Nuclear Free Local Authorities
briefing

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Subject: COMARE 14th Annual Report on low-level radiation and response to the KIKK report – a critical analysis by Dr Ian Fairlie

NFLA Secretariat Introduction

This briefing provides member authorities with a critique of the independent government committee COMARE's (Committee on Medical Aspects of Radiation in the Environment) 14th Annual Report by Dr Ian Fairlie. Dr Fairlie is an independent consultant on radiation in the environment. He was a member of CERRIE - the independent government 'Committee Examining Radiation Risks of Internal Emitters'.

It has been kindly reproduced in full with the permission of Dr Fairlie. The NFLA Secretariat would like to thank Dr Fairlie for allowing it to publish the report as a NFLA Policy Briefing to contribute to the debate on the COMARE findings. The briefing will be of particular interest to environmental health officers and public health officers.

Dr Fairlie expresses his thanks to Dr Alfred Körblein for his help, particularly on statistical tests.

Comments on Committee on Medical Aspects of Radiation in the Environment (COMARE): 14th REPORT. Further consideration of the incidence of childhood leukaemia around nuclear power plants in Great Britain.

A. Leukaemia increases near nuclear power stations

1. The main aim of the 14th COMARE Report was to undertake a further review of the incidence of childhood leukaemia near most UK nuclear power plants (NPPs). In 2008, a previous study[1] commissioned by the Department of Health had found a 36% increase in acute childhood leukaemias between 1969 and 2004 within 5 km of 13 of the 14 UK nuclear power stations [Observed=20: Expected = 14.74 (95% CI= 0.83-2.10) O/E = 1.36]. The observed increase was considered not to be statistically significant as there was a >5% probability that it could have arisen by chance.

2. In November 2009, the Department of Health requested COMARE to extend the 2008 Bithell study to include more recent data in order to increase the statistical strength of its findings. This is reflected in COMARE's Press Release which states that the new study examines data "…for the extended period…"
http://www.comare.org.uk/press_releases/14thReportPressRelease.htm.
However the COMARE Report actually does not do this: it uses the same 1969 to 2004 time period as the 2008 study. The Report states (para 6.6) "….any significant amount of later information

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would have entailed a delay in carrying out the analysis. Later years are also becoming increasingly difficult to analyse satisfactorily because of the ways in which recent census data are made available."

3. This excuse is not transparent and leaves several questions unanswered. One question is - what is therefore the difference between the 2008 study and the present one? The apparent difference is that the COMARE study now includes non-Hodgkins lymphomas (NHL), chronic myeloprolific diseases, and unspecified leukaemias - as well as the acute leukaemias examined in 2008. These are strange inclusions as there are no actual cases of these extra diseases in the 5 km circles near British NPPs in the study period, and these disease categories were used in neither the 2008 Bithell nor the KiKK study which were supposed to be replicated.

4. The Report finds a 22% increase in childhood acute leukaemia + non-Hodgkins lymphoma (NHL) + chronic myeloprolific disease + unspecified leukaemia [Observed= 20; Expected =16.35 (95% CI= (0. 75–1.89) O/E =1.22). Therefore the net result of adding the new disease categories is to reduce the apparent increase in leukaemias/lymphomas near NPPs from 36% in the 2008 study to 22%. The Report states (para 6.40) that its study had a "negative finding". But in statistics, it is incorrect to make negative conclusions merely because a study lacks statistical significance. This important matter is discussed further in Annex A.

5. Care is needed in epidemiology studies in the choice of which disease categories to examine. This is shown in the table below, where leukaemia increases of 47%, 36% or 22% are found depending on which types of leukaemia/lymphoma are selected. The Report chooses to cite the smallest increase, i.e. that for all types of leukaemia + NHL. In addition, the Report tries to downplay this increase. It mentions (para 6.39) "…a very slightly … raised incidence …", but this misrepresents the actual 22% increase in various leukaemias and NHL.

