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THE INDUSTRIAL INJURIES ADVISORY COUNCIL

POSITION PAPER 32

**Work as a dry cleaner and
cancers of the oesophagus
and cervix**

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Work as a dry cleaner and cancers of the oesophagus and cervix

Position Paper 32

Summary

1. The dry cleaning industry has used many solvents since its inception in the middle of the nineteenth century. Initially petroleum-based solvents were used in industrial premises, but around the middle of the 20th century, dry cleaning moved onto the high street with the vast majority of establishments using perchloroethylene as the solvent. This agent remains in use today, although exposures have fallen over time.
2. Some dry cleaning agents are suspected of being carcinogenic and a recent review of the occupational burden of cancer in the UK for the Health and Safety Executive (HSE) (Rushton et al, 2010) led the Council to explore the case for prescription in dry cleaners in relation to two particular cancers: of the oesophagus (gullet) and cervix.
3. A careful review of the evidence – set out in this paper – has led the Council to conclude that, while there may be some evidence of increased risks in certain subgroups of workers in certain settings, overall there is insufficient evidence of a level of risk for either of these two cancers that would justify prescription and addition of them to the list of prescribed diseases. The Council will continue to monitor ongoing research in this area of inquiry.

This report contains some technical terms, the meanings of which are explained in a concluding glossary.

Background

4. In 1995, the International Agency for Research on Cancer (IARC) concluded that work in the dry cleaning industry entails exposure to certain organic compounds that are possibly carcinogenic to humans (IARC, 1995).
5. More recently, the Council's attention has been drawn to a review, commissioned by the HSE, on the burden of occupational cancer in the UK (Rushton et al, 2010). Among other things, this review highlighted potential risks of cancer in the dry cleaning industry with special reference to tumours of the oesophagus and cervix.
6. The Council has conducted a preliminary literature search in these topic areas and subsequently a full review of evidence. This paper describes the Council's review and considers the case for prescription.

The Industrial Injuries Disablement Benefit Scheme

7. The Industrial Injuries Advisory Council (IIAC) is an independent statutory body that advises the Secretary of State for Work and Pensions in Great Britain and the Department for Social Development in Northern Ireland on matters relating to the Industrial Injuries Scheme. The major part of the Council's time is spent considering whether the list of prescribed diseases for which compensation may be paid should be enlarged or amended.
8. The Industrial Injuries Disablement Benefit (IIDB) Scheme provides compensation that can be paid to an employed earner because of the effects of an industrial accident or a prescribed disease.

The legal requirements for prescription

9. The Social Security Contributions and Benefits Act 1992 states that the Secretary of State may prescribe a disease where s/he is satisfied that the disease:
 - a) ought to be treated, having regard to its causes and incidence and any other relevant considerations, as a risk of the occupation and not as a risk common to all persons; and
 - b) is such that, in the absence of special circumstances, the attribution of particular cases to the nature of the employment can be established or presumed with reasonable certainty.
10. In other words, a disease may only be prescribed if there is a recognised risk to workers in an occupation, and the link between disease and occupation can be established or reasonably presumed in individual cases.
11. In seeking to address the question of prescription for any particular condition, the Council first looks for a workable definition of the disease. It then searches for a practical way to demonstrate in the individual case that the disease can be attributed to occupational exposure with reasonable confidence. For this purpose, reasonable confidence is interpreted as being based on the balance of probabilities according to available scientific evidence.
12. Within the legal requirements of prescription it may be possible to ascribe a disease to a particular occupational exposure in two ways – from specific clinical features of the disease or from epidemiological evidence that the risk of disease is at least doubled by the relevant occupational exposure.

Clinical features

13. For some diseases attribution to occupation may be possible from specific clinical features of the form of the disease, or of the circumstances of the individual case. For example, the proof that an individual's dermatitis is caused by their occupation may lie in its improvement when they are on holiday, and regression when they return to work, or in the demonstration that they are allergic to a specific substance with which they come into contact only at work. It can be that the disease *only* occurs as a result of an occupational hazard (e.g. coal workers' pneumoconiosis).

Doubling of risk

14. Other diseases are not uniquely occupational, and when caused by occupation, are indistinguishable from the same disease occurring in someone who has not been exposed to a hazard at work.

