

Committee on Medical Aspects of Radiation in the Environment (COMARE)

FOURTH REPORT

The incidence of cancer and leukaemia in young people in the vicinity of the Sellafield site, West Cumbria: Further studies and an update of the situation since the publication of the report of the Black Advisory Group in 1984

Chairman: Professor B A Bridges

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FOREWORD

i. The Committee on Medical Aspects of Radiation in the Environment (COMARE) was established in November 1985 in response to the final recommendation of the report of the Independent Advisory Group chaired by Sir Douglas Black (Black, 1984). Our terms of reference are to “assess and advise Government on the health effects of natural and man-made radiation in the environment and to assess the adequacy of the available data and the need for further research”.

ii. The Black Advisory Group had been commissioned by the Minister of Health in 1983 to investigate reports of a high incidence of leukaemia occurring in young people living in the village of Seascale, 3km from the Sellafield nuclear site and the suggestion that there might be an association between the leukaemia incidence and the radioactive discharges from Sellafield. The Advisory Group confirmed that there was a higher incidence of leukaemia in young people resident in the area but also concluded that the estimated radiation dose from the Sellafield discharges and other sources, received by the local population, could not account for the observed leukaemia incidence on the basis of knowledge available at that time. The uncertainties in the available data led the Advisory Group to make recommendations for further research and investigation.

iii. Our First Report (COMARE, 1986), examined the implications of some further information concerning discharges of uranium oxide particles from Sellafield in the 1950s, which had not been available to the Black Advisory Group. The Committee concluded that this additional information did not change the essential conclusions of the Black report.

iv. Our Second Report investigated the incidence of leukaemia in young people living near to the Dounreay Nuclear Establishment in Caithness, Scotland (COMARE, 1988). We found evidence of an increased incidence of leukaemia in young people in the area and although the conventional dose and risk estimates suggested that radioactive discharges could not be responsible, we noted that the raised incidence of leukaemia at both Sellafield and Dounreay tended to support the hypothesis that some feature of these two plants lead to an increased risk of leukaemia in young people living in the surrounding area. The report also considered other possible explanations and recommended further investigations.

v. Our Third Report considered suggestions of an increased incidence of childhood cancer near the Atomic Weapons Research Establishment at Aldermaston and the Royal Ordnance Factory at Burghfield (COMARE, 1989). We found a small but statistically significant increase in registration rates of childhood leukaemia and other childhood cancers in children in the vicinity of the two sites. However, we judged that the doses from the radioactive discharges were far too low to account for the observed increase in the incidence of childhood cancer. We considered a number of possible explanations for the findings including other mechanisms by which radiation could be involved, but

there was insufficient evidence to point to any one explanation, although the possibility remained that a combination of factors might be involved. Further investigations were recommended. Our Third Report concluded by saying that the distribution of cases of childhood leukaemia or other childhood cancers around nuclear installations could not be seen in proper context in the absence of comparable information about the pattern throughout the UK. We recommended, therefore, that further work be carried out to determine the national geographical pattern of distribution of childhood cancer and that this work should be given high priority.

vi. This, our Fourth Report is the result of the Committee's review of the dosimetric, epidemiological and other scientific data relating to the Sellafield Site and the village of Seascale, together with other relevant advances in scientific knowledge, that have become available since the publication of the report of the Black Advisory Group in 1984. The review was undertaken in response to a request by Government, made to the Committee in September 1989 and recorded as a commitment in answer to a Parliamentary Question regarding COMARE's work programme which included:

“an update and review of cancer incidence in young people in the vicinity of BNFL Sellafield, in the light of emerging epidemiological work commissioned by Government in 1984 and other relevant work.” [Hansard 10 January 1990, Col 662]

vii. In this report, we review all of the data which has become available since the publication of the Black Advisory Group report and we report our findings and conclusions to Government.

viii. In the course of this review the Committee and its various sub-committees and working groups requested data and information from a number of organisations and researchers. Many individuals have given time to present data to us and we wish to take this opportunity to thank all of them for their co-operation.

ix. During the course of this review the civil litigation case, *Reay v BNFL and Hope v BNFL*, was heard. Many expert witness reports relevant to our deliberations were generated. These expert witness reports were made available to us during the course of our current review.

x. The views expressed in this report are those of the Committee and not necessarily those of the Secretariat, the Assessors, or those providing evidence. A list of Members (of the main Committee, sub groups and working groups), the Secretariat and Assessors is provided in Appendix B. Technical detail is unavoidable in a report such as this and a Glossary of terms is provided in Appendix A. However, a complete picture of the scientific background to this report can only be gained by reference to the scientific material consulted which are listed at the end of the report in the References.

CHAPTER 1

INTRODUCTION

THE INCIDENCE OF CANCER IN YOUNG PEOPLE (0-24 YEARS) AROUND SELLAFIELD

The report and recommendations of the Black Advisory Group.

1.1 In this chapter we describe briefly the findings in the Black Advisory Group report and our previous three reports. The outcomes of our recommendations in previous reports are at Annex A for reference. We conclude with our opinions on these issues and the remaining uncertainties as they stood at the time we started this review.

1.2 In their report (Black, 1984), published in 1984, the independent advisory group chaired by Sir Douglas Black:-

- i. identified (a) 7 cases of leukaemia occurring between 1955 and 1984 in young people aged under 25 years at diagnosis and resident in Seascale and a further eight outside Seascale, but in the same rural district (Millom) adjacent to and south of Sellafield: (b) 7 cases of lymphoma (in Table 3 of the Black Advisory Group report labelled “Lymphomas” one case was listed as a leukaemia and this designation is used here), and (c) 10 cases of other solid tumours in Millom including Seascale.
- ii. confirmed that there was an increased incidence of leukaemia in young people resident in the area around Sellafield, when compared with national rates of leukaemia;
- iii. having considered the assessment of risk of leukaemia and cancer in Seascale, by the National Radiological Protection Board (Stather *et al* 1984), concluded that the estimated doses of radiation received by the local population from the Sellafield discharges could not account for the observed leukaemia incidence, on the basis of current knowledge;
- iv. stressed the uncertainties involved in these dose assessments;
- v. made 10 recommendations all of which were accepted by Government. The current status of these recommendations is detailed in Annex A.

1.3 The final recommendation of the Black Advisory Group (10e) stated “that there should be a designated body with significant health representation to enable decisions on action with regard to the control of permitted radioactive discharges to take account of all relevant factors.” As a consequence of this recommendation the Committee on Medical Aspects of Radiation in the Environment (COMARE) was set up in 1985.

**FURTHER DATA ON
RADIOACTIVE
DISCHARGES FROM
SELLAFIELD**

**COMARE'S First
Report.**

1.4 Our first report (COMARE, 1986) examined the implications of some further information concerning larger discharges of uranium oxide particles from Sellafield in the 1950s, which had not been available to the Black Advisory Group. After calling for and considering a further assessment of dose and risk by NRPB (Stather *et al*, 1986) the Committee concluded that this additional information did not change the essential conclusions of the Black report because the published dose estimates were based largely on environmental monitoring data rather than discharge data. This First Report made no new recommendations although it contained the advice to Government “that they should satisfy themselves as to the adequacy of the current monitoring programme at or near all such installations”.

1.5 Our First Report criticised the way in which this new evidence had come to light and stated that a detailed reconsideration of the epidemiological data was not justified until the results of the first four recommendations of the Black Advisory Group report were available.

**THE INCIDENCE OF
LEUKAEMIA IN
YOUNG PEOPLE
RESIDING NEAR
THE DOUNREAY
NUCLEAR
ESTABLISHMENT**

1.6 During their inquiry concerning the area around Sellafield, in 1984, the Black advisory group requested information about the incidence of leukaemia around Dounreay, the only other nuclear installation in the UK where reprocessing of nuclear fuel is carried out. At that time the available data did not suggest any evidence of an increase in leukaemia incidence at this site.

1.7 A further analysis was prompted by the 1986 public inquiry into a planning application for a new reprocessing plant at Dounreay. This was carried out by the Information and Statistics Division (ISD) of the Common Services Agency of the NHS in Scotland on behalf of the Scottish Home and Health Department (SHHD) (Heasman *et al*, 1986.) The results suggested that there had been an elevated incidence of leukaemia among young people living in the area up to 12.5 km from the site, in the years 1979 to 1984.

**COMARE's Second
Report.**

1.8 In response to this information, the Secretary of State for Scotland asked for our advice on this and other similar reports. To consider these data in the appropriate context, we asked NRPB to produce estimates of dose and risk to the population of the nearest community, Thurso, from exposure to environmental radiation (Hill *et al*, 1986, Dionan *et al*, 1986). The Committee's advice was contained in COMARE's second report (COMARE, 1988) published in 1988, which:-

- i. identified 6 cases of leukaemia among people 0-24 years old resident within 25 km of Dounreay during the period 1968-1984;
- ii. concluded that there was clear evidence of a statistically significant excess incidence of leukaemia in young people living in the area around Dounreay;
- iii. noted that evidence of a raised incidence of leukaemia around both the Dounreay and Sellafield sites, despite the differences in the temporal distribution of the cases and the levels of the discharges, tended to support the hypothesis that some feature of the sites leads to an increased risk of leukaemia in young people living nearby;
- iv. made 8 recommendations, the outcome of which are in Annex A.

THE INCIDENCE OF CHILDHOOD CANCER AROUND THE ALDERMASTON BURGHFIELD AND HARWELL NUCLEAR ESTABLISHMENTS

1.9 The leukaemia incidence in young people living in the areas around these sites was studied because clinicians at the Royal Berkshire Hospital, Reading, suspected that more cases of childhood leukaemia were being referred to the hospital, than would normally have been expected. The topic was the subject of YTV programme entitled "Inside Britain's Bomb" which was broadcast in December 1985.

1.10 A study by Roman *et al* (1987) found that there was a statistically significant increased incidence of childhood leukaemia in an area within 10 km of either Aldermaston or Burghfield in the years 1972 to 1985. This increase was found only in the age-group 0-4 years. Although the incidence was relatively low compared to that at Seascale or the area around Dounreay, the area is much more densely populated and larger numbers of cases were registered.

COMARE's Third Report.

1.11 These studies were referred to COMARE for advice. We also had access to unpublished data from the Childhood Cancer Research Group (CCRG) in Oxford. These data showed that for the years 1971 to 1982 there is also an excess of all childhood cancers other than leukaemia in the same area and in the same age group, 0-4 years as that found by Roman *et al*.

1.12 COMARE again asked NRPB to produce estimates of doses of radiation to the general public living in the vicinity of the sites (Dionan, 1987). Because the levels of discharge were similar to those emitted by coal-fired boilers and power stations in the same area, we asked NRPB to produce estimates of dose from these sources for comparison (Wan and Wrixon, 1988).

1.13 COMARE's Third Report published in 1989,

- i. identified a significant excess of childhood leukaemia cases confined to those aged 0 to 4 years of age, among whom 29 cases were observed resident less than 10 km from a nuclear establishment against 14.4 expected. There were also 30 cases of other cancer in this age group and area compared to 19.4 expected;
- ii. concluded that although there is a small but significant excess of childhood leukaemia and other cancers in the vicinity of Aldermaston and Burghfield, the radioactive discharges from these and the Harwell site were far too low to account for the epidemiological findings;
- iii. could not completely exclude the possibility that these observations around Sellafield, Dounreay, and Aldermaston & Burghfield, are due to chance or due to selection of the sites referred to them for investigation;
- iv. concluded that the distribution of cases of childhood leukaemia, or other childhood cancer, around individual nuclear installations could not be seen in a proper context in the absence of comparable information about the general pattern throughout the rest of the UK;
- v. made 5 recommendations, the outcome of which are given in the annex.

COMARE'S GENERAL VIEW OF POSSIBLE CAUSES AND UNCERTAINTIES.

