regard to respiratory disease it is important to note that animal studies have demonstrated that lung tissues presented emphysema and lung parenchyma inflammation associated with loss of alveolar architecture in the second generation of animals exposed to fluoride in drinking water.[37]

The inflammatory effect of fluoride exposure has also been demonstrated in human lung epithelial cells.[38]

It is evident therefore that while smoking is contributing to CHD amongst the population additional factors are influencing the significantly higher burden of CHD and respiratory disease present in Ireland.

## *Alcohol*

Alcohol use is related overwhelmingly detrimentally to many cardiovascular outcomes, including hypertensive disease (Taylor et al., 2009)[39], haemorrhagic stroke (Patra et al., 2010)[40] and atrial fibrillation (Samokhvalov, Irving & Rehm, 2010)[41].

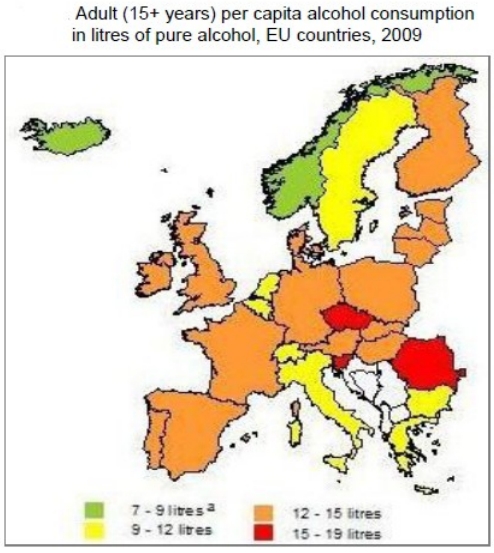
For ischaemic heart disease and ischaemic stroke, the relationship is more complex. Chronic heavy alcohol use has been associated uniformly with adverse cardiovascular outcomes (Rehm & Roerecke, 2011)[42]. But, on average, light to moderate drinking has a protective effect on ischaemic diseases (Roerecke & Rehm )[43]This effect is found to be equal for people who just drink beer or who just drink wine (Di Castelnuovo et al., 2002)[44]

The detrimental effects of heavy drinking occasions on ischaemic diseases are consistent with the physiological mechanisms of increased clotting and a reduced threshold for ventricular fibrillation which occur following heavy drinking (Rehm et al., 2010).[45]

People who are socially disadvantaged people or who live in socially disadvantaged areas experience more harm per gram of alcohol consumed than the better-off (Rehm et al., 2009)[46].

In Finland, areas with higher levels of manual workers or of unemployment and areas with lower social cohesion had higher levels of alcohol-related mortality among men aged 25–64 years (Blomgren, Martikainen & Makela, 2004).[47]

The level of consumption of a country level varies throughout EU. Figure 3 below illustrates the variation across the EU.




Source: Alcohol and the European Union, World Health Organisation,2012

The proportion of alcohol-attributable mortality in Ireland to all deaths in the group aged 15−64 years is <10% for men. This is significantly less than the EU average and below Germany(13%), Spain(12%),Finland(16), France(16),

Austria(16), Poland(16), Luxemburg(14%), Denmark(14%), Switzerland(11.5%) & Belgium(11%).

For woman mortality from alcohol attributable mortality in Ireland is at <7% which is also below the European average. The highest rates of mortality are in the Baltic regions where up to 25% of deaths are attributable to alcohol.

The WHO report on alcohol in the European Union (2012) estimates that there are approximately 110,000 alcohol attributable deaths across EU each year.[48] For men, the highest contribution to alcohol-attributable mortality is made by liver cirrhosis (26%) and unintentional injury (23%), followed by cancer (16%), intentional injury (15%) mental and neurological disorders (8%) and cardiovascular diseases last (7%).

For women, more than two thirds of alcohol-attributable deaths arise from liver cirrhosis (37%) and cancer (31%) (the largest proportion of which concerns breast cancer, with 21%), with cardiovascular disease other than ischaemic heart disease as a distant third cause (11%). Moderate alcohol consumption was also seen to have a beneficial effect on ischaemic heart disease.[49]

Based on this information it can be concluded that while alcohol consumption in Ireland is contributing to CHD, the significantly higher prevalence of alcohol related mortality in other EU countries, as noted above, should see CHD death rates higher in EU than in Ireland.

Yet this is not the case, not only does Ireland have the highest rate of premature deaths from ischaemic heart disease (<65yrs) in the European Union[50] but significantly higher mortality from CHD than the EU 15 or EU 27 countries, where alcohol related deaths and their contribution to CHD deaths are much higher than Ireland.[51]

What is also relevant however is that draught beer sales in Ireland are much higher than in other EU countries and beer, as with any beverage product produced in Ireland, is most likely to be fluoridated as manufacturers use fluoridated public water supplies. Alcohol consumption in Ireland, compared to other EU countries is therefore a potentially significant additional dietary source of fluoride.

### *Vitamin D 12*

Recently Vitamin D deficiency has been identified as a potential risk factor for many diseases not traditionally associated with Vitamin D, such as cancer and CVD.[52]

Vitamin D deficiency has been associated with CVD risk factors such as hypertension and diabetes mellitus, with markers of subclinical atherosclerosis such as intima-media thickness and coronary calcification, as well as cardiovascular events such as myocardial infarction and stroke in addition to congestive heart failure. It is plausible to suggest that vitamin D deficiency contributes to the development of CVD through its association with other known risk factors, such as diabetes and hypertension.

The differences in CHD between Northern, Southern and Western European countries and Central and Eastern European Countries would appear to support this interaction. It is evident that Southern European countries still having lower death rates from CVD than Western European countries apart from Greece and Malta

which have significantly higher mortality rates than other southern European countries for CHD. [53]

There are however significant differences between Ireland and other Northern European countries including England, Iceland, Denmark, Sweden and Norway.

This can be illustrated in the figures for Age-standardized Disability-adjusted life years (DALYs) per 100,000 for CHD, stroke and other CVD in Europe. For Ireland the figure is 671 compared to UK (657), Iceland (470), Norway (503), Sweden (506), Denmark (478), the Netherlands (460), and Germany (574), while the figures for France, Spain and Portugal are 259 and 367 and 431 respectively.[54]

It is likely that V D12 is playing a role in increased CHD in Ireland but these figures would suggest that it is limited and other factors dominate.

### *Obesity and Diabetes.*

Fluoride is a risk factor in both the development of obesity and diabetes.[55] It is now known that biologically relevant doses of fluoride results in impairment of glucose tolerance or increased blood glucose and decreased insulin synthesis.[56] Both of these conditions are major contributors to diabetes and obesity which have also reached epidemic proportions in Ireland. In Ireland, the incidence of type 1 diabetes is 16.8 per 100,000, which is above the European average.[57]

Diabetes is a condition in which the amount of glucose in the blood is too high because the body is unable to use it properly. Normally, the amount of glucose is carefully controlled by the hormone insulin, which is produced in the pancreas.