Oesophageal and cervical cancers, the topics of this review, are examples of such diseases. In these circumstances, attribution to occupation on the balance of probabilities depends on epidemiological evidence that work in the prescribed job, or with the prescribed occupational exposure, increases the risk of developing the disease by a factor of two or more.

15. The requirement for, at least, a doubling of risk follows from the fact that if a hazardous exposure doubles risk, for every 50 cases that would normally occur in an unexposed population, an additional 50 would be expected if the population were exposed to the hazard. Thus, out of every 100 cases that occurred in an exposed population, 50 would do so only as a consequence of their exposure while the other 50 would have been expected to develop the disease, even in the absence of the exposure. Therefore, for any individual case occurring in the exposed population, there would be a 50% chance that the disease resulted from exposure to the hazard, and a 50% chance that it would have occurred even without the exposure. Below the threshold of a doubling of risk only a minority of cases in an exposed population

would be caused by the hazard and individual cases therefore could not be attributed to exposure on the balance of probabilities; above it, they may be.

16. The required epidemiological evidence required should ideally be drawn from several independent studies, and be sufficiently robust that further research at a later date would be unlikely to overturn it.

17. Cancers of the oesophagus and cervix are not currently well recognised as occupationally related and are not regarded as having unique clinical features when they develop in an occupational context. The case for prescription, therefore, rests on reliable evidence of a more than doubled risk in workers with a history of exposure to a putative occupational risk factor, in the case of this enquiry, work in the dry cleaning industry.

Exposures in dry cleaning

18. Dry cleaning involves the use of organic solvents to dissolve oils, waxes, greases and fats that both soil clothing and bind particles to it. The process was first introduced into the UK in the 1850s. The earliest solvents (e.g. petrol, paraffin, benzene) were petroleum-based, and later chlorinated (e.g. carbon tetrachloride, trichloroethylene). These agents gave rise to various practical problems such as fire risk and corrosion, and their fumes had narcotic and toxic effects. Around the time of World War II, perchloroethylene was adopted by the industry as a safer choice, but it in turn had limitations; some colours and prints could not be cleaned safely, it would dissolve certain types of plastic beading and some adhesives and stripped the plasticiser out of polyvinyl chloride (PVC). Today, though, it remains the solvent of choice and is widely used throughout the UK.

19. The main route of exposure to solvents used in dry cleaning is by inhalation, although skin absorption and ingestion may also occur.

Improvements in equipment, solvent reclamation, and engineering control in the industry have led to lower occupational exposures to chlorinated solvents over time. Thus, typical exposures to perchloroethylene in dry cleaning internationally declined from about 350-700 mg/m³ in the 1970s to 70-350 mg/m³ in the late 1980s (IARC, 1985). Data from the UK National Exposure Database suggest that exposures in the UK in the 1980s-1990s were approximately in the range 35-160 mg/m³. However, airborne concentrations remain highly variable with the differences between different dry cleaning shops typically being many times greater than those between staff in different roles within a shop (IARC, 1995).

20. Exposures to high concentrations of dry-cleaning chemicals can cause transient headaches and neurological symptoms such as dizziness and lethargy. Exposures over long periods may give rise to permanent brain damage ('chronic solvent encephalopathy'), but this is less well established. Prolonged exposures at high concentration (atypical of the workplace but possible in those who deliberately misuse solvents for their narcotic effect) can damage the kidneys and liver. In addition, and the focus of this report, dry-cleaning chemicals may pose a risk of cancer over the long-term.

Cancers of the oesophagus and cervix

21. Cancer of the oesophagus exists in two main forms, squamous cell carcinoma (affecting the upper oesophagus and arising from cells lining the inside of the oesophagus) and, more commonly adenocarcinoma (affecting the lower oesophagus and arising from cells inside its mucous glands). Some 8,000 new cases of the disease are diagnosed each year in the UK. Cancer of the cervix is diagnosed in almost 3,000 women per year, and additionally many more women develop a precancerous condition of the cervix called cervical intraepithelial neoplasia.