1.14 The initial hypothesis considered by the Black Advisory Group was that an association existed between the doses received by the environmental exposure of the local population to radioactive discharges and other radiation sources and the incidence of childhood leukaemia and other cancers. In our Second Report we speculated on whether there were any other ways in which exposure to radioactive discharges could be implicated, namely:

- a. that unknown pathways in the environment could have led to a section of the population being exposed to higher levels of environmental radioactivity than expected,
- b. that the carcinogenic effect of particular types of radioactive materials (principally alpha emitters) may be much greater than had been supposed,
- c. that different tissues and cell types, principally fetal haemopoietic tissue and lymphoid tissue in the bronchial and intestinal regions of young people may have different sensitivities to radiation.
- d. that exposure of the gonads could lead to effects in subsequent offspring,
- e. that there were unrecognised pathways of exposure via workers whereby radioactive material was inadvertently removed from the site.

1.15 In our Second Report we noted various factors, other than radiation, which could be relevant to the incidence of leukaemia around the sites examined. These factors were:

- a. the social class distribution of the local population,
- b. exposure to chemicals used in or discharged from a nuclear installation,
- c. the influx of an outside workforce into a previously isolated community,
- d. possible viral causes of leukaemia.

1.16 At the end of our Third Report we considered a number of possible explanations for the findings, including other mechanisms by which radiation may be involved, but we did not have sufficient evidence to point to any one particular explanation and we felt that it was possible that a combination of factors may be involved.

1.17 Thus, at the time that we were asked to review the scientific, epidemiological and other scientific data relating to the Sellafield site and the village of Seascale, we had concluded that there was a statistically significant increase in the incidence of childhood leukaemia in Seascale and in the vicinities of Dounreay and Aldermaston and Burghfield.

1.18 In all three cases we concluded that, on the basis of the authorised and all known accidental radioactive discharges and using accepted radiological estimates of risk, we could not account for the observed increase in childhood leukaemia but we could not exclude completely the existence of some hitherto unknown and unexpected route by which some individuals could have been exposed to increased levels of radiation. We had also considered factors other than radiation exposure including chemical carcinogens, demographic phenomena and viruses. Although we recognised the potential importance of these factors, at that time we were not aware of any specific evidence that these might have been responsible for the increased incidence of childhood leukaemia.

1.19 We could not exclude completely the possibility that these observations were a consequence of chance or due to the selection of the sites referred to us for our enquiries but the evidence tended to support the hypothesis that, some

feature related to the nuclear plants that we had examined had led to an increased risk of leukaemia in young people living in the vicinity of those plants.

1.20 Since that time further evidence has been made available as the result of both the Black Advisory Group's and our recommendations (see the Annex to this chapter) and from other sources. We have also requested further epidemiological and other scientific data for this review.

Our Current Report

1.21. We now review the epidemiological, dosimetric and other scientific data which have become available since the publication of the Black Advisory Group report and our first report. We will draw conclusions about the main advances in scientific knowledge since the time of the Black report and clarify where progress has been made and where uncertainties remain.

1.22 We have considered the current evidence in depth by setting up several subgroups and working groups. The reports of these groups were considered by the full committee in our overall assessment in this report.

1.23 In subsequent chapters we update the epidemiological data (chapter 2), and general radiological assessment (chapter 3); consider a particular occupational radiation hypothesis (chapter 4) and other possible causative factors - chemical exposure (chapter 5) and infectious aetiology (chapter 6).

1.24 During the writing of this review, we asked for further information on local activities and cancer rates prior to the commissioning of the Sellafield Nuclear site and this is given in Chapter 7. Finally, the Committee's Discussion, Conclusions and Recommendations are given in the final three chapters of this report, chapters 8, 9 and 10.

ANNEX

A REVIEW OF BLACK AND COMARE RECOMMENDATIONS

The outcome of the Black Advisory Group's recommendations.

A1 The first four recommendations of the Advisory group concerned major epidemiological studies, largely funded by the Department of Health.

A2 Recommendation 1. A case control study was carried out of leukaemia and lymphoma in young people up to the age of 25 living in West Cumbria (Gardner *et al*, 1990a & 1990b). Using a variety of sources the authors of this study identified 52 cases of leukaemia and 22 cases of non-Hodgkin's lymphoma (NHL) in children who had been born and diagnosed of their illness in West Cumbria. The study concluded that the raised incidence of leukaemia and NHL among children living near Sellafield showed a statistically significant association with paternal employment at Sellafield and the recorded external whole body dose of radiation received prior to conception of the affected child. The highest relative risks recorded were of the order of sixfold for fathers with total radiation doses of 100 mSv or greater before the date of their child's conception, or doses of 10 mSv or greater during the six months before conception.

A3 The results of this study generated what has become known as the "Gardner hypothesis", which suggests that paternal preconception irradiation is associated with the risk of childhood leukaemia in subsequent offspring. Considerable investigation of this hypothesis has been carried out. The results and conclusions of these investigations are considered in Chapter 4 of this report.

A4 The Gardner study also reported that in West Cumbria there was an increase in the incidence of leukaemia in the offspring of fathers working in the chemical, steel and agricultural industries that was as great as that found amongst the offspring of Sellafield workers, although considerably less than the risks suggested for those having the highest levels of paternal preconception irradiation.

A5 COMARE considered the results of this study and made an interim Statement of Advice to Government (Hansard 2 April 1990). COMARE reiterated Recommendation 3 of their Second (Dounreay) Report and Recommendation 2 of their Third Report (Aldermaston and Burghfield) which say that an epidemiological study of the possible health effects on the offspring of parents occupationally exposed to radiation should be undertaken. As a result two studies are in progress: the Nuclear Industry Family Study (NIFS) and a record linkage study being carried out jointly by the Childhood Cancer Research Group (CCRG) at the University of Oxford, the National Radiological Protection Board (NRPB) and the Department of Epidemiology and Public Health of the University of Birmingham.

A6 In their statement COMARE also recommended that a co-ordinating body be set up to ensure that any studies within this area should not duplicate other work, and that approaches to families are minimised so as to avoid undue

Rec 7a Gut transfer factor data have been obtained for adults in volunteer studies carried out by the Ministry of Agriculture, Fisheries and Food (MAFF). These have been considered in the dose assessment for this report.

Rec 7b. Metabolic differences between adults and children. Investigations in children present ethical and technical difficulties. A specific project to investigate the uptake of various stable isotopes in neonates is under consideration.

Rec 7c. Children's habits in relation to radiation exposure pathways. Data continue to accrue in several research projects.

Rec 7d. Biological effects of low dose rate exposures to alpha emitters. Several groups are active in this field using both in vitro and in vivo techniques, but no scientific consensus has as yet emerged.

The results of these studies have been used in the dose and risk assessment covered in Chapter 3 of this report.

A13 Recommendations 8, 9, 10a & 10c. Authorisations to discharge radionuclides. These recommendations were addressed to the authorising departments (ie. MAFF, HMIP, SO). Significant reductions in discharges, the process by which the discharges are reported and changes in the consultation upon draft authorisations were already under way and improvements have continued to be made.

A14 Recommendation 10b Collection of relevant epidemiological data relating to exposure to discharges. Many studies have been completed or are under way and several of the more important studies are described in more detail in this and other sections of this report.

**The outcome of the
Recommendations of
COMARE's Second
Report. (Dounreay)**

A15 Recommendation 1. A case-control study of young people registered as cases of leukaemia or lymphoma in the Dounreay area was undertaken as recommended (Urquhart *et al.* 1991). The authors' objective was to examine whether the observed excess of childhood leukaemia and NHL in the area around the Dounreay Nuclear Establishment was associated with factors related to the plant or parental occupation in the nuclear industry. The study showed that children with leukaemia or NHL were no more likely to have fathers who worked or had worked in the nuclear industry, than were control children. The only statistically significant association was with the use of local beaches prior to diagnosis. In their Statement of Advice to Government COMARE (21 March 1991), noted that these results differ from those obtained by Gardner *et al* (1990a), in regard to paternal employment in the nuclear industry. However, COMARE agreed with the authors that a study based on such a small number of cases could not negate the hypothesis put forward in the Gardner study, even though the latter was itself based on a very small number of cases.

A16 Recommendation 2. Studies to establish whether the leukaemia excess was confined to those born in the Dounreay area (Birth and School cohort studies) were carried out (Black *et al*, 1992). These studies concluded, in contrast to the studies by Gardner at Sellafield, that the place of birth is not a more important factor than place of residence in the series of cases in the Dounreay area. The incidence of leukaemia and NHL was raised in both those born in the area and those resident in the area but born elsewhere.

A17 Recommendation 3. Epidemiological studies were set up to consider any possible effects on the health of the offspring of parents occupationally exposed

to radiation. The Nuclear Industry Family study (NIFS) and the Radiation Record Linkage Study were commissioned in 1990/1. These studies are funded by Department of Health and the Health and Safety Executive.

A18 Recommendations 4a, 4b & 4d. That monitoring of radioactivity in diet, air, household dusts, sea spray and beach sediments should continue. Programmes of such monitoring continue and in many cases have been expanded.

A19 Recommendation 4c. This recommendation encouraged the Authorising Departments to investigate anomalous monitoring results.

A20 Recommendation 5. A study of the chemicals used at Sellafield and Dounreay. The Committee on Mutagenicity (COM) were asked to examine data on the types and quantity and leukaemogenic potential of chemicals used on the Sellafield and Dounreay nuclear sites. This topic is dealt with in detail in Chapter 5 of this report.

A21 Recommendation 6. Dose calculations should, wherever possible, be based on environmental monitoring data since this provides an independent test of discharge data. If this is not possible it should be clearly stated when doses are estimates based on discharge data. At Sellafield, measurements were available for environmental levels of radionuclides so actual population exposures could be calculated from these data. The situation at Dounreay was different in that environmental levels of man-made radionuclides were too low to be distinguished from background levels, so exposures had to be calculated from discharges. In the current Sellafield review dose calculations are based on environmental monitoring data where available.

A22 Recommendation 7. Whole body monitoring of people living near to Scottish nuclear sites. A study was carried out in Scotland which found no unusual levels of radionuclides in the people measured.

A23 Recommendation 8. Further laboratory work on leukaemogenesis. The Medical Research Council (MRC) was consulted and gave details of relevant research under way. COMARE did not identify any major gaps except the research subsequently sponsored by Department of Health and Health & Safety Executive to investigate the “Gardner Hypothesis”.

A24 The Dounreay case-control study raised the possibility of an association between childhood leukaemia and the use of local beaches prior to diagnosis. COMARE noted that these data relate to five cases only and that the data were based on parental recall some years after the event, which may be subject to recall bias. Also, evidence available from the corresponding study at Sellafield did not show a comparable association and the information concerning the levels of radio-activity on public beaches near Dounreay suggested that resulting doses would be too low to account for the excess of leukaemia, on the basis of currently accepted models of leukaemogenesis. However, COMARE agreed that it would be prudent to re-examine the Dounreay beach monitoring data and an appropriate subgroup was set up to carry out this task. COMARE’s combined report with the Radioactive Waste Management Advisory Committee (RWMAC) on this issue was published in May 1995 (COMARE/RWMAC 1995).

A25 The reports from the two Committees address the possible health implications and putative sources of the radioactive particles found in the vicinity of the Dounreay Nuclear Establishment. The COMARE working group visited

the Dounreay site and nearby beaches in May 1994. During this visit the working group were informed of new possible sources of contamination of the Dounreay foreshore. COMARE requested RWMAC to assist in establishing the source of the radioactive contamination. RWMAC is of the opinion that the most likely source for the particles is surface contamination adjacent to the authorised Intermediate Level Waste Disposal Shaft (ILWDS), although other sources could not be ruled out. RWMAC called for further investigations into the source of the particles and wider contamination which is now being carried out by UKAEA. COMARE and RWMAC also noted that the ILWDS is an unacceptable model for the disposal of nuclear waste and recommended that UKAEA propose a solution and timetable for the treatment of the waste in accordance with modern standards. COMARE noted that the possible health effects from the radioactive particles depend upon the likelihood of encountering one and on its activity. The Committee noted that the chance of a member of the public encountering a particle was considered very small and that whilst the most active particles could cause acute effects, the particles are most unlikely to explain the observed excess of childhood leukaemia in the Dounreay area. COMARE and RWMAC have promised to monitor the outcome of their recommendations regarding the discovery and treatment of the sources of contamination at Dounreay.