The prevalence of obesity in Ireland is among the highest in the EU 27.[58] Obesity in18-64 year old adults increased significantly in Ireland between 1990 and 2011, from 8% to 26% in men, and from 13% to 21% in women, with the greatest increase observed in men aged 51-64 years.[59]

Notwithstanding other lifestyle and dietary factors this subgroup also represents those with the highest lifetime exposure to fluoride in the Republic of Ireland since commencement of artificial fluoridation in mid 1960's. It is also worth nothing that figures for obesity in Ireland are considerably above the EU average.

It is now accepted that a high fat diet and obesity induce endoplasmic reticulum (ER) stress in liver, which suppresses insulin production and contributes to diabetes.[60]

The Russian Academy of Sciences recently published a review[61] of scientific literature on the molecular toxicity of fluoride and noted how fluoride induces endoplasmic reticulum (ER) stress. The endoplasmic reticulum (ER) is a cellular compartment responsible for multiple important cellular functions including the biosynthesis and folding of newly synthesized proteins destined for secretion, such as insulin. Accumulating evidence suggests that ER stress plays a role in the pathogenesis of diabetes, contributing to pancreatic β-cell loss and insulin resistance. ER stress has also importantly been linked obesity and insulin resistance in type 2 diabetes.

Disturbances in the normal functions of the ER lead to cell death if ER dysfunction is severe or prolonged. Important roles for ER-initiated cell death pathways have been recognized for several other diseases, including hypoxia, ischemia/reperfusion injury, neuro-

degeneration, diabetes and heart disease.[62]

Researchers Menoyo et al.[63] and Lin et al.[64] demonstrated the effect of fluoride on glucose metabolism using in vivo and in vitro experimental models and confirmed that biologically relevant doses of fluoride result in impairment of an oral glucose tolerance test and decreased insulin synthesis.

It has also been reported by Montalvo et al. [65] that fluoride exposure regulates insulin gene expression in murine beta pancreatic cells, resulting in reduced insulin secretion.

Further studies have shown that fluoride exposure may contribute to impaired glucose tolerance or increased blood glucose.[66],[67],[68]

The influence of fluoride in contributing to diabetes and obesity must consequently to be regarded as a significant risk factor in the high rates of CHD in Ireland. Given these facts the contribution of mass fluoridation of the population to increased CHD cannot be excluded.

An examination of the fluoride as a risk factor in both diabetes and Obesity in Ireland has previously been examined by Waugh.[69]

### *Hypothyroidism*

In humans, effects on thyroid function have been documented with fluoride exposures of 0.05-0.13 mg/kg/day when iodine intake was adequate and 0.01-0.03 mg/kg/day when iodine intake was inadequate.[70]These ranges are well within the exposure levels experienced by the general public in Ireland. Therefore it is a scientific fact that fluoride exposure of sensitive subgroups of the population will clearly impact on the thyroid function of some consumers.

Hypothyroidism is a clinical state resulting from an insufficient amount of circulating thyroid hormone to support normal body function. It may exist in utero or develop in infancy, childhood or even in adult life. The prevalence of unsuspected overt hypothyroidism, defined as the combination of biochemical and clinical findings of hypothyroidism, ranges from 1-18 cases per thousand persons.

Ireland has the highest incidence of congenital hypothyroidism (CHT) in the EU.[71],[72] The incidence of CHT was 1 case per 2296 live births in the Republic of Ireland (ROI) in the past decade with increasing numbers over recent years.[73] The Global mean incidence for Congenital hypothyroidism (CHT) is 1/3800 with a reported incidence of 1:3500 in Caucasian populations.

Subclinical hypothyroidism (SCH), affects about one in six people over the age of 65 in Ireland and has been linked to various health problems, such as heart attacks and strokes, in later life.

Subclinical hypothyroidism is considered a strong risk factor for later development of overt hypothyroidismassociate subclinical thyroid dysfunction with changes in cardiac function and corresponding increased risks of heart disease.[74],[75],[76]

Subclinical hypothyroidism is associated with increased cholesterol concentrations increased incidence of depression, diminished response to standard psychiatric treatment, cognitive dysfunction, and, in pregnant women, decreased IQ of their offspring.[77],[78]

The incidence of hypothyroidism prevalent in Ireland must consequently to be regarded as a significant risk factor in the high rates of CHD in Ireland.[79] This obviously has major implications for water fluoridation, as biological relevant concentrations of fluoride are known to contribute to this disease.

### *Water Hardness & Calcium*

The consumption of soft water is associated with increased risk of cardiovascular mortality from cardiovascular, ischaemic heart and hypertensive heart disease.[80, 81, 82, 83, 84]

Calcium levels in drinking water are also of significance in fluoride absorption and fluoride retention in humans. Fluoride has been implicated in disturbing the functionality of calcium, both directly[85] and indirectly in interaction with Vitamin D.[86] Hammond[87] found that any cause of hypocalcemia or vitamin D deficiency can lead to secondary hyperparathyroidism (elevated PTH) in an attempt by the body to maintain calcium homeostasis.

It is also now known that secondary hyperparathyroidism in response to calcium deficiency may contribute to a number of diseases, including osteoporosis, hypertension, arteriosclerosis, degenerative neurological diseases, diabetes mellitus, some forms of muscular dystrophy, and colorectal carcinoma.[88]

In high calcium waters most of the fluoride is excreted while in low calcium waters the majority of fluoride is absorbed; resulting in elevated blood plasma fluoride levels, and retention of fluoride in various organs of the body.[89]

Furthermore Dr. G. W. Rapp, Professor of Biochemistry and Physiology, noted that multiple smaller doses of fluoride (such as by drinking fluoridated water) will result in greater retention of fluoride than exposure to a single large dose.

Consequently dietary retention of fluoride will vary considerably by individual depending on the source and chemistry of drinking water that is fluoridated, the individuals metabolism and nutritional health.

The indirect action of fluoride decreases calcium absorption from the gastrointestinal tract increasing in the body's calcium requirement. If dietary calcium is inadequate to support the increased requirement, the response is an increase in secondary hyperparathyroidism.[90]

This view is supported by Krishnamachari in his review[91] when he found that In the presence of inadequate calcium, fluoride directly or indirectly stimulates the parathyroid glands, causing secondary hyperparathyroidism leading to bone loss.

It is also now accepted that altered calcium homeostasis is recognized as a key pathophysiological mechanism in heart failure, leading to altered contractile function and transcriptional activity.[92]

Calcium homeostasis depends on efficient energy-driven calcium and sodium pumps, while calcium concentration in turn determines energy expenditure through cellular ATPases and mitochondrial dehydrogenases. Disturbances in these finely controlled cellular processes make the myocyte enter a vicious cycle of energy mismatch and calcium dysregulation that may turn out to be highly detrimental.[93]

Given the sharp increase in CHD post water fluoridation and the geographical association of CHD with low calcium areas of Ireland, the role of water fluoridation and the bioavailability of fluoride in low calcium drinking waters must therefore be considered a risk factor in the high prevalence of CHD in Ireland.

This evidence of high CHD in communities that are fluoridated in England supports this view. The widespread implementation of water fluoridation in Ireland is the only known variable and identifiable risk factor that is present in Ireland and absent in mainland European countries. Its contribution to CHD cannot be overlooked.