Childhood Cancer Increases within 5 km of most UK NPPs, 1969-2004

	Observed/ Expected	**Result**	**95% CI**
Bithell et al, 2008	20/14.74= 1.36	36% increase in acute (lymphoblastic and myeloid) leukaemias	0.83-2.10
COMARE 14	20/16.34 = 1.22	22% increase in acute leukaemias + non-Hodgkins lymphomas + chronic myeloprolific diseases + unspecified leukaemias	0.75-1.89
From data in table 6A.2 of COMARE 14	19/12.97 = 1.47	47% increase in lymphoid leukaemias	0.88-2.29

N.B. Data in blue is abstracted from COMARE 14

6. Para 6.40 also states that the risk observed by the Report "...is extremely small if not actually zero." This confuses the background risk of childhood leukaemia which is small with the observed increase in that risk near NPPs, i.e. 22% to 47%, which is not small.

7. Care is also needed in the choice of the level of statistical significance. In many studies, a level of 5% is chosen for no better reason than it is conventional. This was the level chosen by Bithell et al (2008) and by the COMARE Report. However a level of 10% is also commonly used. It is important not to discount results which lie just outside chosen confidence limits[i]. In other words, if an observed increase were not statistically significant using a 5% level but was at a slightly higher level; then this should be reported[ii].

8. Also, COMARE should have carried out the categorical test used in the KiKK study: that is, it should have compared risks within 5 km with risks outside 5 km. The KiKK study did this because, being a case-control study, it did not determine incidence ratios. If COMARE had carried out this test using the data in table 6A.2, then the relative risk for lymphoid leukaemias (risk<5 km vs risk>5 km) would be 1.61 (i.e. a 61% increase) which is significant at the 10%

level (p=0.074). Also, COMARE should have discussed the evident relationship between increased leukaemia risk and proximity to UK nuclear power stations found by the Report's table 6A.2. This clear indication of a dose-response relationship is quite important but, apart from its regression coefficient, it is not commented upon.

B. Evidence on leukaemias near Nuclear Power Plants (NPPs)

9. The COMARE Report refutes the clear pattern of epidemiological evidence across the world indicating increased leukaemia risks near NPPs. In a study[iii] not cited by COMARE, Laurier and Bard examined the literature on childhood leukaemias near NPPs world-wide. They listed a surprising total of 50 studies (29 ecological, 7 case-control and 14 multi-site studies) the majority of which revealed small increases in childhood leukaemia near NPPs although most were not statistically significant. In a later study, Laurier et al[iv] reviewed epidemiological studies on childhood leukaemia at 198 nuclear sites in 10 countries, including 25 major multi-site studies. They found that increased risks of childhood leukaemia near nuclear installations were a recurrent issue. The authors, employees of the French Government's Institut de Radioprotection et Sûreté Nucléaire (IRSN), confirmed that clusters of childhood leukaemia cases existed locally near NPPs but they declined to generalise their findings.

10. In fact, the 2008 Laurier et al study, taken together with Laurier and Bard's 1999 study, indicate over 60 studies world-wide on increased childhood cancers near nuclear facilities, most of them finding cancer increases. It is hard to think of any other toxicity studies, e.g. with chemicals or biological agents, which remotely approach this number.

11. The findings of all these studies have been discussed by Fairlie and Körblein [v] who concluded that "the copious evidence indicating increased leukaemia rates near nuclear facilities, specifically in young children, is quite convincing, at least to independent observers." The COMARE Report comes to the opposite conclusion and fails to discuss the preponderance of the evidence of the above-stated studies, i.e. the finding of increased leukaemias near NPPs.

12. Most important, is the German KiKK study[vi] [vii] (**K**inderkrebs **i**n der Umgebung von **K**ern**K**raftwerken = Childhood Cancer in the Vicinity of Nuclear Power Plants) which found a 120% increase in leukaemias and a 60% increase in solid cancers among children under 5 years old living within 5 km of all German nuclear power plants. The KiKK report is significant because it is a large well-conducted study; because it is scientifically rigorous; because its evidence is particularly strong; and because the German Government, which commissioned the study, has confirmed its findings. The COMARE Report gives a number of reasons for refusing to acknowledge the KiKK study. These reasons are disingenuous and unconvincing: they are discussed below in Annex B.