A26 In the light of the DH request for a review of the situation at Sellafield since the time of the Black enquiry, COMARE considered that it would be reasonable to ask for a 5 yearly update of the epidemiological data at Dounreay. A study was undertaken by the Information and Statistics Division of the Scottish Office Home and Health Department and has now been published (Black *et al*, 1994).

A27 The objective of this study was to review the geographical incidence of leukaemia and NHL in children and young adults resident in the area less than 25km from the Dounreay nuclear installation, and in the remainder of the postcode area in which the Dounreay installation is situated (ie. postcode area KW). The full time period 1968-91 was studied to determine whether the excess incidence reported in the period up to 1984 had continued in subsequent years. In comparing observed and expected numbers of cases of leukaemia and non-Hodgkin's lymphoma, the expected numbers were based on Scottish national rates.

A28 The authors reported that in 1968-91, 12 cases were observed compared with 5.2 expected in the zone within 25km of the Dounreay plant ($p=0.007$, 1-sided test). In the latest period 1985-91, which was not included in the second COMARE report, 4 cases were observed compared with 1.4 expected ($p = 0.059$).

A29 COMARE'S advice to government on this finding (Hansard 19 July 1994 Col 120.) concluded that the findings reinforced the view held in the Second Report that

“Although chance cannot be entirely dismissed as an explanation of the raised incidence of childhood leukaemia in the vicinity of Dounreay, we consider that it is now less likely* than when Sellafield was considered in isolation”. [* ie. as an explanation of the increased risk of leukaemia in young people living in the vicinity of Dounreay or Sellafield (paragraphs 5.26-5.28 of COMARE's 2nd Report)]

Regarding the causation of leukaemia and non-Hodgkin's lymphoma in the area, the Committee considered that this study neither adds nor removes support for the "population mixing" hypothesis suggested by Professor Kinlen. [see chapter 6] The Committee also noted that the data in the case-control study (Urquhart *et al*, 1991), which examined parental exposure to radiation, showed that the "paternal preconception irradiation" hypothesis put forward by Professor Gardner could not account for the observed excess and that the new data did not change this position.

The Committee concluded that further epidemiological research in the Dounreay area to try to determine causal mechanisms was not considered to be a practicable way forward at present, because of the small number of cases involved. However, we stated that the incidence of any new cases of childhood leukaemia which might arise should continue to be monitored at appropriate time periods. Rigorous analysis of pathological material from such individuals should continue to be strongly encouraged.

**The outcome of the
Recommendations of
COMARE's Third
Report.
(Aldermaston and
Burghfield)**

A30 Recommendation 1. This recommended a case-control study of young people registered as cases of childhood cancer in the vicinity of the Aldermaston and Burghfield sites with the objective of this study being to investigate any relationship between parental employment in the nuclear industry (Aldermaston and Burghfield) and childhood leukaemia and NHL. This was undertaken by Roman *et al* in (1993) and the results published in 1993. The subjects were 54 cases of childhood leukaemia and NHL diagnosed at ages 0-4 years between 1972 and 1989 and living in West Berkshire and North Hampshire at the time of diagnosis. Three of these cases had fathers who had been monitored for radiation exposure before the conception of their children compared to 2 (out of 324) fathers of controls. The authors concluded that the children of fathers who had been monitored for exposure to external ionising radiation in the nuclear industry, may be at increased risk of developing leukaemia before their 5th birthday, but noted that this finding is based on small numbers and could be due to chance and also that it does not explain the above average rates of childhood leukaemia in the study area.

A31 COMARE issued its Statement of Advice on this study on 18 May 1993 suggesting that conclusions regarding pre-and post-conception exposures could not be drawn from this study in view of the very small numbers of families affected. Furthermore, it was agreed that the study provided no new evidence to distinguish between the various hypotheses previously suggested regarding causative agents or chance effects in relation to childhood cancer incidence in the vicinity of certain nuclear installations.

A32 Recommendation 2. This recommendation reiterated the need to investigate any health effects in the offspring of nuclear workers. The Nuclear Industry Family Study (NIFS) and radiation record linkage studies (linking the National Registry for Radiation Workers NRRW and the National Register of Childhood Cancers NRCT) are in progress.

A33 Recommendation 3. Cancer registration. The national cancer registration system was reviewed in 1990, and a DH Steering Committee under the chairmanship of the Deputy Chief Medical Officer was set up to oversee the implementation of the recommendations (Hansard 19.2.93 col 391). Cancer registrations have been postcoded for patients diagnosed from 1974 onwards. For

children below age 15, postcode data are available from 1962 onwards. Place of birth is being added for children with cancer, born in 1965 or later.

A34 Recommendation 4. The national distribution of childhood cancer should be investigated. Studies of childhood leukaemia rates have been completed and published and are discussed in chapter 2 of this report.

A35 Recommendation 5. An overall review of childhood cancer incidence around all nuclear installations should be undertaken on the completion of Recommendation 4. The results of these studies of childhood leukaemia around nuclear installations in England and Wales (Bithell *et al*, 1994) and Scotland (Sharp *et al*, in press) are also discussed in chapter 2 of this report. The corresponding analyses for other childhood cancers are in progress.

CHAPTER 2

THE INCIDENCE OF CANCER AND LEUKAEMIA IN YOUNG PEOPLE LIVING IN THE VICINITY OF SELLAFIELD

INTRODUCTION

2.1 Over the past thirteen years or so, there have been many suggestions of an increased incidence of cancer, or of 'clusters' of cases, in young people living in the vicinity of nuclear installations. The most detailed investigations have concerned the area around the Sellafield nuclear reprocessing plant in West Cumbria. The Black Advisory Group investigated the suggestion that there was an increased incidence of cancer in the vicinity of this installation and reported in 1984 (Black, 1984). Our current report reviews the data which has become available since then.

2.2 Areas around some other nuclear installations have also been the subject of systematic epidemiological studies: in the UK such studies include those of Dounreay (COMARE, 1988), Aldermaston and Burghfield (COMARE, 1989) and of nuclear installations in England and Wales generally (Cook-Mozaffari *et al*, 1989a). The results of our enquiries into these specific sites have been summarised in the previous chapter. The more general issues are discussed later in this chapter.

2.3 Since the Black report, further cohort and case-control studies of the area around Sellafield have been carried out (Gardner *et al*, 1987a, 1987b and 1990a). The Black Advisory Group also recommended that childhood cancer data for the North of England should be re-analysed using data from the 1961, 1971 and 1981 censuses. Craft, (1989 and 1993) analysed the Northern England data from 1968 to 1985 in this way and showed that when the significance level of the observed incidence rate of ALL and NHL for each census ward was evaluated under the null hypothesis that the true rate was equal to the average rate for this disease group in the North of England and the UK, the ward of Seascale was ranked first. For other cancers there were wards with more extreme significance levels than Seascale.

2.4 Following the request from the Department of Health for COMARE to review the epidemiological and dosimetric data for the Sellafield area, we requested a study to update the epidemiological data. As a result of this request Draper *et al* (1993) published a comprehensive analysis of childhood cancer rates at ages 0-24 years in Seascale up to and including 1990. The present chapter includes the data in the Draper paper but the analysis is extended and updated to cover the incidence rates for the period up to 1992. The analyses are based partly on data collected in the course of research studies and partly on improved cancer registration data, to which postcodes have been added; such data were not available to the authors of the Black report.

2.5 The main body of this chapter is concerned with the period following the publication of the Black report, i.e. 1984 to 1992. In planning the analyses for this latter period it was necessary to avoid the biases which inevitably tend to affect the analyses of the period up to and including 1983. For these years, the general area and the age-group and types of disease to be studied were selected as a result of the observed 'cluster'. The hypothesis thus tested was not

determined *a priori* but was formulated, at least partly, after the results had been obtained. The significance levels attached to the data for the period up to 1983 cannot accurately reflect this process. The analysis for the post-Black period, 1984-1992, has therefore been designed principally to test the hypothesis that no excess of leukaemia or other cancers in 0-24 year olds has occurred in the vicinity of the Sellafield plant from 1984 to 1992.

2.6 In discussing the significance of these results, we have also considered the epidemiological data for Seascale and Cumbria in the context of studies around nuclear sites in general and also in context of the national geographical distribution.

2.7 In order to minimise the possibility of bias, we agreed in advance on a plan for analysing the results. Therefore we carefully selected the diagnostic groups, time periods and geographical areas in advance of requesting the data for analysis.

THE CHOICE OF METHODS AND DATA

Diagnostic groups

2.8 It was agreed that the analyses would cover both all malignant disease around Sellafield and also a number of specific diagnostic groups defined below. The disease categories in brackets refer to the standard classification for childhood cancer (Birch and Marsden 1987). This classification is based on the topographical and morphology (M) codes in the International Classification of Diseases for Oncology (ICD-O) (WHO 1976). The diagnostic groups analysed in the present report were defined as follows:

- i. Lymphoblastic leukaemia and non-Hodgkin's lymphomas (NHL), including Burkitt's lymphoma, unspecified lymphoma and hairy cell leukaemia; (I(a),I(b),II(b),II(c),II(d), plus ICD-O M-code 9940/3)
- ii. All other and unspecified leukaemias; (I(c),I(d),I(e) except ICD-O M-code 9940/3)
- iii. Hodgkin's disease; (II(a))
- iv. Brain and spinal tumours (including non-malignant); (III(a) to III(e))
- v. All other malignant diseases; (II(f), IV to XII).

2.9 The first diagnostic group was chosen in the light of discussions in the COMARE report on Dounreay (1988), paras 2.27-2.30, together with the conclusion that acute lymphoblastic leukaemia (ALL) could be adequately distinguished from other leukaemias in the present data. Chronic lymphocytic leukaemia (CLL) is very rare in the age group 0-24 years and so lymphoid leukaemia in this age group is essentially equivalent to ALL. Hairy cell leukaemia is now regarded as a variant of chronic lymphocytic leukaemia and has been grouped with it (Birch and Marsden, 1987). Langerhans Cell Histiocytosis (formerly histiocytosis X) is not included in the analysis as this group is increasingly recognised to be not only rare, but a heterogeneous group of diseases some of which are thought to be malignant and some of which are not. It is impossible to classify these different entities retrospectively and in view of that and of their rarity they have been excluded.

2.10 Acute lymphoblastic leukaemia (ALL) accounts for approximately 75-80% of all cases of childhood leukaemia (approximately 350 new cases per year in the UK) but it is now recognised that it is not in itself a single entity. Over the last 30 years new technology has increasingly enabled the identification of sub-

types. Although many leukaemias represent a clonal expansion of cells representing a specific and identifiable stage of normal differentiation many, especially the childhood B-cell lineage cases, do show patterns of surface antigen and immunoglobulin gene rearrangements that are not recognisable within normal differentiation pathways. Furthermore a smaller but important group have characteristics of more than one lineage (Poplack, 1993).