### *Homocysteine*

There are a number of risk factors associated with cardiovascular disease including homecysteine.[94],[95],[96] Homocysteine is an intermediate product of methionine metabolism. Any substance that may inhibit secondary metabolism of methionine would result in increased homocysteine levels resulting from less homocysteine being metabolized into (L)-Cystathionine.

Fluoride is known to be an inhibitor of enzymatic activity and research has identified fluoride as an inhibitor of homocysteine hydrolase.[97]

Inhibition of homocysteine hydrolase would result in cellular accumulation of homocysteine[98] and therefore contribute to the development of cardiovascular disease.

The impact of fluoride on homocysteine must consequently to be considered a risk factor in the high rates of CHD in Ireland.

### *Fluoride and Heart Physiology*

Research published in 2010 demonstrated that fluoride also affects the aorta (main artery) and heart in ways that lead to increased heart attacks. [99],[100] This confirms earlier studies showing that high blood-fluoride levels have an effect on body calcium, leading to calcification of the aorta and other arteries.[101],[102]

Animal studies by Ebert et al.[103],[104] demonstrated that fluoride exposure resulted in retarded development of heart muscle and inhibition of heart function in developing chic embyros.

Research undertake by Spratt[105] concluded that primary site of fluoride action was enolase, which is distributed predominantly in the heart and skeletal muscles and is a biomarker for myocardial damage.

In addition to enolase inhibition, fluoride is recognized as a potent inhibitor of non-specific phosphatases and mitochondrial adenosine triphosphatase.[106],[107]

Slater & Bonner[108] found succinic dehydrogenase to be the site of fluoride inhibition in the succinoxidase system of heart-muscle preparations.

Subsequently it has been found that a depression of all known energy-liberating reactions in the heart may play an important role in the further development of chronic and acute heart disease.[109] The implications for cardiovascular health for a population of increasing exposure of a population, through addition to drinking water, of a compound that is known to inhibit both glycolysis and mitochondria respiration are therefore significant.

Turla et al.[110] observed that fluoride inhibits calmodulin, loss of calmodulin

activity has been linked to contractile dysfunction which causes congestive heart failure as characterized by a high incidence of Sudden Adult Death Syndrome (SADS.)[111]

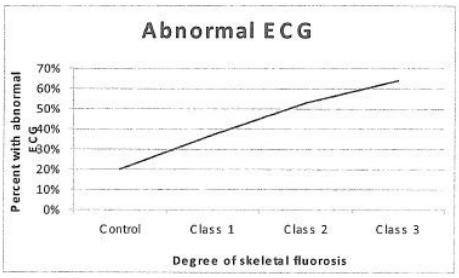
Varol et al. examined the effect of fluoride exposure on cardiovascular system in a clinical setting. and observed that elastic properties of ascending aorta were impaired in patients with endemic chronic fluorosis and that chronic fluoride toxicity can cause aortic stiffness in patients as well as ventricular diastolic and global dysfunctions.[112],[113]

Furthermore Varol et al. found that fluoride toxicity can cause atherosclerosis at molecular level, as well as aortic stiffness and disturbed ventricular distensibility at clinical level. [114]

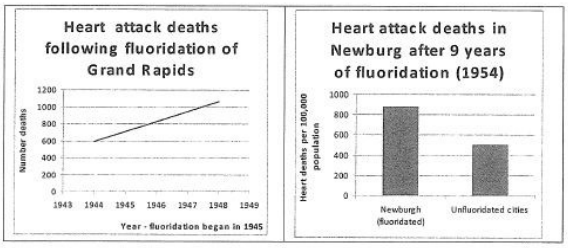
Research has also demonstrated that fluoride accumulates in aorta vascular walls and that a significant correlation exists between fluoride uptake and coronary calcifiation.[115]

Further research has shown that the heart beat rate slows, and heart rate abnormalities increase, in direct proportion to increasing fluoride levels. Since fluoride is a cumulative poison, lower levels of fluoride will have a more subtle long-term effect, thus increasing heart problems and other disease burdens within society.

Due to the that fact that fluoride bioaccumulates in the human body over a lifetime even relatively low levels of used for water fluoridation, taken in additon to other dietary sources of fluoride the burden or toxic affect can easily reach the "Class 1" level (shown in the chart below that can contribute to this effect). Fluoride's effects were evident at water levels of 0.2mg/L or more of Fluoride.[116],[117]




This supports the findings from the earliest days of fluoridation in the USA which found that following the introduction of fluoridation, deaths from heart attacks significantly increased in fluoridated communities, compared to the non-fluoridated communities.[118],[119],[120]




The data from the USA has appears to collerate with CHD data for the England where it can be seen that the highest prevalance of CHD is geographically located in areas where water fluoridation programmes are currently in use.

It has also been documented by Professor T. Takamori and his researchers in Japan that fluoride damages the heart muscle, especially in subjects deficient in Vitamins A and D.[121] They further observed that fluoride decreases the energy building glycogen in the muscles,[122] and that it adversely affects the functions of the kidneys.[123]

Dr. Mitsugi Hirao, another member of the research group, produced anemia and abnormal changes in the bone

marrow by fluoride.[124] He recorded an increase in blood platelets, an indication of a disturbance in the clotting mechanism of blood. These experiments correlate with clinical observations by Dr. Waldbott who measured on patients with fluorosis, significantly elevated blood platelets, at levels multiples above what would be considered normal.[125]

Dr. Albert Schatz, discoverer of the antibiotic Streptomycin, which was the first antibiotic remedy used to treat tuberculosis and a number of other diseases, and a distinguished recipient of the Rutgers medal in 1994 (for his contribution to medicine) investigated mortality rates in Chile pre and post commencement of water fluoridation programmes in the 1960's and found that fluoridation of drinking water resulted in increased death rates in Chile.

He demonstrated that poor, malnourished children, especially infants, are the most sensitive barometer of fluoride toxicity. Dr. Schatz examined the data for the three "test" cities in Chile including, Curico, (F 1 ppm), San Fernando (F 0.0 ppm), and La Serena (0.67 ppm) and noted that the only possible conclusion was that fluoridation was causing significant numbers of deaths.

In examining the deaths resulting from congenital malformations as a percentage of the total number of deaths in the three test cities, he found that Curico the optimally fluoridated community had 244% more such deaths than San Fernando, and 94% more than La Serena while infant mortality rates in Curico were 69% greater than in San Fernando and La Serena.

Research undertaken by Dr. Schatz and supported by Dr. Albert W. Burgstahler of the University of Kansas Department of Chemistry, demonstrated that exposure to low levels of fluoride was a contributory cause of sudden infant death syndrome (SIDS), particularly within the lower income communities where poor nutrition was already prevalent.[126],[127]

On the subject of infant deaths, researchers at the New York State University (Department of Epidemiology and Biostatistics,School of Public Health).documented that municipal water fluoridation causes more premature births, after controlling for age, race/ethnicity, neighbourhood poverty level, hypertension and diabetes.[128]

The impact of fluoride on heart function and physiology must consequently to be regarded as a significant risk factor in the high rates of CHD in Ireland.

### *Inflammatory Response*

Fluoride exposure has been implicated in inflammation. Inflammation is the first response of the immune system to infection or tissue damage, leading to the protection of the human body against these insults.