13. The COMARE Report chooses to downplay the KiKK study, but it simply cannot invalidate the more sophisticated and rigorous KiKK study, as it attempts to do. First, the KiKK study found statistically significant cancer increases. The p-values in the KiKK study were 0.0034 for all cancers and 0.0044 for leukaemias (both one-tailed), in other words they are more stringent than the usual p=0.05. Second, the KIKK study determined precise distances between the homes of cancer cases and NPPs to within 25 metres. In contrast, the COMARE study measured the distances between NPPs and the population centroids of irregularly-shaped electoral wards.

14. Finally KiKK is a case-control study, that is, it examined 593 leukemic children together with 1,766 controls. On the other hand, the COMARE study used geographical averages rather than parameters characterising individual cases and controls. Such studies are termed 'geographical' or 'ecological' and they are much less reliable than case-control studies. Policy makers who should be guided by the best available scientific evidence should rely on the better KiKK study rather than the COMARE study.

C. Exclusion of Calder Hall reactors

15. Only 13 of the 14 UK NPPs were used in COMARE's leukaemia study. The Report states (para 6.12) that the former Calder Hall nuclear power station at Sellafield was excluded from its study. This raises the question as to why. This is an important matter because in the 1980s and 1990s several epidemiology studies revealed relatively large numbers of excess leukaemias (> 7) at Seascale a small village less than 5 km from Sellafield. If these had been included, the Report acknowledges (para 6.13) "…the result would have yielded a higher estimate of risk…".

16. The COMARE Report (para 6.12) gives the following reasons for the exclusion:
    (i) "The observation of an excess of childhood leukaemia near Sellafield was the 'hypothesis-generating' observation and good scientific practice proceeds by attempting to test hypotheses on independent sets of data.
    (ii) Power generation has always been an incidental part of the activities on the Sellafield site, which have included nuclear operations (e.g. reprocessing) that release considerably more radioactivity into the environment than Calder Hall.
    (iii) The well-known excess of childhood leukaemia cases in the village of Seascale adjacent to the Sellafield site would have an undue influence on the overall results, and distort the findings for the group of NPPs."

17. These reasons do not stand scrutiny. As regards (i), the purpose of the COMARE study was to ascertain the number of increased leukaemias near all UK nuclear facilities, not to test a hypothesis. The phenomenon of increased leukaemias near NPPs had already been convincingly shown by KiKK and many other studies: scientifically speaking, there was little reason to have to test any such "hypothesis" again.

18. Reasons (ii) and (iii) are largely the same. Reason (ii) contains an interesting admission that the release of radioactivity into the environment may be a causative factor for the increased leukaemias. However its attempt to divorce reprocessing from nuclear power is disingenuous: most UK nuclear power generation would be impossible without a means for dealing with spent nuclear fuel - the large majority of which is still reprocessed. Reprocessing is therefore an integral part of nuclear power in Britain and its radioactive discharges should logically be included in any reckoning of its health effects. From the point of view of the health of nearby citizens, it does not matter whether the radiation emanates from a reprocessing plant or from nuclear reactors.

19. This problem could have been addressed by presenting the data with and without Calder Hall: in other words, by widening the study to include all nuclear installations not just NPPs. Indeed this was indicated by the title of the Bithell et al (2008) study "Childhood Leukaemia near British Nuclear Installations". Reason (ii) states that reprocessing releases considerably more radioactivity than NPPs: this is true for sea discharges but not necessarily for air emissions which are responsible for the majority of the collective dose to local people. Annual air emissions for some nuclides (especially C-14) from the four Calder Hall reactors could be of similar magnitudes to those from reprocessing. For example, using data available to the author, C-14 releases from Calder Hall in 1995 were 1.4 TBq[viii] compared with 2.62 TBq[ix] for all Sellafield facilities (including Calder Hall) in 1998.