2.11 Since 1985, when COMARE was first established, diagnostic classification of ALL has progressed from three types (T, B, non-T non-B) to six broad categories (T, B, pre B, Common, null and mixed lineage) with an increasing number of subtypes being identified. However, the majority (60%-70%) of childhood ALL in the UK represents a B-cell lineage disorder with a peak incidence between 3 and 6 years of age which tends to emerge in countries as socio-economic conditions improve and appears to parallel industrialisation and urbanisation (Miller, 1979). A subset of these disorders have a consistent translocation involving chromosomes 1 and 19. Mature B-cell ALL is rare in the UK, but morphologically similar to both endemic and sporadic Burkitt's lymphoma. There appears to be a close association between the majority (95%) of African B-cell lymphomas and Epstein Barr virus (EBV) (ie. genome in tumour) and to a lesser extent in European cases (20% have genome inclusion). High titres to EBV are found in many B cell leukaemias as well as lymphomas (even those which are genome negative), but the exact role of the virus is as yet unclear. Both B cell leukaemia and lymphoma are associated with characteristic chromosomal translocations which involve the c-myc oncogene, although the break points are variable (Henderson *et al*, 1991). A number of co-factors with EBV have been implicated as contributory at least in B cell lymphomas, including phorbol esters from plants, chronic malaria, malnutrition and chronic immunosuppression (Aya *et al*, 1991).

2.12 T-cell ALL accounts for 10-15% of childhood cases and has a very distinctive clinical pattern and a number of consistent chromosomal rearrangements, all involving T-cell receptor loci, with a peak incidence in males during adolescence. Infants (those less than 1 year old) with leukaemia (ALL) have consistent abnormalities involving the MLL-1 gene on chromosome 11 (q23) (Greaves, 1993).

2.13 Table 2.1 below demonstrates the way in which increasingly sophisticated markers have demonstrated the heterogeneity of ALL. Table 2.1a shows similar data for acute myeloblastic leukaemia (AML, otherwise known as acute non-lymphoblastic leukaemia or ANLL) (Grier and Weinstein, 1993). Non-lymphoblastic leukaemia is usually diagnosed on morphological grounds with the clinical features and cell surface markers not appearing to be especially helpful in distinguishing the sub-types. Increasingly, as for ALL, non-random and consistent rearrangements are being defined in the non-lymphoblastic leukaemias, although the rarity of the diseased sub-groups has not yet enabled clear cut differences in epidemiological features to be defined.

Table 2.1 ACUTE LYMPHOBLASTIC LEUKAEMIA: DIAGNOSTIC CRITERIA

DIAGNOSIS AND APPROX DIAGNOSTIC FREQUENCY (in % as seen in MRC UKALL XI Trial 1990-1995)	CLINICAL FEATURES					EARLY MARKERS		MONOCLONAL ANTIBODY SCREEN (C.D.)					INTRA CELLULAR		REARRANGEMENTS			SPECIFIC CYTOGENETIC EXAMPLES	
	Sex M:F	Median Age of Onset Years	White Blood Count	Organ Enlarged	French American British	Sheep Red Cell Rosettes E+	Surface Ig+	Class 7 10 11 19 20 13/33					Cytoplasmic Ig	Tdt	Ig Heavy %	Ig Light %	T Cell Receptor Gene %		
T	10%	12:1	10-14	Usually High	+++	Often L2	+	+	±	-	-	-	-	+	10-15	≥80	80	*14q 11-q13 7q 32-36 7q 15	
Common	57%	1.2:1	3-6	Variable	±	L1 or L2		+	+	±	-	+	-	+	100	40	20	Most show no consistent structural changes. Numbers vary.	
preB	10%	?1:1	5	Variable	±	L1 or L2	-	-	-	+	+	±	+	+	100	40	20	t (1, 19)	
B	2-3%	♂>♀	Variable	Usually High	++	L3		+	-	+	+	-	+	-	(+)	Very low	Very low	t (8, 14) t (2, 8) t (8, 22)	
Null (N.B. Hetero-Group)	2%	?	Common <Y	Usually High	+	L1 or L2 or Monocytoid	-	-	-	+	-	±	+	-	±	<70 in infants	<1	<1	t (4, 11) t (11, 19)
Mixed Lineage Ph+	?	?	Older	< 30	±	Variable	±	±	+	+	±	±	+	±	+	?	?	?	t (9, 22)
Ph	?	?	Variable	High	±	L1 or Undiff	-	-	+	-	-	±	-	+	?	?	?	?	Variable

Note: Frequency of positive results - the remainder of cases are unclassifiable (2%), of unusual lineage (2%) or had failed investigation (3%).

Table 2.1a ACUTE MYELOBLASTIC LEUKAEMIA: DIAGNOSTIC CRITERIA

DIAGNOSIS AND DIAGNOSTIC FREQUENCY IN % IN THE AML 10 STUDY	CLINICAL FEATURES			MONOCLONAL ANTIBODY SCREEN (CD)	INTRA CELLULAR Cytoplasmic	SPECIFIC CYTOGENETIC EXAMPLES
	TYPE	DIAGNOSTIC FEATURES	MORPHOLOGY			
M1	19%	AML	Common 1 Year	Blasts >90% Few Granulocytes	- (+) - - - + -	*** - 5-10 +
M2	31%	AML	Morphological distinction	Blasts >30% and some Maturation	- (+) - - - + -	Rarely - +
M3	7%	APL	Morphological distinction	Hypergranulated promyelocytes	- - - - ± ±	t (15 17) (40%)
M4	18%	AMML	Morphological distinction	Granulocytic + Monocytic Differentiation	- - - - + ±	Inv 16
M5	14%	AMOL	Usually high WBC and more extra medullary disease	Monoblast ± Monocytes	- - - - + +	
M6	3%	AEL	Often has a preceding pre leukaemic phase	>50% Erythroid Precursors	- - - - -	Many + Bizarre Chromosomes
M7	5%	Megakaryocytic	Morphological distinction	Megakaryocytic	- - - - -	

Note: A small percentage of cases are unclassifiable

2.14 The progressive use of more complex typing of leukaemia in general and childhood leukaemia in particular has led to a greater realisation that both of the disease groups - ALL and AML - show remarkable heterogeneity but that within certain sub-types there are consistent features. When considering the aetiology of any particular leukaemia these should be borne in mind.

Areas to be analysed

2.15 The areas used throughout the study (see map, Figure 2.1) were as follows:

- a. Seascale ward
- b. Allerdale and Copeland county districts excluding Seascale ward - these are the two county districts nearest to Sellafield;
- c. Cumbria county excluding Allerdale and Copeland.

These areas represent the areas of concern (Seascale) together with the surrounding local area of a sufficient size to give a reasonable comparison.

All boundaries are those which came into force with the local government reorganisation of 1974. Cases were assigned to areas according to their residential address at diagnosis as defined for the National Cancer Registration Scheme (Swerdlow, 1986).

Calendar periods

2.16 Data are presented for 1963-83 and for 1984-92 (0-24 years) for Seascale. The latter period does not overlap with any of the analyses covered in the Black report. For Allerdale, Copeland and the rest of Cumbria the period 1963-92 has been used for the analysis of childhood (ages 0-14) cancer rates in this report because the data for Cumbria are believed to be almost complete for this period; for ages 15-24 the period 1969-92 has been used and for the ages 25-74 the period 1984-92 has been used, for the same reason.

Case ascertainment for the study area

2.17 For the analyses of childhood cancers, that is those diagnosed at ages 0-14 years, the data have been taken from the National Registry of Childhood Tumours (NRCT) at the Childhood Cancer Research Group (Stiller *et al*, 1991). Cases in the NRCT are ascertained from cancer registries, the Northern Region Children's Malignant Disease Registry (NRCMDR) (from 1968 when this register began), the Manchester Children's Tumour Registry (for cases occurring before 1974 in the area now called South Cumbria) (Craft *et al*, 1987), death certificates, entries to the Medical Research Council leukaemia trials (1970 onwards) and the register of the United Kingdom Children's Cancer Study Group (1977 onwards). Details of the methods of ascertainment of cases and verification of diagnostic and other information have been published (Stiller *et al*, 1991). For the study areas defined above there is a high degree of completeness of ascertainment from 1968 onwards for children aged 0-14, because these areas are included in the prospectively collected NRCMDR and all these cases are included in the NRCT.

2.18 The analyses for the age-group 15-24 are based mainly on data from the NRCMDR. This originally covered only the age-group 0-14 but was extended as a result of the Black Advisory Group recommendations to ages 15-24. For 1969-83 cases in the NRCMDR at ages 15-24 were obtained retrospectively from the Northern Region Cancer Registry and the North Western Regional Cancer Registry (for 1969-73 in what is now South Cumbria). Ascertainment through such regional cancer registries may not be complete (Birch, 1988), and so for this study a special search of hospital and pathology department records was made to ascertain any cases of leukaemia/lymphoma in Allerdale and Copeland for the period 1969-83 that might not previously have been registered. This resulted in

From 1984 onwards cases in the NRCMDR have been ascertained directly from hospitals throughout the Northern Region. Cumbria has been included in the Leukaemia Research Fund Data Collection Study (DCS) (Cartwright *et al*, 1990) since it began in 1984. The DCS also ascertains cases of leukaemia and lymphoma directly from diagnostic sources within hospitals in its study areas and these are cross-checked with cancer registration records; ascertainment for these diagnostic groups is believed to be virtually complete. For the period 1984-92 a comparison between the NRCMDR and the DCS found no additional cases for Allerdale and Copeland but for the rest of Cumbria seven were added to the NRCMDR.

2.19 Among persons aged 25-74, the only analyses in the present paper are of leukaemia and lymphoma for 1984-92, using data derived from the DCS. These data were included to investigate whether there were excesses of cancer in adults in the area as well as 0-24 year olds.

Population data

2.20 For the calculation of incidence rates population estimates were required for five-year age groups for each of the years 1963-92. Census data and OPCS estimates were used wherever these were available. For Seascale in 1986 estimates from CACI Ltd were used. For other years, estimates were made by linear interpolation, a proportionate adjustment being made if the total of the estimates so obtained for individual age groups did not agree with the independent OPCS estimate for all ages taken together.

2.21 The results for broad age groups at five-year calendar intervals are summarised in Table 2.2 below:

Table 2.2 SUMMARY OF POPULATION ESTIMATES FOR AREAS WITHIN CUMBRIA

Age Groups	Year	0-14	15-24	25-74
Seascale ward	1961*	606	176	-
	1966+	604	218	-
	1971*	602	259	-
	1976+	506	299	-
	1981*	411	339	-
	1986***	320	291	1126
	1990+	302	234	1129
Copeland & Allerdale county districts excluding Seascale ward	1961*	41990	21852	-
	1966+	41718	23215	-
	1971**	39898	23441	-
	1976**	37694	24101	-
	1981**	34224	25719	-
	1986**	30885	25514	98988
	1990**	30717	22836	102614
Rest of Cumbria	1961*	67854	37794	-
	1966+	69227	39683	-
	1971**	70400	42400	-
	1976**	69200	42400	-
	1981**	61049	46624	-
	1986**	56721	49464	189621
	1990**	55926	44855	196978

* Census ** OPCS *** CACI + INTERPOLATED

Incidence Rates

2.22 Incidence rates are expressed in this chapter as annual rates per million population. For ages 0-14 and 15-24, age standardised rates (ASRs) have been calculated as simple averages of the age-specific incidence rates for the five-year age groups they contain.

Comparisons with national data

2.23 The incidence rates in the study areas have been compared with national data using the following sources: for childhood cancer, NRCT data for 1969-90 for which years we believe the NRCT to be virtually complete; for young persons aged 15-24, cancer registration statistics for England and Wales for 1971-88, national cancer registration data being acceptably complete for these years (though these data have not been subjected to the review processes carried out for the specialist registries); for leukaemias and lymphomas at ages 25-74, data from the DCS 1984-92, covering about one third of the population of England and Wales (Cartwright *et al*, 1990). Age-standardised annual cancer incidence rates for England and Wales calculated as described in the paragraph 2.22 are given in Table 2.3.