As noted in the review by Barbier et al[129] chronic inflammation is harmful and has an important role in the development of several chronic diseases such as diabetes and atherosclerosis, both of which contribute significantly to CHD.

The review further discusses how fluoride contributes to inflammatory processes that may play a significant role in cardiovascular disorders and recommends more research be undertaken on the role of low to moderate fluoride exposure in vascular disease.

An article published by Ma et al.[130] (2012) investigated the effect of exposure to fluoride alone on inflammatory response in rabbit aorta. It was found that fluoride increased the expression of VCAM-1, P-sel, MCP-1, IL-8, and IL-6 at the RNA and protein levels. All of these are now known to play a critical role in development of heart disease.[131, 132, 133, 134, 135, 136, 137, 138]

The role of fluoride in inflammatory response mechanisms must consequently to be regarded as a significant risk factor in the high rates of CHD in Ireland.

### *Oxidative Stress*

Oxidative stress is a recognized mode of fluoride action.[139] Oxidative stress is also related to the pathogenesis of many chronic disorders including cancer, inflammation, and neurological diseases.[140]

Researchers Varol et al. reported that in addition to fluoride exposure causing oxidative stress, it may have an important role in cardiovascular disease. [141] He also observed that in addition to promoting inflammatory mechanisms, oxidative stress contributes to atherosclerosis, vascular stiffness, and myocardial cell damage. Researchers have also found that oxidative stress and inflammation are important pathophysiological mechanisms involved during ischemic stroke.[142, 143]

In addition endothelial dysfunction and vascular disorders have been associated with fluoride exposure in humans.[144, 145]

According to Barbier et al. "*the data suggest an important role played by factors related to oxidative stress and vascular inflammation, providing future directions for research into the cardiovascular effects of fluoride exposure.*" [146]

The role of fluoride in oxidative stress must consequently to be regarded as a significant risk factor in the high rates of CHD in Ireland.

### *Dietary Intake of Fluoride*

The amount of bioavailable fluoride will also depend on the total dietary intake which will not be the same for any two individuals. For example high tea drinkers, smokers as well as fish eaters and consumers of processed food will ingest more fluoride than non tea drinkers, non smokers and vegetarians or red meat eaters.

Infants will retain more fluoride due to the developing kidneys not been able to remove fluoride from the body and through the consumption of formula milk or other beverages made from fluoridated water[147].

Similarly diabetics are a high risk group to the toxicity of fluoride[148], as are active sportsmen and woman who consume much larger volumes of water daily.[149].

Finally once cannot control for fluoride itake from prescribed medication, which can be significant as many pharamacautical drugs are fluoride based medications. The EFSA have estimated that up to 75% of an infants total dietary intake may come from prescribed medication at any one time.[150]

The dietary intake of fluoride in Ireland is expected to be much higher than the European average due to a combination of water fluoridation, (nnly EU country with a national policy mandating all public water supplies are fluoridated) high consumption of tea (highest in World), high prevalence of bottle fed infants (highest in EU), high consumption of fluoridated alcoholic

beverages such as draft beer produced in Ireland, high prevlance of smokers (tobaccco contains very high levels of fluoride) and high level of prescribed medication (highest in EU) in Ireland.

### *Dental Fluorosis*

Dental Fluorosis is a biomarker for CHD. Professor Takamori's research team observed that children with dental fluorosis have a higher incidence of heart damage and an increase in abnormal heart rhythm than those without fluorosis.[151] These observations have been supported by studies conducted by Wang et al. in China.[152]

This is extremely worrying as the NHS York Review, undertaken for the Chief Medical Officer of the UK, concluded that in communities where artificial fluoridation or high natural fluoride levels was present a very significant percentage of the population were overexposed to fluoride, resulting in a high level of dental fluorosis amongst the population.

The NHS York Review found that in fluoridated communities up to 48% of the population may experience dental fluorosis. [153]

A recent EU study funded under the **FLINT Project** demonstrated that children in Ireland have the highest prevalence of dental fluorosis in the EU.

The study also compared dental fluorosis levels in both fluoridated and non-fluoridated communities in Ireland and found that for children up to age 8 in fluoridated areas up to 24% had abnormal teeth due to exposure to fluoride.

For children up to 12 years of age, 37% had abnormal teeth due to fluoride overexposure. In comparison, for children up to age 8 living in non-fluoridated communities < 10% had abnormal teeth and for children up to age 12 approximately 17% had abnormal teeth.

Astonishingly the study found that the level of dental fluorosis was 100% higher in fluoridated areas compared to non-fluoridated communities.

Not surprisingly, the EU study also found that Ireland had the highest level of dental fluorosis amongst children and teenagers.

Given the previous findings in the Japanese study and the alarmingly high prevalence of dental fluorosis in Ireland, this presents an alarming biomarker of future health burdens for society and the healthcare system in Ireland.

## Concluding Remarks

The distinguished scientist Dr. Schatz believed that **"fluoridation of drinking water is not safe at any level" and** believed that *"artificial fluoridation of drinking **water** may well dwarf the thalidomide tragedy, which was dramatic because it produced crippled children who are living testimonials to what that drug has done. Many victims of artificial fluoridation, on the other hand, die quietly during the first year of their lives, or at a later age under conditions where their deaths are attributed to some other cause."*[154]

Furthermore Dr. Schatz stated: *"(b)ecause artificial fluoridation causes deaths among individuals who are for one reason or another more sensitive to fluoride toxicity than the total population taken as a whole, the controversy over whether fluoridation*

*does or does not reduce caries is purely academic. It is criminal to implement a so-called public health measure which kills certain people even if it does reduce tooth decay in some of the survivors."*

In an affidavit[155] dated 1993 Dr. Schatz gave sworn evidence that *"(i)t is my best judgment, reached with a high degree of scientific certainty, that fluoridation is invalid in theory and ineffective in practice as a preventive of dental caries. It is dangerous to the health of consumers."*

Given the observations of Dr. Schatz and the additional information provided in this document it is not surprising to find that Ireland (the only country in the EU with a mandatory legislative policy requirng artificial fluoridation of all public water supplies) has the highest prevalence of mortality from ischemic heart disease in all of the European member states.

The Department of Health recently stated "*Current cardiovascular disease risk profiles in Ireland, must now provide a national 'wake-up call' to the health sector and beyond – that the cardiovascular health of the nation is in a precarious state. Cardiovascular health needs to be robustly addressed at both population and individual level.*" [156]

This is certainly the case and it is about time that the Irish Government and its Agencies "woke up" to the public health dangers posed by water fluoridation. These were previously comprehensively examined by Waugh in his report of March 2012 and have yet to be adequately and independently assessed by a panel of suitably qualified experts in Ireland.

According to Dr. Eoin O Brien, Professor of molecular pharmacology, University College Dublin, deaths rates in Ireland from CVD will soon begin to rise "*pointing towards a dismal epidemic for future generations".*[157]

The risk group that he refers to represent individuals born since 1965 who are the longest exposed to the dangers of mass fluoridation. They are a generation exposed since birth to fluoride and silicofluorides compounds, providing experimental proof of the biological effects of artificial fluoridation on the health of a population.