20. Para 6.13 states "... had the data from this site been included – the results would certainly have yielded a higher estimate of risk, but it would have been entirely unclear what implications this had for purpose-built power-generating plants." But surely COMARE was established to concern itself primarily with the health of people living near NPPs rather than the need to construct purpose-built power-generating plants?

D. Resurrection of discredited reason for leukaemia increases

21. The new Report states (para 1.3) "There is growing epidemiological evidence that childhood leukaemia is linked to infections...either a rare response to a common infection...or a rare

response to general exposure to infectious agents...however the biological mechanism underlying these hypotheses remain the subject of considerable scientific debate."

22. No such agent has been remotely identified, and the source, pathway and receptor for any such infectious agent are unknown. This myth is periodically recycled but it has been comprehensively criticised[x] [xi] in the past. The resurrection of the evidence-free notion of an infectious agent being responsible for the increased leukaemias is an embarrassment, and will act to discredit UK science in other countries.

E. Conclusions

23. The data in the COMARE Report indicate a 22% increase in various types of leukemias and non-Hodgkins lymphoma. However it concluded "that the latest British data has *(sic)* revealed no significant evidence of an association between risk of childhood leukaemia … and living in proximity to an NPP".

24. This statement pivots on the equivocal meaning of the word "significant". COMARE rejects the 22% increase by incorrectly implying that, as its findings did not meet a significance test, the findings were negative - a type II error in statistics. COMARE's Report is regrettable as it may mislead members of the public into thinking there are no increases in leukaemias near UK nuclear power stations when in fact this may not be the case. The Report should have said that it found increases ranging between 22% and 47%; that these increases did not meet the statistical test used by COMARE; but that this could be due simply to the low numbers in the study and not to lack of effect.

25. In three areas, the COMARE Report's handling of epidemiological data is not transparent
- it excludes recent data on child leukaemias near NPPs after 2004, despite being established to do precisely that
- it includes new categories of lymphomas and leukaemias although none were actually observed and although neither KiKK nor the 2008 Bithell study examined these types
- it excludes data from the Calder Hall nuclear power station although they state "...their inclusion would certainly have yielded a higher estimate of risk."

26. This irregular handling of data unfortunately lays the COMARE Report open to accusations of selecting or 'cherry picking' their data. In order to dispel any doubts in this area and increase transparency, it is recommended COMARE should release its data
- on the observed numbers of childhood acute lymphoblastic leukaemias within 5 km of NPPs between 2004 and 2010, and
- on the observed numbers of childhood acute lymphoblastic leukaemias within 5 km of Sellafield between 1969 and 2010.

27. The table below lists a number of questionable aspects in the COMARE 14th Report for ease of reference.

para 1.2	myth of "infectious agent" held responsible for increased leukaemias
chapter 4	discounts important KIKK study
chapter 4	ignores considerable evidence that geographical studies are less reliable and should not be used where case-control studies (like KiKK) exist
chapter 6	refutes clear pattern of epidemiological evidence across the world indicating increased leukaemia risks near NPPs
para 6.2	inclusion of leukaemia/lymphoma categories not used in 2008 Bithell and KiKK studies
para 6.6	does not include more recent data after 2004, despite specific DH request to do so
para 6.13	excludes Calder Hall NPP although it "… would have yielded a higher estimate of risk…"
para 6.39	22% leukaemia risk increase termed "very slight..."
para 6.40	states its study had a "negative finding": type II error to make a negative

	conclusion merely because study lacks statistical significance
table 6A.2	does not compare risks <5km with those >5 km. If it had done so, the 61% increase is statistically significant at p = 10%
table 6A.2	relationship between increased risk and proximity to NPPs: clear indication of dose-response relation not discussed

ANNEX A - STATISTICAL SIGNIFICANCE

The COMARE Report states (para 6.40) that its study had a "negative finding". But in statistics, it may be incorrect to make a negative conclusion merely because a study lacks statistical significance. In statistics, concluding there is no association when in fact there may be one is a type II error. The Report should have reported that a leukaemia increase was found but that the increase was not statistically significant. However this could be due to the fact that small studies, like the COMARE study, fail to obtain statistically significant results simply because their data numbers are too small, i.e. they lack statistical power.