Table 2.3 AGE-STANDARDISED ANNUAL CANCER INCIDENCE RATES PER MILLION, ENGLAND AND WALES

	Age 0-14 (1)		Age 15-24 (2)	
	1969-83	1984-90	1971-83	1984-88
Lymphoid Leukaemia and NHL	35.6 (5732)	38.4 (2559)	18.8 (1790)	21.5 (863)
Other Leukaemia	8.5 (1380)	7.9 (528)	11.1 (1054)	9.4 (379)
Hodgkin's Disease	4.5 (762)	5.0 (329)	33.5 (3166)	32.2 (1301)
Brain (inc benign)	25.8 (4214)	27.2 (1808)	27.7 (2596)	26.2 (1055)
Other Malignancies	35.6 (5710)	42.3 (2835)	93.1 (8780)	99.4 (4044)
All registrations	110.0 (17798)	120.8 (8059)	183.8 (17386)	188.6 (7642)
Source (1) National Registry of Childhood Tumours (2) Cancer Registration statistics for England and Wales () = number of cases on which rates are based				

Age standardised rates calculated for populations with equal numbers in each five-year age-group for the age-range shown.

2.24 In analysing the sets of rates presented in this report, some idea of the precision of any rate can be obtained by regarding the number of cases observed as a Poisson variable and approximating the standard error of a rate R based on M cases by R/\sqrt{M} . This formula is reasonably accurate where the age distribution of the population considered is similar to that of the population used as a basis for standardising the rates. For values of M larger than 20, confidence limits for R based on the normal distribution can then be constructed.

DATA GATHERED FOR ANALYSIS

Cases of cancer in young people aged 0-24 years in Seascale since 1953

2.25 A list of all the cases of cancer in persons aged 0-24 in Seascale known to have been diagnosed during 1953-95 is given in Table 2.4. As far as possible the information for the cases listed in Tables 2.2 to 2.5 of the Black report has been checked; cross-references are given to cases listed in those tables and where necessary the information has been corrected.

Table 2.4 CANCER AMONG PERSONS AGED 0-24 AND RESIDENT IN SEASCALE AT DIAGNOSIS, 1953 - 1995

Case	Year of Birth	Year of Diagnosis	Age	Sex	Diagnosis	Included in present analysis	Ref number in Black Report
A	1947	1954	6	M	Neuroblastoma	No	22
B	1952	1955	2	F	NHL	No	14
C	1947	1955	7	F	ALL	No	1
D	1957	1960	2	M	AML	No	3
E	1957	1968	11	M	ALL	Yes	2
F	1964	1968	4	M	ALL	Yes	5
G	1968	1971	2	F	ALL	Yes	6
H	1960	1975	15	F	Rhabdomyosarcoma*	Yes	26
I**	1958	1978	19	M	CML	No	4
J	1974	1979	5	F	ALL	Yes	7
K	1974	1983	9	M	NHL	Yes	16
L	1982	1984	1	F	NHL	Yes	17
M	1966	1985	18	M	Pinealoma	Yes	--
N	1965	1988	23	F	NHL	Yes	--
O	1970	1988	17	F	Hodgkin's Disease	Yes	--
P	1975	1991	16	M	ALL	Yes	--
Q	1988	1995	6	F	Ganglio-neuroblastoma	No	--

* Previously described as retroperitoneal sarcoma.

** This patient also had an address in another region of England at which he was resident at the time of diagnosis, and he is therefore excluded from all the analyses (see Paragraph 2.26).

ALL - Acute lymphoblastic leukaemia. AML - Acute myeloid leukaemia.

CML - Chronic myeloid leukaemia. NHL - Non-Hodgkin lymphoma.

2.26 Eleven cases diagnosed during 1963-92 (cases E-H and J-P) are included in the present analyses. One from the most recent period, 1984-92, (case L in Table 2.4) is included in the Black report, but with the year of diagnosis given wrongly as 1983 instead of 1984. This case was notified to the Black advisory group during the course of their investigation but does not appear in any of the analyses in their report. This case is included in the present analysis for the post-Black period 1984-92 and is regarded as part of the group used in testing rather than generating the hypothesis. Case I in Table 2.4 had a second address in another part of Britain, to which the case should correctly be allocated under the rules followed by the National Cancer Registration Scheme; this person has therefore been excluded from the analyses. Four other cases (A-D) in Table 2.4 (diagnosed 1954-1960) are excluded from the analyses for the present report because they occurred before complete registration data were available and any analysis of incidence rates for this early period would be unreliable. Case P, diagnosed in 1991, is the only Seascale case included in the present analysis that is not included in the analysis performed by Draper *et al* (1993). Case Q was notified in 1995 after the analysis for this report was completed.

Incidence rate at ages 0-14, 1963-92

2.27 Table 2.5 shows the numbers of cases of cancer together with the age standardised incidence rates (ASRs) for ages 0-14 for each diagnostic group in the three study areas during 1963-83 and 1984-92. The rates of malignant disease and, specifically, of lymphoid leukaemia/NHL for children in Seascale are substantially higher than those for the remainder of Copeland/Allerdale, Cumbria or England and Wales. In Allerdale and Copeland (excluding Seascale) the rates for lymphoid leukaemia/NHL are similar to or lower than those for other parts of Cumbria and for England and Wales. In the remainder of Cumbria the rates are similar to those for England and Wales in the period 1969-83, and slightly higher in the period 1984-92.

Table 2.5: Age standardised annual incidence of specific cancers per million children aged 0-14 in specified areas of Cumbria

	Seascale Ward		Allerdale and Copeland minus Seascale Ward		Rest of Cumbria		England and Wales	
Years	Age Standardised No.	Age Standardised Rate	Age Standardised No.	Age Standardised Rate	Age Standardised No.	Age Standardised Rate	Year	Age Standardised Rate
Lymphoid leukaemia and non-Hodgkin lymphomas								
1963-83	5	459.1	19	24.2	50	35.9	1969-83	35.6
1984-92	1	389.4	10	35.9	34	67.0	1984-90	38.4
1963-92	6	449.2	29	27.3	84	44.3	1969-90	36.5
Other Leukaemias								
1963-83	0	0.0	7	8.7	11	7.8	1969-83	8.5
1984-92	0	0.0	3	10.7	4	7.8	1984-90	7.9
1963-92	0	0.0	10	9.3	15	7.8	1969-90	8.3
Hodgkins's disease								
1963-83	0	0.0	0	0.0	4	2.7	1969-83	4.5
1984-92	0	0.0	1	3.5	4	7.6	1984-90	5.0
1963-92	0	0.0	1	0.9	8	4.0	1969-90	4.7
Brain Tumours (including benign)								
1963-83	0	0.0	21	26.2	45	31.8	1969-83	25.8
1984-92	0	0.0	6	21.6	8	15.7	1984-90	27.2
1963-92	0	0.0	27	25.0	53	27.6	1969-90	26.2
Other malignant tumours								
1963-83	0	0.0	31	39.3	43	30.8	1969-83	35.6
1984-92	0	0.0	17	60.9	17	33.5	1984-90	42.3
1963-92	0	0.0	48	44.9	60	31.7	1969-90	37.7
All registrations								
1963-83	5	459.1	78	98.4	153	109.0	1969-83	110.0
1984-92	1	389.4	37	132.6	67	131.7	1984-90	120.8
1963-92	6	449.2	115	107.4	220	115.3	1969-90	113.4

2.28 Thus there is no overall evidence over the period from 1963 onwards that the excess found in Seascale extends to a wider area around Sellafield though for the most recent period there is a slight non-significant increase in the incidence of lymphoid leukaemia/NHL in the ‘rest of Cumbria’. The age standardised rate in the rest of Cumbria is 67.0 per million per year, with 95% confidence limits 44.5 to 89.5, as compared with a national rate of 38.4 per million per year. Since this excess is found only in the period 1984-92 and not in Allerdale/Copeland, we regard it as a chance finding.

Incidence rates at ages 15-24 years, 1969-92

2.29 Results for ages 15-24 during the period 1969-92 are given in Table 2.6. In Seascale there were 5 cases of “all cancers”, which represents a considerable increase over the national rates whether one considers lymphoid leukaemia/NHL or all malignant disease for the period 1969-92. In the period 1984-92 (the period subsequent to the Black report) there were 4 cancer cases in this age range in Seascale; one ALL, one NHL, one Hodgkin’s disease, and one pineal tumour. In the remainder of Copeland and Allerdale and in the rest of Cumbria the rates are unremarkable, except that for all registrations, rates for the rest of Cumbria are slightly lower than those for England and Wales (rate for rest of Cumbria 1969-92 = 142.5 (95% confidence interval 119.8-165.2); rate for England and Wales 1971-88 = 185.1).

Table 2.6: Age standardised annual incidence of specific cancers per million people aged 15-24 in specified areas of Cumbria

Years	Seascale ¹ Ward		Allerdale and Copeland minus Seascale Ward		Rest of Cumbria		England and Wales	
	No	Age Standardised Rate	No	Age Standardised Rate	No	Age Standardised Rate	Year	Age Standardised Rate
Lymphoid leukaemia and non-Hodgkin lymphomas								
1969-83	0	0.0	12	32.4	8	13.0	1971-83	18.8
1984-92	2	850.7	5	22.9	3	7.1	1984-88	21.5
1969-92	2	304.4	17	29.1	11	10.5	1971-88	19.6
Other Leukaemias								
1969-83	0	0.0	4	11.0	5	7.6	1971-83	11.1
1984-92	0	0.0	2	9.3	4	9.5	1984-88	9.4
1969-92	0	0.0	6	10.3	9	8.4	1971-88	10.6
Hodgkin’s Disease								
1969-83	0	0.0	16	44.1	19	31.1	1971-83	33.5
1984-92	1	400.6	12	55.2	17	40.5	1984-88	32.2
1969-92	1	124.8	28	48.2	36	34.3	1971-88	33.1
Brain Tumours (including benign)								
1969-83	0	0.0	8	21.7	12	18.4	1971-83	27.7
1984-92	1	400.6	7	32.6	7	16.7	1984-88	26.2
1969-92	1	124.8	15	25.7	19	17.8	1971-88	27.3
Other malignant tumours								
1969-83	1	181.2	24	65.8	48	74.6	1971-83	93.1
1984-92	0	0.0	15	68.8	28	66.6	1984-88	99.4
1969-92	1	124.8	39	67.1	76	71.5	1971-88	94.9
All registrations								
1969-83	1	181.2	64	174.9	92	144.6	1971-83	183.8
1984-92	4	1652.0	41	188.8	59	140.4	1984-88	188.6
1969-92	5	678.7	105	180.5	151	142.5	1971-88	185.1

¹For Seascale ward (although not for Allerdale and Copeland or the rest of Cumbria) registration data for the period 1963-68 are thought to be reasonably complete. No cases in the age group 15-24 occurred (see Table 2.3).

**Incidence at ages 25-74
(leukaemia and
lymphoma only),
1984-92**

2.30 Table 2.7 shows the numbers of cases of leukaemia and lymphomas for ten-year age groups in the age range 25-74, together with overall incidence rates, in the three study areas during 1984-92. In Seascale there were two cases of NHL, both occurring at ages 55-64. On the basis of the national DCS rates one case would be expected. The excess incidence of leukaemia and NHL found among young people does not extend to the older age groups.