What is particularly disturbing is that not only has Ireland the highest mortality and incidence of CHD in EU but diabetes and hypothyroidism, neurological disorders and certain cancers. Where fluoride is a known risk factor in each of these diseases and with a high prevalence of these diseases now present in the population of Ireland, increasing their exposure to fluoride through mass fluoridation is not only unwise but unsafe. Clearly, it is now evident, with a tsunami of health crisis facing the country, that the blunt, ineffective and dangerous policy of fluoridation should be discontinued. This is particularly the case with current and predicted future rises in CHD, especially knowing what is now known about fluoride, silicofluorides and their affect on the heart as well as other organs such as the thyroid, kidneys, pineal gland and brain.

Fluoride is now well acknowledged as an accumulative toxin with detrimental impacts on health that accumulates over time in calcified tissues such as bone and soft tissues.[158] Fluoride has been identified by Harvard researchers as a development neurotoxin.[159] This is a matter of great concern given the

findings of Dr. G.W Rapp who documented that "the fluoride ion crosses the placental barrier" and who noted "the importance of this is that the fetus has already accumulated fluoride during its development." [160] Therefore fluoridation of drinking water combined with other dietary sources of fluoride may contribute to a total maternal fluoride intake that could cause neurological damage to unborn babies.

Fluoride has also been identified by the U.S National Research Council as a toxin "that can cause and pro mote cancers" and negatively impact on endocrine systems.[161] Masters and Copland also demonstrated that silicofluorides in drinking water can contribute to a wide range of neurological diseases contributing to learning behavioral problems, violent crime and substance addiction.[162],[163] Given the scientific information provided in this communication, the Government of Ireland and the Department of Health have no alternative but to comply with the 'precautionary principle' and end the policy of mandatory fluoridation of the population of Ireland immediately.

Failure to act presents a substantial and unjustifiable risk to the population of Ireland and in light iof the findings presented here would demonstrate criminal neligence of the authorities concerned.

---

[1] Risk Factors for Heart Disease, Heartbeat Wexford.http://heartbeatwexford.com/RiskFactor.pdf
[2] Risk Factors for Heart Disease, Cardiac Rehabilitation Unit, Wexford General Hospital. May 2006
[3] Changing Cardiovascular Health, National Cardiovascular Health Policy 2010 – 2019, Department of Health and Children May 2010.
[4] Moolenburgh H. Fluoride: the freedom fight. Edinburgh: Mainstream Publishing; 1987. p. 46-7.
[5] Lamberg et al. Symptoms experienced during periods of actual and supposed water fluoridation, Community Dent Oral Epidemiol 1997: 25: 291-5
[6] Kunzel W,Fischer T. Rise and fall of caries prevalence in German towns with different F concentrations in drinking water. Caries Res. 1997;31(3):166-73.
[7] Künzel W, Fischer T, Lorenz R, Brühmann S. Decline of caries prevalence after the cessation of water fluoridation in the former East Germany. Community Dent Oral Epidemiol.2000 Oct;28(5):382-9.
[8]Changing Cardiovascular Health, National Cardiovascular Health Policy 2010 – 2019, Department of Health , May 2010.
[9] Hobdell MH, O'Hickey S. Public water fluoridation in Ireland: twenty five years on. Br Dent J 1989:36 - 38.
[10] Braunwalds Heart Disease, A textbook of Cardiovascular Medicine, Ninth Edition
[11] Irish Heart Factsheet, Mortality from cardiovascular disease (CVD), WHO HFA database 2007

12 Coronary Heart Disease and Stroke Deaths — United States, Centres for Disease Control and Prevention, January 2011.

[13] AIHW National Mortality Database, National Health Priority Areas.
[14] Bennett K, Kabir Z, Unal B et al. Explaining the recent decrease in coronary heart disease mortality rates in Ireland, 1985-2000. *J Epidemiol Community Health* 2006; 60: 322-7.
[15] Central Statistics Office. *Population and labour force projections* 1991-2021. Dublin: Stationery Office, 1988.
[16] Changing Cardiovascular Health, National Cardiovascular Health Policy 2010 – 2019, Department of Health and Children May 2010.
[17] Dr Emer Shelley, Changing Levels and Trends in Mortality, HSE, 2006
[18] Risk Factors for Heart Disease, Cardiac Rehabilitation Unit, Wexford General

Hospital. May 2006
[19] Institute of Public Health, Making Chronic Conditions Count, Hypertension Stroke Coronary Heart Disease. Diabetes, 2010
[20] Institute of Public Health, Making Chronic Conditions Count, Hypertension Stroke Coronary Heart Disease. Diabetes, 2010
[21] American Heart Association, Statistical Update, Heart Disease and Stroke Statistics, *Circulation. 2006; 113*
[22] WHO HFA Database 2007

[23] Changing Cardiovascular Health: National Cardiovascular Health Policy 2010 – 2019, Department of Health, 2010
[24] Human Toxicity, Environmental Impact and Legal Implications of Water Fluoridation, Waugh D, 2012.
[25] WHO Calcium and Magnesium in Drinking water, Public Health Significance, 2009
[26] Risk Factors for Heart Disease, Heartbeat Wexford General Hospital
[27] Coronary Heart Disease Statistics in Northern Ireland, 2012
[28] Ref: England CHD Factsheets Statistics Factsheet 2012.
[29] World Health Organization (2004) The World Health Report 2004. WHO: Geneva
[30] European Cardiovascular disease statistics, 2012.
[31] Brennan et al. Inhale Report Second Edition, Irish Thoracic Society. http://www.imj.ie/Archive/February%20Supplement.pdf
[32] World Health Organisation (2007) European Health for All Database (3).
[33] Fewtrall et al. An attempt to estimate the global burden of disease due to fluoride in drinking water, Journal of Water and Health,04.4 2006
[34] Global Atlas on cardiovascular disease prevention and control, World Health Organisation, 2011
[35] National Vital Statistics Reports, Vol. 61, No. 6, October 10, 2012
[36] Barbier et al.Molecular mechanisms of fluoride toxicity, Chemico-Biological Interactions 188 (2010) 319–333
[37] G. Aydin, E. Cic¸ek, M. Akdo˘gan, O. Gokalp, Histopathological and biochemical changes in lung tissues of rats following administration of fluoride over several generations, J. Appl. Toxicol. 23 (2003) 437–446
[38] P.E. Schwarze, M. Lag, R. Becher, E.V. Thrane, J.T. Samuelsen, R.B. Hetland, M. Refsnes, Role of signal transduction pathways in lung inflammatory responses, Toxicol. Lett. 112–113 (2000) 165–170.
[39] Taylor B et al. (2009). Alcohol and hypertension: gender differences in dose–response relationships
determined through systematic review and meta-analysis. *Addiction,* 104:1981–1990.
[40] Patra J et al. (2010). Alcohol consumption and the risk of morbidity and mortality from different stroke types – a systematic review and meta-analysis. *BMC Public Health,* 10: 258.
[41] Samokhvalov AV, Irving HM, Rehm J (2010). Alcohol as a risk factor for atrial fibrillation: a systematic review and meta-analysis. *European Journal of Cardiovascular Prevention and Rehabilitation*, 17:706– 712.
[42] Rehm J, Roerecke M (2011). Alcohol, the heart and the cardiovascular system – what do we know and where should we go? *Drug and Alcohol Review,* 30:335–337.
[43] Roerecke M, Rehm J (in press). The cardioprotective association of average alcohol consumption and ischaemic heart disease: a systematic review and meta-analysis. *Addiction*.
[44] Di Castelnuovo A et al. (2002). Meta-analysis of wine and beer consumption in relation to vascular risk. *Circulation*, 105(24):2836–2844.
[45] Rehm J et al. (2010). The relation between different dimensions of alcohol consumption and burden of disease – an overview. *Addiction,* 105:817–843.
[46] Rehm J et al. (2009). *Alcohol, social development and infectious disease*. Toronto, Centre for Addiction and Mental Health.
[47] Blomgren J, Martikainen P, Makela P (2004). The effects of regional characteristics on alcohol-related mortality – a register-based multilevel analysis of 1.1 million men. *Social Science & Medicine*, 58:2523– 2535.