22. Tobacco smoking is a risk factor for both types of cancer. Other risk factors for oesophageal cancer include drinking alcohol, being overweight, having a diet low in fruit and vegetables and other medical conditions such as achalasia.¹ Other risk factors for cervical cancer include infection with human papilloma virus (the major cause of the disease) and having a weakened immune system (e.g. patients with HIV or AIDS). Thus, any apparent association with occupation should not arise simply as a result of the greater propensity of workers in certain occupations to have these other non-occupational risk factors. More generally, the potential for confounding to create spurious relationships needs to be considered in weighing the case for prescription.

Consideration of the Evidence

23. A search of the recent literature was carried out by the IIAC Secretariat and the relevant papers were obtained, cross-checked for completeness with studies scheduled for inclusion in a forthcoming IARC report, and reviewed by the Council's Research Working Group.

Oesophageal cancer

24. Evidence on the risk of oesophageal cancer arising from work in the dry cleaning industry comes from studies with various designs and outcomes, some based on workers in the industry, others on the general population; some reporting on cancer mortality, others on cancer incidence. Some of these studies had overlapping populations or provided several update reports. In all, nine studies are considered below, featuring in more than a dozen reports. With a few exceptions, outcomes have not been reported separately for squamous cancers and adenocarcinomas. A challenge in investigation is the rarity of the tumour, which limits statistical power, even for quite large studies.

¹A disorder of the oesophagus that results in difficulty swallowing.

25. An early Japanese study of mortality involved 1,711 deaths among members of the All-Japan Laundry and Dry Cleaning Association between 1971 and 1980 (Nakamura, 1985). The relative risk (RR) for oesophageal cancer was lower than expected in men and somewhat higher in women, but findings (based on 12 and 4 cases respectively) were not significant statistically.
26. A cohort study from Finland concerned workers biologically monitored for exposure to three halogenated hydrocarbons (trichloroethylene, tetrachloroethylene, 1,1,1-trichloroethane) (Anttila et al, 1995). However, only one case of oesophageal cancer occurred and no useful conclusions could be drawn.
27. A general population-based mortality study from the US identified 8,163 deaths from cancer in 28 states during 1979 to 1990 (Walker et al, 1997). Occupations were determined by the attending physician, medical examiner, coroner, or funeral director. Information on length of employment was incomplete and no data were available on smoking or alcohol intake. Various sub-analyses were conducted (in men vs. women, black vs. white subjects, and in various subgroups). Although some RRs were elevated, effects in general were not statistically significant. However, the RR in black male workers aged 15-64 years, was 2.15 (95% confidence interval (95% CI) 1.11 to 3.76), based on 12 cases of the cancer.
28. A population-based case-control study from Washington State (Vaughan et al, 1997) compared subjects with cancer of the oesophagus or gastric cardia (upper stomach) and matched controls, in terms of lifetime exposures to dry cleaning agents (ever vs. never worked in the industry; years in the industry; probability of exposure to perchloroethylene; and estimated cumulative exposure to perchloroethylene). Comparatively few of those studied had worked in the industry, limiting the power to draw strong conclusions; but allowance could be made in analysis for smoking habits, alcohol

consumption and education. Many estimates of risk were made and several of these were elevated. Only one, that for squamous cancer of the oesophagus in relation to cumulative exposure of 1-29 ppm (parts per million) -years (RR 11.9, vs. no exposure), was statistically significant and with wide uncertainty around this estimate (95%CI 1.1 to 124), which was based on only two deaths from the cancer.

29. A study by Travier et al (2002) linked routine data on cancer incidence and mortality (the Swedish Cancer Environment Register III and national register of causes of death) with census information on dry cleaning and laundering jobs held in 1960 and 1970. None of the groups exposed to dry cleaning had a statistically significantly elevated risk of oesophageal cancer.
30. A US cohort study identified 5,369 members of a dry cleaning union in Missouri admitted to the union before 1978 and followed their mortality experience from 1948 to 1993 (Blair et al, 2003). An exposure score was assigned for jobs held, based on published exposure data from the industry. The overall standardised mortality ratio (SMR) for oesophageal cancer was 2.2 (95% CI 1.5 to 3.3, 26 cases). However, risks of oesophageal cancer did not increase with level of exposure (little or no exposure: 2.1, 95% CI 0.9 to 3.3, 7 cases; medium and high exposure: 2.2, 95% CI 1.2 to 3.5, 16 cases) or with increasing duration of exposure. The study lacked information on tobacco smoking and alcohol consumption, and job histories whilst employed in the dry cleaning industries were basic. (The former would be unlikely to have led to an underestimate of risk, but the latter could have.)
31. A report by Lynge et al (2006) pooled cohort information on 44,678 laundry and dry cleaning workers, identified from the 1970 censuses in Denmark, Finland, Norway and Sweden and followed during the period 1970-2001 for cancer incidence. New cases of oesophageal cancer were compared with matched non-cases in terms of occupational history (e.g. length of employment in dry cleaning shops; unexposed

laundry working). None of the RRs for oesophageal cancer were significantly raised.