Table 2.7: Age specific annual incidence of leukaemia and lymphomas per million people aged 25-74 in specified areas of Cumbria, 1984-92

	Age (years)											
	25-34		35-44		45-54		55-64		65-74		Total* 25-74	
	No	Rate	No	Rate	No	Rate	No	Rate	No	Rate	No	Rate
	Seascale ward											
Lymphoid leukaemia and non-Hodgkin's lymphoma	0	0.0	0	0.0	0	0.0	2	922.5	0	0.0	2	196.2
Other leukaemias	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Hodgkin's disease	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	Allerdale and Copeland minus Seascale ward											
Lymphoid leukaemia and non-Hodgkin's lymphoma	7	31.9	5	24.1	19	108.7	30	179.0	53	391.0	114	125.9
Other leukaemias	1	4.6	3	14.4	6	34.3	17	101.4	23	169.7	50	55.2
Hodgkin's disease	4	18.2	4	19.2	2	11.4	2	11.9	6	44.3	18	19.9
	Rest of Cumbria											
Lymphoid leukaemia and non-Hodgkin's lymphoma	7	17.3	25	64.3	38	114.6	83	253.3	127	450.6	280	161.5
Other leukaemias	6	14.9	10	25.7	11	33.2	16	48.8	43	152.6	86	49.6
Hodgkin's disease	9	22.3	12	30.9	6	18.1	13	39.7	7	24.8	47	27.1

* The 'total' rate over the whole range 25-74 is not standardised.

DISCUSSION

Statistical significance of rates of malignant disease in Seascale at ages 0-24, 1963-83 and 1984-92

2.31 In tables 2.5 and 2.6 the rates for Seascale are clearly based on very small numbers of diagnosed patients. The method that we have used to carry out a formal test of the hypothesis that there is no raised incidence of cancer among young persons aged 0-24 is the same as that in the Black report and is based on a comparison with the national rates for England and Wales summarised in Table 2.3. Expected numbers of cases in Seascale during the periods 1963-83 and 1984-92 in the age range 0-24 years are calculated on the assumption that the true age specific rates are the same as those for England and Wales. In Table 2.8 the observed numbers of cases at ages 0-24 are compared with those expected for lymphoid leukaemia/NHL, for all other cancers and for all cancers combined, separately for 1963-83 and 1984-92.

Table 2.8: OBSERVED AND EXPECTED NUMBERS OF CASES OF CANCER AT AGE 0-24 IN SEASCALE 1963-92 AND POISSON PROBABILITY OF OBSERVED OR GREATER NUMBER OF CASES. EXPECTED NUMBERS ARE CALCULATED ON THE BASIS OF INCIDENCE RATES FOR ENGLAND AND WALES (TABLE 2.2)

Year	Lymphoid Leukaemia & NHL	Other Cancers	All Malignancies
1963-83			
No. of cases	5	1	6
Expected	0.49	1.69	2.18
Probability that at least the observed number of cases would occur if national rates were to apply	0.000160	0.815	0.0240
1984-92			
No. of cases	3	2	5
Expected	0.16	0.62	0.78
Probability that at least the observed number of cases would occur if national rates were to apply	0.000572	0.129	0.00124

2.32 In 1963-83 a total of six cases, of which five were lymphoid leukaemia/NHL, occurred. The expected number of cases of lymphoid leukaemia/NHL on the basis of national rates is 0.49 (O/E = 10.16); the expected number for all malignant disease is 2.18 (O/E = 2.75). The probabilities of values as high as this or higher occurring by chance, if the true age-specific rates in the Seascale area were the same as those for England and Wales, are respectively $p=0.00016$ and $p=0.024$. These probabilities are low and accordingly support the findings of the Black report. In interpreting the findings it must be remembered that the hypothesis to be tested was not determined *a priori* but was formulated, at least partly, after the results had been obtained. That is to say that to some extent the process was a circular one of selecting a result which appeared remarkable from a large and unspecified number of possible results and then using a statistical test that could not take into account the selection procedure to judge whether it was in fact remarkable.

2.33 This difficulty of interpretation does not extend to analyses of subsequent periods (ie from 1984 onwards). Table 2.8 contains the data for cancer occurring among young persons in Seascale during 1984-92, when a total of five cases occurred in the age group 0-24, three of these being leukaemia/NHL. The expected number of cases of lymphoid leukaemia/NHL in this period and age group is 0.16 (O/E = 19.1); for all diagnostic categories taken together, the expected number is 0.78 (O/E = 6.4). Whether we consider just the three cases of lymphoid leukaemia/NHL, or the total of five cases, there is a significant ($p=0.0006$, and $p=0.0012$, respectively) excess of cases in Seascale in the period 1984-92. For 'Other cancers' the expected number of cases is 0.62 (O/E = 3.2, p -value = 0.129). This excess is not statistically significant. Although the O/E values are higher in 1984-1992 than in 1963-1983 both for 'lymphoid leukaemia/NHL' and for 'all malignancies', this difference is not statistically significant for either group. As explained in paragraph 2.26, one additional case (a six year old child with ganglioneuroblastoma) was diagnosed in 1995 and is excluded from our analyses. It is not, in fact, possible with conventional methods of analysis to assess the statistical significance of this observation but, taken together with the results for 1984-92, it suggests the possibility that the Seascale excess may not be confined to leukaemia/lymphoma; on the other hand there is no evidence for such an excess for the period before 1984.

Studies around nuclear sites in general with relevance to the Sellafield situation.

2.34 We have reviewed the current information that is available on studies around nuclear sites in general and we have noted that studies using either incidence or mortality (Cook-Mozaffari *et al*, 1987, 1989a and Forman *et al*, 1987) data have shown a significant excess from leukaemia in young people aged 0-24 in county districts with more than 0.1% of the population near to nuclear installations, compared with remaining areas. There was a statistically significant excess around Sellafield and around the grouped pre-1955 sites (Springfield, Capenhurst, Amersham, Aldermaston, Harwell and Sellafield). The combined nuclear power stations showed an excess of leukaemia mortality but this excess was not statistically significant. Studies of cancer around nuclear facilities have also been carried out in France, the United States, Canada, Germany and Sweden. Most of these analyses have found either negative results or small excesses which could be attributable to chance. Goldsmith (1989) found an excess of childhood (0-9 years) mortality in four counties near two major US nuclear facilities (Hanford and Oak Ridge), though this might have been due, at least in part, to underestimation of the population at risk. Viel *et al*, (1995) found an excess of childhood leukaemia in the immediate vicinity of the French nuclear reprocessing plant at La Hague, though this was based on only four cases.

2.35 Leukaemia mortality rates in areas which had been considered as potential sites for nuclear power stations, but where no actual building took place, were also studied (Cook-Mozaffari *et al*, 1989b) and compared to the rates found around nuclear power stations and it was found that the rates in both types of area were raised to similar degrees. This finding raises the possibility that some aspect of the type of area in which nuclear installations are built, is associated with a raised incidence of leukaemia in young people.

2.36 A study by Bithell *et al*, (1994) using incidence data, examined the relationship between the risk of childhood leukaemia and NHL and proximity of residence to 23 nuclear installations in England and Wales. In this study the numbers of cases were compared with expected numbers using standard methods and also a new method designed to detect a relationship between the magnitude of the risk and the distance from an installation. Six control sites were chosen because they were areas which had been considered as suitable for building nuclear generating stations, although so far unused. The results of this study show that there is no evidence of an increase in incidence of childhood leukaemia and NHL within 25 km of nuclear sites generally in England and Wales, nor is there evidence for a general effect of proximity to nuclear sites. The only significant results were for Sellafield, Burghfield and one of the control sites. The Sellafield result was attributable to the recognised excess at Seascale. The authors considered it unlikely that the excess at Burghfield was due to environmental radiation or paternal exposure.

2.37 A very similar study to that described in paragraph 2.36, examining the relationship between the risk of childhood leukaemia and lymphoma and the proximity of residence to the 7 nuclear installations in Scotland has been also been carried out at the request of COMARE (Sharp *et al*, in press). This study also compared the observed and expected numbers of cases and the trend of risk with increasing distance from the sites. The results confirmed the known excess of cases around the Dounreay nuclear site but failed to demonstrate any generalised raised incidence of childhood leukaemia and NHL near nuclear sites in Scotland.

National Geographical Distribution

2.38 Any search for clusters of disease of any sort is likely to reveal some spatial aggregations of cases which are simply due to chance. This is particularly true if the age groups, areas, calendar periods and diagnostic groups to be studied are not specified in advance. When a cluster at Seascale was first identified it seemed plausible that chance was a possible explanation. However, similar findings around Dounreay and, on a lesser scale around Aldermaston and Burghfield, have weakened this suggestion. The current report, having defined diagnostic groups, time periods, area and age groups in advance and tested the hypothesis for the post-Black period *a priori*, further reduces the likelihood that the findings are due to chance.

2.39 Recommendation 4 of COMARE's third report pointed out that studies of the geographical distributions of childhood cancer incidence on a nationwide basis were needed to enable the patterns around nuclear installations to be seen in the context of patterns of the rest of the UK. Two studies of the general distribution of childhood leukaemias and other cancers have been carried out in response to this recommendation.

2.40 A series of analyses was carried out as part of a collaborative study on data for childhood leukaemia and NHL in Britain during the period 1966-83 using postcoded data from the National Registry Childhood Tumours (Draper, 1991).

2.41 One group of analyses was to identify possible variations in incidence rates and the extent to which such variations could be explained by factors known to vary geographically - for instance the socioeconomic status of an area and whether it was urban or rural. Many of these analyses relate to lymphocytic and unspecified leukaemia (LUL) - virtually equivalent, for children, to ALL. Significant differences in rates for LUL were found between Regional Health Authority areas, and, for some sub-groups, between counties. For county districts and census tracts incidence rates for LUL were found to be higher in areas of higher socioeconomic status.

2.42 A second group of analyses was carried out to determine whether there was any evidence for a general tendency for clustering to occur. Some positive findings emerged though no attempts were made to identify individual cluster locations.

2.43 These analyses did not suggest that the findings at Seascale could be accounted for by the high socioeconomic status recorded in census data for Seascale, because the increase in risk found in such studies is much lower than the increased incidence of leukaemia and NHL actually found in Seascale, though the measures of social status are not directly comparable. Similarly, analyses of clustering do not suggest that the Seascale findings are simply part of some widespread phenomenon.

2.44 The results of a study by Craft *et al*, (1993) in response to Black recommendation 4 also provide information about geographical distributions. In this paper they calculated childhood cancer incidence rates for ages 0-24 in every census ward in the North of England in the period 1968-85, ranking the wards according to the probability of that incidence, or a greater value, occurring by chance and thus identified wards which were "extreme".

2.45 The authors noted an excess of leukaemia/lymphoma in numerous wards throughout the North and North West of England. In such an analysis it is inevitable that some areas will have an excess of cases and some a deficiency. A significant excess of cases was found in Egremont North, one of a number of wards in the area containing an appreciable number of BNFL Sellafield workers. The fathers of these children did not, however, have any recorded dose of preconception exposure to external irradiation (Wakeford and Parker, In Press); moreover the excess in Egremont North is less marked if a longer period than that analysed by the authors, is considered (1968-85). Data for the age-group 0-14 are available for the period 1962 - 1967 and data for the full 0-24 age group are available from 1986 onwards. Examination of both these sets of data identified only one additional case. Craft *et al* concluded that Seascale ward was the highest ranked in the North of England for ALL or ALL/NHL for the period 1968-85 and that the incidence of these conditions was indeed high when set in the context of rates and geographical variation in Northern England generally. Since their data did not go beyond 1985 the Seascale rates are based on much the same data as those available to the Black Advisory Group.

2.46 We conclude from these wider geographical studies that when Seascale is examined in the context of the national distribution of ALL/NHL, the pattern of these diseases in Seascale village is confirmed to be highly unusual.

CONCLUSIONS

2.47 Two principal questions have been considered in this chapter. First, do the findings of the Black report relating to the period up to and including 1983 remain unchanged now that more comprehensive data sets and analyses are available? Secondly, did the excess incidence of childhood leukaemia in Seascale found in the various analyses summarised in the Black report persist in later years? This chapter deals with the periods 1963-92 for children aged 0-14, 1969-92 for the 15-24 age group, and 1984-92 for leukaemia and lymphomas in adults. As explained earlier, the diagnostic groups, age groups, calendar periods and areas to be analysed were agreed in advance of the analyses being carried out.