[48] Alcohol and the European Union, World Health Organisation,2012
[49] Alcohol and the European Union, World Health Organisation,2012, Page 20
[50] Risk Factors for Heart Disease, Cardiac Rehabilitation Unit, Wexford General Hospital. May 2006
[51] WHO HFA Database 2007
[52] Gouni-Berthold I, Krone W, Berthold HK. Vitamin D and cardiovascular disease. Curr Vasc Pharmacol. 2009 Jul;7(3):414-22.
[53] European Cardiovascular Disease Statistics 2012 edition
[54] World Health Organization (2004) The World Health Report 2004. WHO: Geneva
[55] Muthuswamy Balasubramanyam, Raji Lenin and Finny Monickaraj, Endoplasmic Reticulum Stress In Diabetes: New Insights Of Clinical Relevance, *Indian Journal of Clinical Biochemistry, 2010 / 25 (2) 111-118,*
[56] O. Barbier et al. Molecular mechanisms of fluoride toxicity, Chemico-Biological Interactions *188 (2010) 319–333*
[57] Diabetes: The Policy Puzzle, Is Europe Making Progress? The International Diabetes Federation (2012).
[58] EU Director General for Health and Consumers, Strategy for Europe on nutrition, overweight and obesity related health issues, Implementation progress report, December 2010
[59] The cost of overweight and obesity on the island of Ireland, Safefood November 2012, ISBN: 978-1-905767-335
[60] Décio L. Eizirik,Alessandra K. Cardozo and Miriam Cnop, The Role for Endoplasmic Reticulum Stress in Diabetes Mellitus, *Endocrine Reviews February 1, 2008 vol. 29 no. 1 42-61*
[61] Natalia Ivanovna Agalakova and Gennadii Petrovich Gusev, *Sechenov Institute of Evolutionary Physiology and Biochemistry Russian Academy of Sciences,* Molecular Mechanisms of Cytotoxicity and Apoptosis Induced by Inorganic Fluoride, International Scholarly Research Network ISRN Cell Biology Volume 2012, Article ID 403835, 16 pages doi:10.5402/2012/403835
[62] Xu C, Bailly-Maitre B, Reed JC. Endoplasmic reticulum stress: cell life and death decisions. J Clin Invest. 2005 Oct;115(10):2656-64.
[63] I. Menoyo, A. Rigalli, R.C. Puche, Effect of fluoride on the secretion of insulin in the rat, Arzneimittelforschung 55 (2005) 455–460.
[64] B.J. Lin, M.J. Henderson, B.B. Levine, B.R. Nagy, E.M. Nagy, Effects of iodoacetate and fluoride on islate respiration and insulin biosynthesis, Horm. Metab. Res. 8 (1976) 353–358.
[65] E.A. Garcia-Montalvo, H. Reyes-Perez, L.M. Del Razo, Fluoride exposure impairs glucose tolerance via decreased insulin expression and oxidative stress, Toxicology 263 (2009) 75–83.
[66] E.A. Garcia-Montalvo, H. Reyes-Perez, L.M. Del Razo, Fluoride exposure impairs glucose tolerance via decreased insulin expression and oxidative stress, Toxicology 263 (2009) 75–83.
[67] A. Rigalli, J.C. Ballina, R.C. Puche, Bone mass increase and glucose tolerance in rats chronically treated with sodium fluoride, Bone Miner. 16 (1992) 101–108.
[68] O. Barbier et al. Molecular mechanisms of fluoride toxicity, Chemico-Biological Interactions *188 (2010) 319–333*
[69] Fluoride and it's contribution to the Epidemic of Obesity and Diabetes, Fact Sheet, Waugh D., Nov 2012.
[70] USA National Research Council, Fluoride in Drinking Water: A Scientific Review of EPA's Standards, Committee on Fluoride in Drinking Water, (2006), Page 263
[71] Congenital hypothyroidism – A thirty year audit of the National Newborn Screening Programme in the Republic of Ireland, Endocrine Abstracts (2009) 23 P30.
[72] Comparison of epidemiological data on congenital hypothyroidism in Europe with those of other parts in the world. Horm Res. 1992;38(5-6):230-5.
[73] Clara McDonnell et al. Congenital hypothyroidism – A thirty year audit of the National Newborn Screening Programme in the Republic of Ireland, Endocrine Abstracts (2009) 23 P30
[74] Helfand, M. 2004. Screening for subclinical thyroid dysfunction in nonpregnant adults: A summary of the evidence for the U.S. Preventive