This is because p values - that is, the probabilities that observed effects may be due to chance - **are affected by both the magnitude of the effect and the size of the study**[xii]. This means statistical tests must be used with caution because a negative finding can lead to incorrectly concluding there is no effect merely because the result is not statistically significant[xiii] [xiv]. In statistics, this is termed a type II error. This often occurs in small studies due to their low sample sizes rather than lack of effect[xv]. As Axelson has pointed out[xvi], many non-positive epidemiology studies (like the COMARE study) are "of questionable validity as they may obscure existing risks".

Some scientists[xvii] question the excessive or inappropriate use of statistical testing, especially significance tests. They point out that if data are omitted or are missing, the use of statistical tests can result in erroneous conclusions. In March 2011, the US Supreme Court in the landmark case of Matrix Initiatives v Siracusano, http://www.americanbar.org/publications/preview_home/publiced_preview_briefs_jan2011.html#matrixx agreed with this view and decided against the use of statistical tests. The Court held that a pharmaceutical company should not have withheld the results of drug tests (which had showed many side effects) on the grounds that the tests were not "statistically significant". The Court relied on the amicus curiae brief of economics Professor Ziliak which can be obtained at
http://www.americanbar.org/content/dam/aba/publishing/preview/publiced_preview_briefs_pdfs_09_10_09_1156_RespondentAmCu2Profs.authcheckdam.pdf

ANNEX B - KIKK REPORT

The COMARE press release discounts the important KIKK study. First it states its results are heavily influenced by cases in the earliest period (1980-1990), compared with the later periods (1991-1995 and 1996-2003) when the risks were lower. But it has been surmised that the reason for the decline in risk is that plant operators learned to depressurise nuclear reactors at night when most people were indoors and thus less exposed.

Second, it states in the later periods, the results are influenced heavily by the known cluster around the Krümmel plant. But this is not the case: the KIKK results were examined as to the effect of withdrawing each NPP in turn from the analyses: the risks were significantly increased – even when Krümmel was withdrawn.

Third, it states KiKK was not able to take potential confounders, such as socio-economic status, into account. But this is untrue as well. Socio-economic factors affect most epidemiology studies to some extent or other. Suggesting this confounder could be a possible explanation for cancers near NPPs is unconvincing.

The COMARE Report states that the KiKK authors acknowledged their study could not account for the confounder of socio-economic status, which could influence their results. But Kaatsch et al were more nuanced: they stated their results "may possibly be influenced by confounders (like social class, pesticides, factors influencing immunological factors, exposure to other ionizing radiation)." In other words, social class was merely one of four possible factors. More important, the companion study by the same team (Spix et al, 2008) stated that, as regards uncontrolled confounding "no risk factors of the necessary strength for this [KIKK] effect are known for childhood cancer and specifically childhood leukaemia." The KiKK team actually tried to control for these confounders in a separate analysis but there was some self-selection among the interviewed controls, meaning they might not have been representative of the study population. For this reason, the results of the separate confounder analysis were not presented in the KiKK published reports. However the team revealed that "none of them [i.e. the confounders] changed the distance parameter by more than one standard deviation". In other words, the confounders studied by the KiKK team, including socio-economic status, appear to have had little effect on the KiKK findings.

Finally the COMARE press release states that there is disparity in the risk for childhood leukaemia for 1980-1990 between additional German geographical studies and the case-control KiKK study. But this again ignores the considerable evidence indicating geographical studies are less reliable and should not be used where better evidence – e.g. case-control studies (i.e. KiKK) exist.

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