2.48 Our conclusions are consistent with those of the Black report insofar as they relate to malignant disease occurring in young people between 1963 and 1983; on the basis of the six cases included in Table 2.4 we conclude that the excess in Seascale is highly unlikely to have arisen by chance (Table 2.8). All of the six cases are included in the report by Craft *et al.*, (1993). As explained above, case I in Table 2.4 has been omitted from the present analyses, since this person had an address in another part of Britain which was regarded as his area of residence for the purposes of the National Cancer Registration Scheme (Swerdlow, 1986). Inclusion of this case would have increased the excess number of cases in the period 1963-83.

2.49 For the period before 1984 the analyses rely on much the same evidence as the Black report, though more complete registration data are now available. There is, however, no way of overcoming the difficulty of interpretation of analyses of Seascale data for this period that arises from the fact that the area, age-group and types of disease to be studied were selected as a result of the observed 'cluster'.

2.50 This difficulty does not affect the results for 1984-92. Even the case from this period that was mentioned in the Black report (with the year of diagnosis wrongly given as 1983 rather than 1984) was diagnosed after concern had been raised about the high incidence in Seascale. For the age group 0-24 there is an excess of malignant disease which is highly unlikely to have arisen by chance (Table 2.8). These more recent data, therefore, strengthen the suggestion that there is an increased incidence in Seascale for the age group 0-24 years. The original findings related mainly to lymphoid leukaemia at ages 0-14. Of the five cases found in the Seascale ward in the period 1984-92, one had leukaemia (ALL aged 16 years) two had NHL (ages 1 and 23 years), one had Hodgkin's disease (aged 17 years) and one a pineal tumour (aged 18 years). Since the publication of Draper *et al.*, (1993) case P of Table 2.4 has been identified strengthening the conclusion that there is an excess of lymphoid leukaemia/NHL at ages 0-24 in Seascale. As regards cancers other than leukaemia and NHL in this age group there is a small, non-significant excess during 1984-92. Inclusion of case Q would increase the excess of cancers other than leukaemia and NHL but we have not included this case in our analyses, since to do so would invalidate the statistical approach used here which is based on a prior decision to include only cases diagnosed between 1984 and 1992.

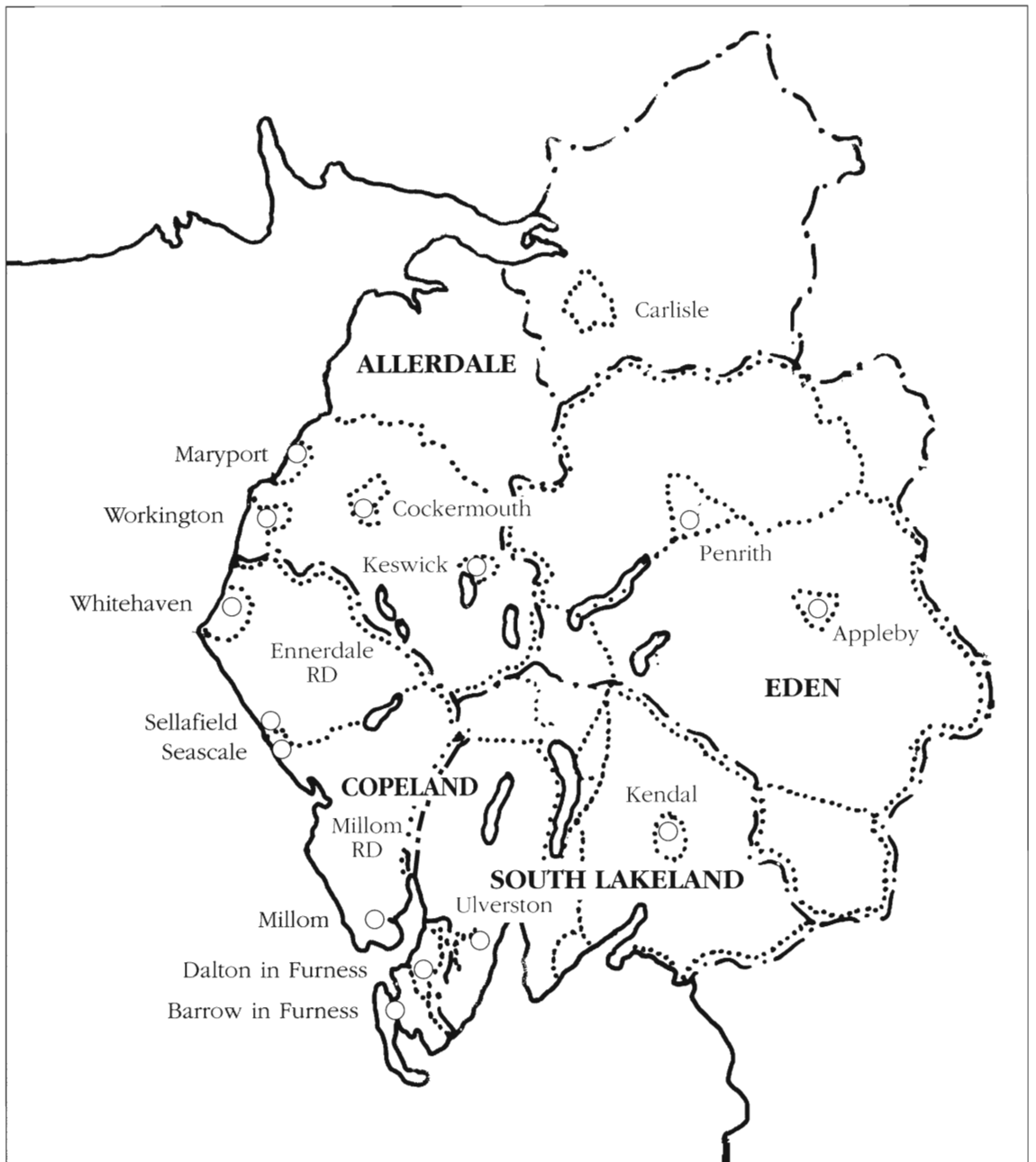
2.51 There is no evidence that the raised incidence at ages 0-24 in Seascale extends to those aged 25 and over in Seascale or to the two county districts nearest to Sellafield or to Cumbria generally.

2.52 National data of the same quality as those used for the present analyses are not always available. However, even if there were a 20% under-registration in national data, which is unlikely, this would not have affected the conclusions of

this report, the only material change in the probabilities given in Table 2.8 being that for all malignancies in the period 1963-83, which becomes non-significant ($p = 0.059$).

2.53 In conclusion, there is good evidence for a persistent excess in the incidence of lymphoid leukaemia/NHL among young people in Seascale for the period 1984-92. We conclude from the wider geographical studies that when Seascale is examined in the context of the national distribution of ALL/NHL, the pattern of these diseases in Seascale village is confirmed to be highly unusual. Possible causes for this significantly higher rate of leukaemia/NHL incidence covering three decades, are discussed in subsequent chapters.

Figure 2.1



County of Cumbria showing districts before (···) and after (- · - · -) its creation in 1974 (based on figure 2.3 of Black report')

CHAPTER 3

RADIATION EXPOSURE AND THE RISK OF RADIATION INDUCED LEUKAEMIA AND CANCER IN YOUNG PEOPLE LIVING IN SEASCALE

INTRODUCTION

3.1 Since the time of publication of the Black Advisory Group report (Black, 1984) a very large body of new scientific data has been produced which relates to the methods used to estimate radiation doses received by the general public from environmental exposures to radionuclides. The volume of data was so large that a number of joint COMARE/NRPB working groups were established to consider the detailed data that would need to be taken into account in a new assessment of doses and risks to the Seascale population. These working groups considered the data required for this exercise under the following broad category headings:

- i. Discharges and environmental monitoring data.
- ii. Modelling procedures.
- iii. Habit data.
- iv. Biokinetic data and fetal dosimetry.
- v. Risk data.

3.2 When the various factors had been considered, recommendations were made to the COMARE Sellafield Dosimetry subgroup, who in turn reported to the full Committee. When COMARE had agreed on the specifications to be considered, NRPB was asked to carry out a full re-assessment of the doses and risks to the population of Seascale from discharges from the Sellafield plant and other sources of environmental radiation, during the time of the site operation. This re-assessment is contained in NRPB Report R276 (Simmonds *et al*, 1995). In order to undertake this assessment, British Nuclear Fuels PLC (BNFL) was asked to provide NRPB with records, on an annual basis, of airborne and liquid radioactive discharges from Sellafield as well as records of the environmental monitoring data gathered from the programme agreed with the appropriate Authorising Departments (Her Majesty's Inspectorate of Pollution - HMIP and Ministry of Agriculture, Fisheries and Food - MAFF). Albright and Wilson Ltd of Whitehaven have discharged various naturally-occurring radionuclides during the time period under investigation. Doses from these discharges to the population of Seascale have also been considered in NRPB's reassessment. We are grateful to NRPB for undertaking this work for us and also to BNFL and Albright and Wilson for making their data available.

3.3 The NRPB assessment of the risks of leukaemia and other cancers to the population of Seascale in West Cumbria covers all sources of ionising radiation. The study also considered the population of Seascale born between 1945 and 1992, with their radiation doses and risks followed to age 24 or 1992 inclusive, whichever is sooner. This represents a longer period than the previous study carried out for COMARE (NRPB reports R171 and R171 Addendum, ie. Stather *et al*, 1984; Stather *et al*, 1986) which considered risks only up to the 20th birthday or the beginning of 1980. As previously, the aim was to estimate the average exposure to radiation of the population due to intakes of radionuclides

into the body and external radiation. The Chernobyl accident and discharges from Albright and Wilson, which had not been considered in previous assessments, have been included in the new study.

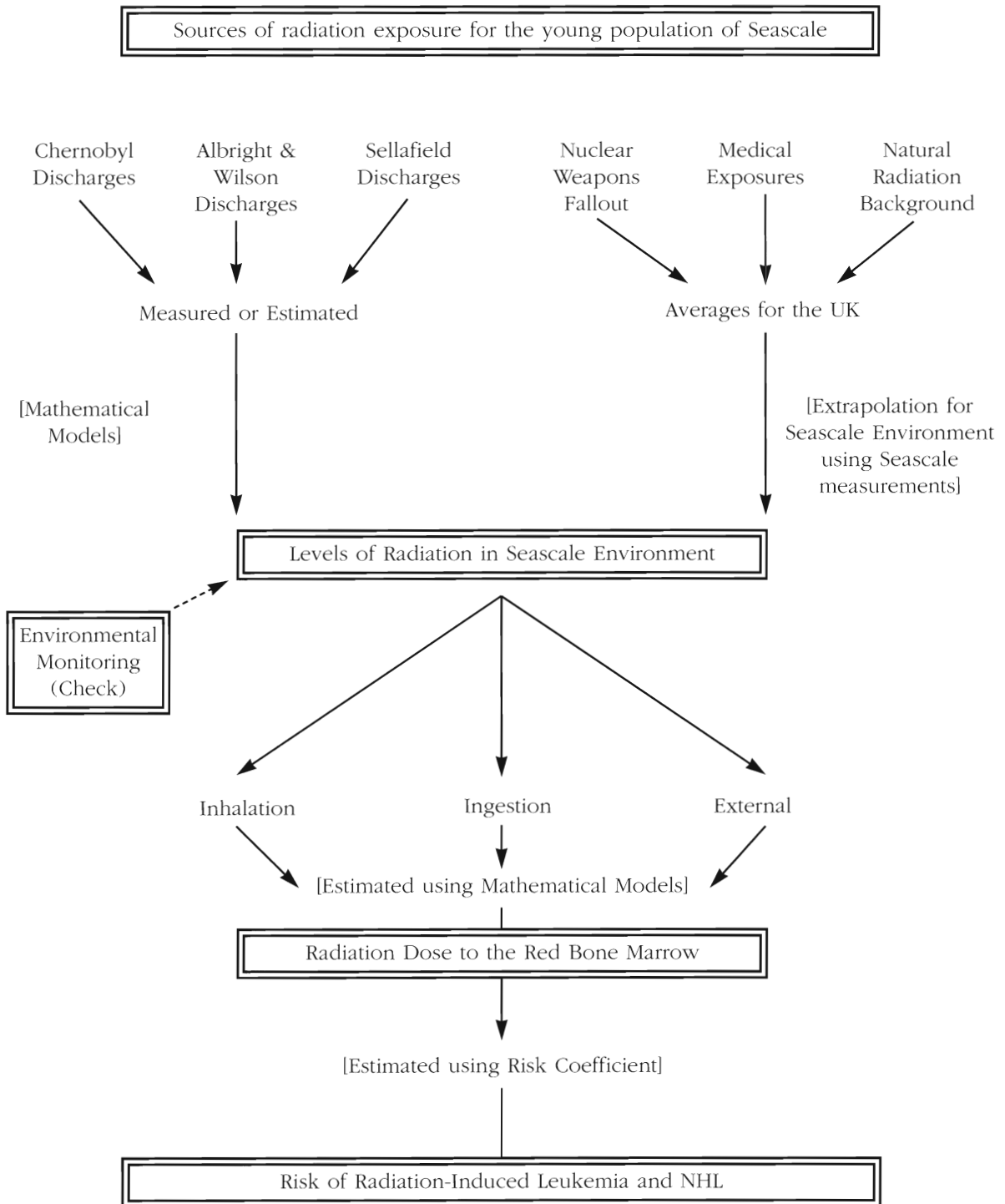
3.4 In assessing the risks to the Seascale population, the number of children born in each year was based on birth statistics for Seascale and so varied from year to year; this approach differs from previous assessments in which the same number of children were assumed to be born in each year.