Services Task Force. Ann. Intern. Med. 140(2):128-141.
[75] Weetman, A.P. 1997. Hypothyroidism: Screening and subclinical disease. Br. Med. J. 314(7088): 1175-1178.
[76] Biondi, B., E.A. Palmieri, G. Lombardi, and S. Fazio. 2002. Effects of subclinical thyroid dysfunction on the heart. Ann. Intern. Med. 137(11):904-914.
[77] Gold, M.S., A.L. Pottash, and I. Extein. 1981. Hypothyroidism and depression. Evidence from complete thyroid function evaluation. JAMA 245(19):1919-1922.
[78] Brucker-Davis, F., K. Thayer, and T. Colborn. 2001. Significant effects of mild endogenous hormonal changes in humans: Considerations for low-dose testing. Environ. Health Perspect. 109(Suppl. 1):21-26.
[79] Fluoride, thyroid disorders, autism and other health concerns, Fact Sheet, Waugh, 2012,http://ffwireland.blogspot.ie/2012/11/fluoride-thyroid-disorders-autism-and.html
[80] Crawford M.D. Gardner. M.J. Morris J .N. Cardio Vascular Disease and the mineral content OF drinking Water. British Medical Bulletin, VOL 27 No 1. Pp 21-24
[81] Sauvant, M-P. and Pepin, D. (2002) Drinking water and cardiovascular disease. *Food* Chem. Toxicol. 40, 1311-1325.
[82] Waugh D, Human Toxicity, Environmental Impact and Legal Implications of Water Fluoridation, March 2012.
[83] Kožíšek, M.D., Ph.D. National Institute of Public Health, Czech Republic, Health Significance of Drinking water Calcium and Magnesium, 2003
[84] Calcium and Magnesium in Drinking Water, Public Health Significance, WHO, 2009
[85] ATSDR, Toxicologial Profile for fluorides, Hydrogen Fluoride, and Fluorine Wastington: US. Department of Health and Human Services (TP-91/17), 1993
[86] Bayley TA, Harrison JE, Murra VM, Josse RG, Sturtridge w, Pritzker KP, Strauss a, Vieth R, Goodwin s. Fluoride-induced fractures: Relation to osteogenic effect: J Bone Miner Res. 1990 Mar; 5 Suppl 1:S217-22.
[87] Ahmad, R., and J.M. Hammond. 2004. Primary, secondary, and tertiary hyperparathyroidism. Otolaryngol. Clin. N. Am. 37(4):701-713.
[88] Fujita, T., and G.M. Palmieri. 2000. Calcium paradox disease: Calcium deficiencyprompting secondary hyperparathyroidism and cellular calcium overload. J. BoneMiner. Metab. 18(3):109-125.
[89] Dr. G. W. Rapp, "The Pharmacology of Fluoride," Professor of Biochemistry and Physiology, Loyola University School of Dentistry Department of Chemistry and physiology, Chicago College of Dental Surgery, The Bur, April 1950
[90] USA National Research Council, Fluoride in Drinking Water: A Scientific Review of EPA's Standards, Committee on Fluoride in Drinking Water, (2006)
[91] Krishnamachari, K.A. 1986. Skeletal fluorosis in humans: A review of recent progressin the understanding of the disease. Prog. Food Nutr. Sci. 10(3-4):279-314.

[92] Ventura et al. Energy metabolism in heart failure, *The Journal of Physiology, 555, 1-13 February 15, 2004*
[93] De Sousa E, Veksler V, Minajeva A, Kaasik A, Mateo P, Mayoux E, Hoerter J, Bigard X, Serrurier B & Ventura-Clapier R (1999). Subcellular creatine kinase alterations – Implications in heart failure. Circ Res 85, 68
[94] Weiss N, Keller C, Hoffman U, Loscalzo j, Endothelial Dysfuntion And Atherothrombosis In Mild Hyperhomocysteinemia. Vasc Med 2002; 7:227-239.
[95] Risk Factors for Heart Disease, Cardiac Rehabilitation Unit, Wexford General Hospital. May 2006
[96] Ari Chodos, Homocysteine and Cardiovascular Disease: Implications for Screening and Prevention in Ireland, *TSMJ* Volume 6
[97] Mehdi S, Jarvi ET, Koehl JR, McCarthy JR, Bey P. The mechanism of inhibition of S-adenosyl-L-homocysteine hydrolase by fluorine-containing adenosine analogs. J Enzyme Inhib. 1990;4(1):1-13.
[98] Liu S, Wnuk S F, Yuan C, Robins M J, Borchardt R T, Adenosine-5'-carboxaldehyde: a potent inhibitor of S-

adenosyl-L-homocysteine hydrolase, *J. Med. Chem.*, 1993, *36* (7), pp 883–887
[99] Ercan Varet al, Biological Trace Element Research, Violume 133, Number 2/February, 2010
[100] Ercan Varol et al, Science of the Total Environment, Volume 408, Issue 11, 1 May 2010 Pages 2295-2298
[101] Song et al, Observations on fluoorotic aorta sclerosis by two doimensional echo cardiography "Endemic diseases Bulliten 5, 1990, (1) 91-93
[102] Liang et al., Investigation and analysis of cardiovascular disease in endemic and non-endemic fluorosis areas, He Bei Province Journal of Endemiology 12, (1984) 44.
[103] Lowell M. Duffey *and* James D. Ebert, Metabolic Characteristics of the Heart-forming Areas of the Early Chick Embryo, J. Embryol. exp. Morph. Vol. 5, Part 4, pp. 324-339, December 1957
[104] James P Elbert, First Heartbeats, Scientific America, March 1959
[105] Spratt, N. T. Nutritional requirements of the early chick embryo. III. The metabolic basis of morphogenesis and differentiation as revealed by the use of inhibitors. *Biol. Bull. Wood's Hole,* **99,** 120-35. (1950).
[106] Judah, J. D., & Williams-Ashman, H. G. The Inhibition Of Oxidative Phosphorylation. *Biochem. J.* 48, 33-42. (1951).
[107] Potter, V. R., Le Page, G. A., & Klug, H. L. The Assay On Animal Tissues For Respiratory Enzymes. Vii. Oxaloacetic Acid Oxidation And The Coupled Phosphorylations In Isotonic Homogenates. *J. Biol. Chem.* **175,** 619-34. (1948).
[108] Slater, e. c. & Bonner, w. d. The effect of fluoride on the succinic oxidase system. *Biochem. J.* **52,** 185-96. (1952).
[109] Study of Heart Mitochondria and Glycolytic Metabolism in Experimentally Induced Cardiac Failure Arnold Schwartz And Kwang Soo Lee *Circ Res.* 1962; 10:321-332
[110] Turla, M, B. Gnegy,. Margaret, E,. Epps, S,. Shlafer, M. Loss of calmodulin activity in cardiac sarcoplasmic reticulum after ischemia. Biochemical and Biophysical Research Communications Volume 130, Issue 2, 31 July 1985, Pages 617–620
[111] Pogwizd SM, Bers DM. Na/Ca exchange in heart failure: contractile dysfunction and arrhythmogenesis. Ann N Y Acad Sci. 2002 Nov;976:454-65.
[112] Varol E, Akcay S, Ersoy IH, Ozaydin M, Koroglu BK, Varol S (2010a) Aortic elasticity is impaired in patients with endemic fluorosis. Biol Trace Elem Res 133(2):121–127
[113] Varol E, Akcay S, Ersoy IH, Koroglu BK, Varol S (2010b) Impact of chronic fluorosis on left ventricular diastolic and global functions. Sci Total Environ 408(11):2295–2298
[114] Ercan Varol • Simge Varol, Effect of fluoride toxicity on cardiovascular systems: role of oxidative stress, Arch Toxicol (2012) 86:1627
[115] Yuxin Li et al. Association of vascular fluoride uptake with vascular calcification and coronary artery disease, Nuclear Medicine Communications 2012, 33:14–20.
[116] Wang et al, Toxicity from Water Containing Arsenic and Fluroide in Xinjiang, Fluoride Volume 30 No 281-84 1997.
[117] Teitz N., Clinical Chemistry, W B Saunders, Philadelphia. 1976
[118] Data from United States Public Health Service. March 24, 1952
[119] The Fluoride Deception, Christopher Bryson
[120] Mass Harm From Fluoridation, by Lee Hardy, Oct. 1997.
[121] Takamori,T.et al, Electrocardiographical Studies of the inhabitants in High Fluorine Districts, Tokushima J of Exp. Med. 3:50, (1956)
[122] Iwasi, Tadashi, Studies on the Glycogen and Phosphorylase Variations in Myocardium, Skeletal Muscle and Liver in Experimental Fluorosis, Shikoku Actu Medica 12:616, (1956)
[123] Kawahara, H, Experimental Studies on the Changes of the Kidney due to Fluorosis, Shikoku Acta Medica 8:266, (1958)
[124] Hirao, M,. Blood Picture of Experimental Fluorosis, Shikoku Actu Medica 5:344, 1954