32. A study of 9,440 dry cleaning and laundry workers employed in the industry for at least one month before the mid-1980s was carried out in Sweden, with new cases of oesophageal cancer ascertained over follow-up between 1985 and 2006 (Sélden et al, 2011). All estimates of RR were close to unity (i.e. significantly increased risks were not found).
33. Finally, a cohort study of mortality was conducted among 1,704 dry cleaning workers from four US cities, identified from union records (Calvert et al, 2011). Subjects were employed for at least one year in a shop using tetrachlorethylene (perchloroethylene). The overall SMR for oesophageal cancer was 2.44 (95% CI 1.40 to 3.97), based on 16 deaths from the cancer. A sub-cohort of 618 subjects worked only in shops where perchloroethylene was the primary cleaning solvent and for this group the risk estimate was marginally higher at 2.68 (95% CI 0.98 to 5.83, 6 related deaths), and was of borderline statistical significance. Workers with five or more years of employment in a job involving exposure and a time from first exposure of at least 20 years had even higher risks, with an SMR of 4.78 (95% CI 2.68 to 7.91, 11), based on 11 relevant deaths. Information on possible confounders, such as smoking and alcohol consumption, was not available, but the elevation in risk in this last group is likely to be higher than might be explained by smoking alone.

Cervical cancer

34. Many of the studies providing evidence on the risk of oesophageal cancer in dry cleaners also provided evidence on risks of cervical cancer.
35. In the study by Nakamura of workers from the All-Japan Laundry and Dry cleaning Association (paragraph 25), the RR for all cancers of the

uterus was not raised (risks for the cervix were not separately distinguished). In the study by Walker et al (paragraph 27), most estimates of RR were decreased, although not significantly different statistically from the no effect level. In the investigation by Travier et al (paragraph 29), some RRs for cervical cancer were elevated and statistically significant, but none approached a doubling of risks, the highest risk estimate being 1.34 (based on 129 cancers). In the cohort study from Missouri (paragraph 30), RRs for cervical cancer were elevated 1.6-fold overall but only 1.4 (P (probability value) >0.05) in the group with highest exposure; in the Scandinavian nested case-control study by Lynge et al (paragraph 31), risks were inconsistently increased and less than doubled; and in the Swedish morbidity study (paragraph 32), while risks overall were non-significantly elevated (standardised incidence rate (SIR) 1.25, $P>0.05$, 25 cancers), only one subgroup had a doubling of the risk, laundry workers employed for between five and 11 years, and this finding was not statistically significant.

36. Set against these largely negative findings, in the cohort study of workers biologically monitored for three halogenated hydrocarbons (paragraph 26), SIRs were raised more than two-fold overall ($P<0.05$, 9 cases). Risk estimates were even higher for use of 1,1,1-trichlorethane (SIR 8.3) and tetrachloroethylene (SIR 3.2), although based on only one to two cases, and not statistically significant; and significantly elevated risks were found when the level of the urinary metabolite trichloroacetic acid was $\geq 100 \mu\text{mol/L}$ (SIR 4.35, 95% CI 1.41 to 10.1, based on five cases).
37. The cohort study by Calvert et al (paragraph 33) also reported elevated risks (see table below). In some analyses RRs were more than doubled, notably when more than 20 years had elapsed from first exposure; but findings were based on comparatively few cases and did not reach statistical significance. The study was limited also by its inability to allow for smoking as a potential confounder.