[125] Dr. G. L. Waldbott. A Struggle with Titans, Carlton Press, (1965)
[126] Increased death rates in Chile associated with artificial fluoridation of drinking water. Journal of Arts, Sciences and Humanities. 1976; 2:1.
[127] Schatz, A., and Martin J.J. The importance of paradoxical effects of fluoride with respect to fluoridation and the toxicology of fluoridation. Pakistan Dental Review 14:1-16, 1964
[128] 197468 Relationship between municipal water fluoridation and preterm birth in Upstate New York Rachel Hart, BA, MPH, et al. Department of Epidemiology & Biostatistics, School of Public health, University at Albany, State University of New York, Rensselaer, NY HTTP://apha.confex.com/apha/137am/webprogram/Paper197468.html
[129] O. Barbier et al. Molecular Mechanisms of Fluoride Toxicity, Chemico-Biological Interactions *188 (2010) 319–333*
[130] Ma Y, Niu R, Sun Z, Wang J, Luo G, Zhang J, Wang J (2012) Inflammatory responses induced by fluoride and arsenic at toxic concentration in rabbit aorta. Arch Toxicol
131 Klaus Ley and Yuqing Huo, VCAM-1 is critical in atherosclerosis, J Clin Invest. 2001 May 15; 107(10): 1209–1210.
132 Harrington J.R. The role of MCP-1 in Atherosclerosis. Stems cells Fundamentals of Cancer medicine, Stem Cells 2000; 18:65-66
133 Apostolakis S, Interleukin 8 and cardiovascular disease, Cardiovascular Research (2009) 84, 353–360
134 Jan H. Von der Thüsen, et al, Interleukins in Atherosclerosis: Molecular Pathways and Therapeutic Potential, Pharmacol Rev March 1, 2003 55:133-166; published online March 1, 2003, doi:10.1124/pr.55.1.5
135 Schieffer B,.et al. Impact of interleukin-6 on plaque development and morphology in experimental atherosclerosis.Circulation. 2004 Nov 30;110(22):3493-500.

136 Dong, M.Z et al. Prominent Role of P-Selectin in the Development of Advanced Atherosclerosis in ApoE-Deficient Mice, American Heart Association, 2000; 101: 2290-2295.
[137] Molenaar J.M. et al. P-selectin as a candidate target in atherosclerosis, Biochemical Pharmacology Volume 66, Issue 5, 1 September 2003, Pages 859–866
[138] Burger PC, Platelet P-selectin facilitates atherosclerotic lesion development, Blood 2003 Apr 1;101(7):2661-6. Epub 2002 Dec
[139] Agalakova et al. MolecularMechanisms of Cytotoxicity and Apoptosis Induced by Inorganic Fluoride, ISRN Cell Biology Volume 2012, Article ID 403835
[140] Tsubota K. (Department of Ophthalmology, Keio University School of Medicine, Tokyo, Japan) Oxidative stress and inflammation: hypothesis for the mechanism of aging. Nihon Ganka Gakkai Zasshi. 2007 Mar;111(3):193-205;
[141] Ercan Varol • Simge Varol, Effect of fluoride toxicity on cardiovascular systems: role of oxidative stress, Arch Toxicol (2012) 86:1627
[142] Shaheen E Lakhan et al. Inflammatory mechanisms in ischemic stroke: therapeutic approaches, *Journal of Translational Medicine* 2009, 7:97
[143] Profumo E et al. Oxidative Stress in Cardiovascular Inflammation: Its Involvement in Autoimmune Responses, International Journal of InflammationVolume 2011 (2011), Article ID 295705
[144] A. Rønneberg, Mortality and cancer morbidity in workers from an aluminium smelter with prebaked carbon anodes—part III: mortality from circulatory and respiratory diseases, Occup. Environ. Med. 52 (1995) 255–261.
[145] E. Varol, S. Akcay, I.H. Ersoy, M. Ozaydin, B.K. Koroglu, S. Varol, Aortic elasticity is impaired in patients with endemic fluorosis, Biol. Trace Elem. Res. 133 (2010) 121–127
[146] O. Barbier et al. Molecular mechanisms of fluoride toxicity, Chemico-Biological Interactions *188 (2010) 319–333*
[147] Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Level of Fluoride, EFSA Journal (2005)192,1-65
[148] International Programme on Chemical Safety. (1984). Environmental Health Criteria 36: Fluorine and Fluorides.

Geneva, Switzerland: World Health Organization.
[149] U.S. National Research Council, Examination of Fluoride Standards in Drinking Water, 2006
[150] Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies on a request from the Commission related to the Tolerable Upper Intake Level of Fluoride, EFSA Journal (2005)192,1-65
[151] The Lancet, Jan 28 1961, p. 197, Tokushima J. Exper., Med. 3-50-53, 1956
[152] Wang et al, Toxicity from Water Containing Arsenic and Fluroide in Xinjiang, Fluoride Volume 30 No 281-84 1997.
[153] NHS York Review, Systematic Review of Public Water Fluoridation, NHS Centre for Reviews and Dissemination, University of York, 2000
[154] Albert Schatz, Ph.D, Low-Level Fluoridation And Low-Level Radiation Two Case Histories Of Misconduct In Science. http://www.fluoridation.com/schatz.htm
[155] Affidavit Of Dr. Albert Schatz, PhD. Circuit Court of Wisconsin, Fond Du Lac County, Case No. 92 cv 579, March 1993
[156] Changing Cardiovascular Health, National Cardiovascular Health Policy 2010 – 2019, Department of Health and Children May 2010.
[157] Eoin O'Brien, Ph.D, Professor of molecular pharmacology at The Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Ireland failing in the battle against CVD, FORUM,May 2008
[158] L. Valdez-Jiménez et al, Effects of the fluoride on the central nervous system, Neurología. 2011;26(5):297—300
[159] Anna L. Choi, Guifan Sun, Ying Zhang, Philippe Grandjean, Developmental Fluoride Neurotoxicity: A Systematic Review and Meta-Analysis, Environmental Health Perspectives, July 2012
[160] Dr. G. W. Rapp, "The Pharmacology of Fluoride," Professor of Biochemistry and Physiology, Loyola University School of Dentistry Department of Chemistry and physiology, Chicago College of Dental Surgery, The Bur, April 1950
[161] U.S. National Research Council, Fluoride in Drinking Water: A Scientific Review of EPA's Standards, Committee on Fluoride in Drinking Water, National Research Council, 2006
[162] Masters, R. and Coplan, M. (1999a) "Water Treatment with Silicofluorides and Lead Toxicity," *International Journal of Environmental Studies*, 56: 435-49
[163] Masters, R.D., Coplan, M. J., Hone, B.T., and Dykes, J.E. (2000)."Association of Silicofluoride Treated Water with Elevated Blood Lead," *Neurotoxicology* 21: 1091- 1100.