Subgroup	SMR	95% CI	Number of cases
All	1.84	0.98 to 3.14	13
PCE as the primary agent	2.10	0.68 to 4.90	5
First exposed < 20 years ago; exposed < 5 years in total	0.84	0.15 to 2.66	2
First exposed < 20 years ago; exposed ≥ 5 years in total	2.63	0.90 to 6.03	4
First exposed ≥ 20 years ago; exposed < 5 years in total	2.75	0.94 to 6.30	4
First exposed ≥ 20 years ago; exposed ≥ 5 years in total	2.08	0.57 to 538	3

PCE = perchloroethylene

38. Katz and Jowett (1981) reported on a mortality study of 671 white female laundry and dry cleaning workers from Wisconsin, USA, who had been followed up from 1963 to 1977. The RR for cancer of the cervix uteri was statistically significantly elevated, although the relative risk was not quite doubled (1.95, based on 10 deaths).

39. Duh and Asal (1984) followed 440 laundry and dry cleaning workers from Oklahoma, USA from 1975 to 1981 and noted their mortality experience. RRs of cervical cancer were marginally raised, but not statistically significant.

Potential for prescription

40. The two cohort studies by Blair et al (2003) and Calvert et al (2011) provide some evidence that risks of oesophageal cancer can be as much as doubled by dry cleaning agents; but the balance of evidence from most other studies, including those by Travier et al (1995), Lynge et al (2006), and Sélden et al (2011), points to lower levels of risk than this. Moreover, the study by Blair et al failed to find an exposure-response relationship, while many studies, including Blair's, could not

control for known non-occupational risk factors for oesophageal cancer, such as alcohol and tobacco consumption, and positive reports have tended to arise from analyses involving many comparisons (increasing the possibility that they arise from chance alone). On balance, therefore, the Council regards the evidence for a doubling of the risk as insufficient, and does not recommend prescription for work as a dry cleaner in relation to oesophageal cancer.

41. Partial evidence also exists of a doubling of risk for cervical cancer (Anttila et al, 1995; Sélden and Ahlborg 2011; Calvert et al, 2011), although risk estimates have fallen well short of this threshold in most reports (e.g. Nakamura et al, 1995; Walker et al, 1997; Travier et al, 2002; Blair et al, 2003; Lynge et al, 2006; Duh and Asal, 1984). The study by Calvert et al is of interest in implying higher risks with greater assumed latency (interval from first exposure), longer total exposure, and use of perchloroethylene as a primary agent; but even here the number of cases was small, none of the risks greater than two was statistically significantly, there were no exposure estimates at the individual or company level and no adjustment was possible for potential confounding factors. In the study by Anttila et al, findings were inconsistent, risks being doubled within ten years since first exposure but not after that (a pattern that would not be expected). On balance, the Council regards the evidence to be insufficient to recommend prescription for work as a dry cleaner and cervical cancer.

Prevention

42. The Control of Substances Hazardous to Health Regulations 2002 (as amended) (COSHH) apply to work with hazardous substances – such as tetrachloroethylene – in the dry cleaning industry. COSHH requires that employers undertake a suitable and sufficient assessment of the risks created by work involving hazardous substances and prevent exposures by substituting with safer options or by totally enclosing the work process. Where this is not feasible, exposures should be

controlled as low as reasonably practicable using work processes/systems, engineering controls, local ventilation systems or – as a last resort – suitable personal protective equipment. Workers should also be informed of the hazards/risks and be provided with relevant training.

43. Modern dry cleaning machines are designed to minimise the loss of the cleaning solvent and this means that the cleaning process is totally enclosed. Dry cleaning machines also incorporate ventilation systems that should prevent contamination of the wider work environment. Ensuring exposures are kept as low as reasonably practical therefore largely depends on adequate maintenance of such machines. Where this is achieved any exposures are likely to be kept well below current workplace exposure limits.

Diversity and equality

44. IIAC is aware of issues of equality and diversity and seeks to promote them as part of its values. The Council has resolved to seek to avoid unjustified discrimination on equality grounds, including age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender and sexual orientation. During the course of the review of dry cleaning and oesophageal cancer and cervical cancer, no diversity and equality issues became apparent.

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Glossary of terms

Types of study

Case-control study: A study which compares people who have a given disease (cases) with people who do not (controls) in terms of exposure to one or more risk factors of interest. Have cases been exposed more than non-cases? The outcome is expressed as an **Odds Ratio**, a form of **Relative Risk**. If the case-control study is described as nested, then this means the case and controls are obtained from a **Cohort study**.

Cohort study: A study which follows those with an exposure of interest (usually over a period of years), and compares their incidence of disease or mortality with a second group, who are unexposed or exposed at a lower level. Is the incidence rate higher in the exposed workers than the unexposed/less exposed group? Sometimes the cohort is followed forwards in time ('prospective' cohort study), but sometimes the experience of the cohort is reconstructed from historic records ('retrospective' or 'historic' cohort study). The ratio of risk in the exposed relative to the unexposed can be expressed in various ways, such as a **Relative Risk** or **Standardised Mortality Ratio**.

Measures of association

Statistical significance and P values: Statistical significance refers to the probability that a result as large as far from that expected, or more extreme still, could have arisen simply by chance. The smaller the probability, the less likely it is that the findings arise by chance and the more likely the expected value is not the true value. A 'statistically significant' result is one for which the chance alone, probability is suitably small, as judged by reference to a pre-defined cut-point. (Conventionally, this is often less than 5% ($P<0.05$)). Results around $p = 0.05$ are often described as being of borderline statistical significance.

Relative Risk (RR): A measure of the strength of association between exposure and disease. RR is the ratio of the risk of disease in one group to that in another. Often the first group is exposed and the second unexposed or

less exposed. *A value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

Odds Ratio (OR): A measure of the strength of association between exposure and disease. It is the odds of exposure in those with disease relative to the odds of exposure in those without disease, expressed as a ratio. For rare exposures, odds and risks are numerically very similar, so the OR can be thought of as a **Relative Risk**. *A value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

Standardised Mortality Ratio (SMR): A measure of the strength of association between exposure and mortality; a form of **Relative Risk (RR)** in which the outcome is death. The SMR is the ratio of the number of deaths (due to a given disease arising from exposure to a specific risk factor) that occurs within the study population to the number of deaths that would be expected if the study population had the same rate of mortality as the general population (the standard).

By convention, SMRs (and standardised incidence rates (SIR) as described below) are usually multiplied by 100. Thus, an SMR (or SIR) of 200 corresponds to a RR of 2.0. For ease of understanding in this report, SMRs (or SIRs) are quoted as if RRs, and are not multiplied by 100. Thus, *a value greater than 1.0 indicates a positive association between exposure and disease.* (This may be causal, or have other explanations, such as bias, chance or **confounding**.)

Standardised incidence ratio (SIR): An SIR is the ratio of the observed number of cases of disease (e.g. cancer) to the expected number of cases, multiplied by 100. The ratio is usually adjusted to take account of differences in the population evaluated with the comparison or “normal population”, due to age, gender, calendar year, and sometimes geographical region or socioeconomic status.

Other epidemiological terms

Confidence Interval (CI): The **Relative Risk** reported in a study is only an estimate of the true value in the underlying population; a different sample may give a somewhat different estimate. The CI defines a plausible range in which the true population value lies, given the extent of statistical uncertainty in the data. The commonly chosen 95%CIs give a range in which there is a 95% chance that the true value will be found (in the absence of bias and confounding). *Small studies generate much uncertainty and a wide range, whereas very large studies provide a narrower band of compatible values.*

Confounding: Arises when the association between exposure and disease is explained in whole or part by a third factor (confounder), itself a cause of the disease, that occurs to a different extent in the groups being compared.

For example, smoking is a cause of lung cancer and tends to be more common in blue-collar jobs. An apparent association between work in the job and lung cancer could arise because of differences in smoking habit, rather than a noxious work agent. Studies often try to mitigate the effects of ('control for') confounding in various ways such as: restriction (e.g. only studying smokers); matching (analyzing groups with similar smoking habits); stratification (considering the findings separately for smokers and non-smokers); and mathematical modelling (statistical adjustment).

µmol/L: A **Mole** is a unit of measurement used in chemistry to express amounts of a chemical substance. Thus µmol/L is a concentration of a substance, usually expressed per litre of volume.

Morbidity: Morbidity refers to the state of being diseased or unhealthy within a population

Mortality: Mortality is the term used for the number of people who died within a population

PPM-Years: This is a measure of cumulative exposure to a substance. PPM is the average intensity of exposure expressed in parts per million in air and this is multiplied by the number of years exposed to obtain cumulative exposure in ppm-years.

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