3.5 Any assessment of the dose received by the local population and the consequent risk of cancer or leukaemia is a multistage process involving the following steps (shown diagrammatically in Figure 3.1):

- i. The quantity of radioactivity discharged to air and to sea from any nuclear site is measured by the site operator. These measurements usually include both the quantity (in becquerels) and type of radioactivity with additional data on the quantities of certain individual radionuclides discharged. These measurements are reported regularly to HMIP and MAFF who are the Authorising Departments. Where measurements are not available, estimates can be made on the basis of operations on the site.
- ii. Levels of radioactivity in the environment e.g air, soil and grass and in food are measured both by the site operator as a condition of the discharge authorisation and by HMIP and MAFF as an independent check on the environmental situation. Where measurements are not available, or not sufficiently sensitive, the levels of radioactivity in the environment can be estimated by applying mathematical models to the discharge data.
- iii. Data on population habits including pattern of food consumption and house occupancy are available either nationally, for example, from the Ministry of Agriculture, Fisheries and Food (MAFF) or from local habit surveys. These data taken with those from (ii) above on the levels of radioactivity in food etc, enable an estimate to be made of the exposures members of the public could receive via either external radiation, or ingestion or inhalation of individual radionuclides.
- iv. Consideration of metabolic factors which include: the proportion of each radionuclide absorbed into the body; the distribution of radionuclide in tissues within the body; metabolic changes undergone by materials while in the body; excretion pattern of the radionuclide plus knowledge of the type of radiation emitted by the radionuclide (alpha, beta or gamma); the energy of its emissions and the half-life of the material. These enable an estimate of the dose from the exposure to be calculated.
- v. Doses can be calculated to individual organs or can be converted to corresponding effective 'whole body doses' which are estimated to carry the same risk of fatal cancer as the dose from all the different radionuclides combined.
- vi. From a knowledge of the risks of cancer associated with human exposures to radiation in the past the estimated doses can be converted to estimated risks of cancer, or estimated risks of specific cancers (such as leukaemia) over time periods of interest.

Figure 3.1 Pathways of exposure to man.

The Main Stages in the Assessment Procedure of the Risk of Radiation Induced Leukaemia and NHL from Radioactive Discharges and other sources.



3.6 In this chapter, we give a brief outline of the main activities which have occurred on the Sellafield site and summarise the discharge and environmental monitoring data used by NRPB in its calculations of estimates of dose and risk to the population of Seascale, for the period of time covering the operation of the Sellafield nuclear plant up to the end of 1992. We have focused on the factors which have changed since the exercise was last carried out and described in the NRPB reports R171 and R171 Addendum (Stather *et al*, 1984; Stather *et al*, 1986). Finally, we consider how these dose and risk estimates might relate to the incidence of childhood cancer in Seascale over the same time period.

THE SELLAFIELD SITE

3.7 The Sellafield site is located in West Cumbria near to the coast (see Figure 3.2). It was acquired by the Ministry of Supply in 1947 for the production of plutonium for defence purposes. Two nuclear reactors and a spent fuel reprocessing plant were in operation by 1952. Responsibility for the site was transferred to the United Kingdom Atomic Energy Authority (UKAEA) when that body was formed in 1954 and subsequently transferred to British Nuclear Fuels Limited (BNFL) when the company was formed in 1971. The various stages in the development of the site up to the time of the publication of the report of the Black Advisory Group (Black, 1984) are set out in table 3.1.

Table 3.1 Stages in the development of the Sellafield nuclear site up to 1984

	Date operational	date shut down
Site available July 1947	Work commenced September 1947	–
First and second pipeline to sea	Laid June 1950	Isolated from sea 1992
No. 1 pile	Critical October 1950	October 1957
No. 2 pile	Critical June 1951	October 1957
1st reprocessing plant and associated facilities	January 1952	Reprocessing plant converted to head end plant for oxide fuel:- used 1969-1973
1st Calder Hall reactor	August 1956	–
All Calder Hall reactors	1958	–
Prototype Advanced gas cooled reactor	1963	April 1981
2nd reprocessing plant (Magneox fuel)	1964	–
Spent oxide fuel storage plant	1968	–
Fast reactor fuel fabrication plant	1970	1992
3rd pipeline to sea	Laid 1976	–

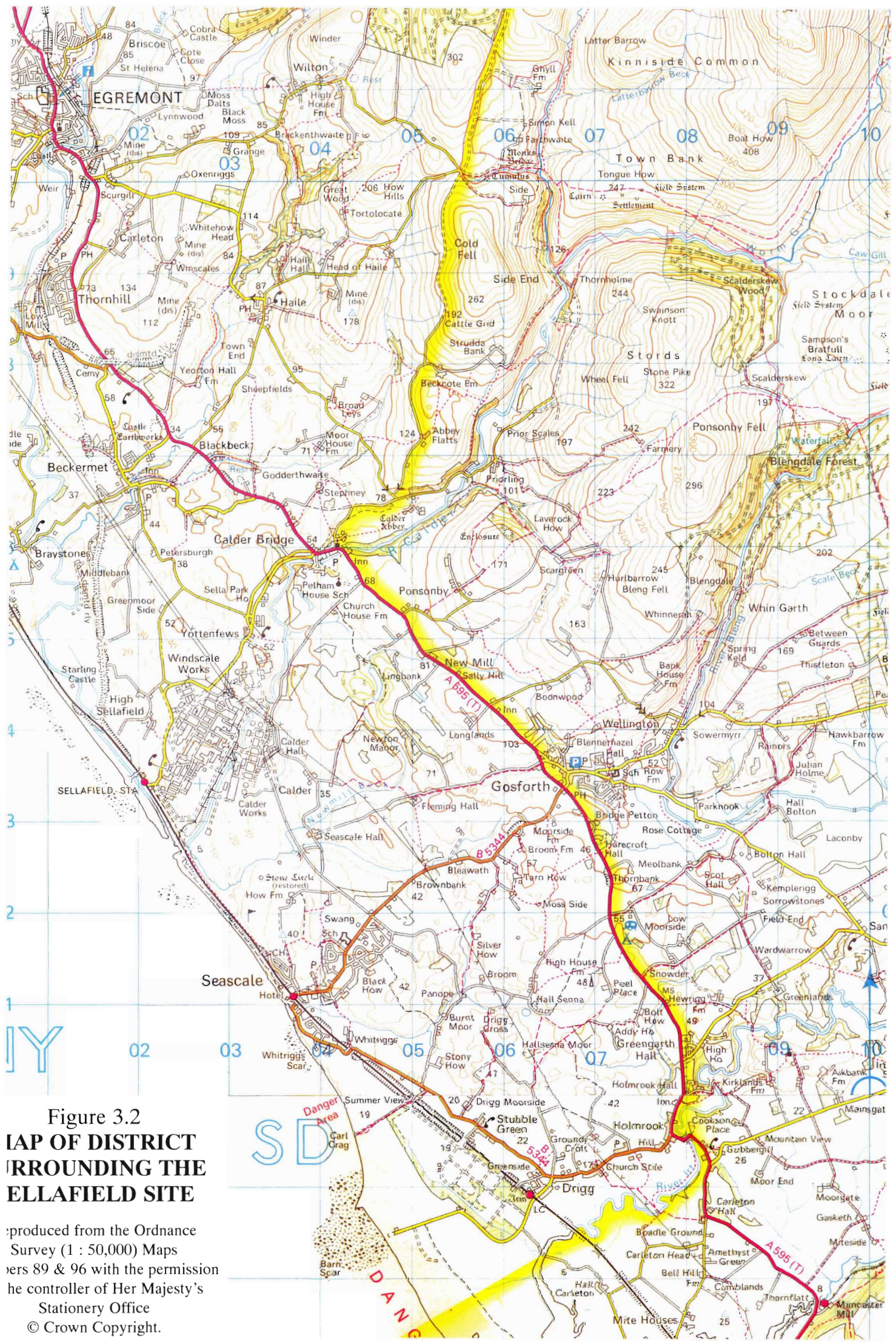


Figure 3.2
MAP OF DISTRICT
SURROUNDING THE
SELLAFIELD SITE

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3.8 Since 1984 many other facilities have been brought into operation on the site. Many of these facilities have been built to manage waste material and have contributed to the considerable reduction in radioactive discharges from the site in the 1980's. Table 3.2 gives a list of the main facilities brought on line up to the end of 1992, the time period with which this report deals.

Table 3.2 Stages in the development of the Sellafield site from 1984-1992

	Date Operational
Site ion exchange plant (SIXEP)	1985
Salt evaporator	1985
New spent fuel storage and decanning	1986
THORP receipt and storage	1988
Vitrification plant for high activity (HA) liquid waste	1990
Magnox encapsulation plant	1990

3.9 Although there are four magnox reactors at the Calder Hall section of the site, by far the greatest volume of site discharges is attributable to spent fuel reprocessing. In the period with which we are concerned (1947-92) most of the discharges have arisen from the reprocessing of "Pile" cartridges or "Magnox" fuel rods. However, during the time period under consideration, facilities on the site have also been used for the storage of spent oxide fuel and the production of fuel for the UK prototype fast breeder reactor. In addition, there is also a UKAEA research laboratory on site. Approximately 7 kilometres south of Sellafield, situated on the coast at Drigg, is an authorised disposal site for low level radioactive waste, which is also owned and operated by BNFL. Table 3.3 lists the principal functions of the Sellafield site in 1992.

Table 3.3 Sellafield site-principal civil functions 1992

i.	Receipt, storage and reprocessing of spent magnox fuel
ii.	Treatment and storage of products of processing
iii.	Receipt and storage of spent oxide fuel
iv.	Fabrication and storage of fuel elements for fast breeder reactor
v.	Operation of Calder Hall reactors
vi.	UKAEA research laboratory
vii.	Treatment, storage or disposal of waste products

3.10 BNFL have supplied us with a list of major new plant brought on line since 1992 or under construction at the Sellafield site. These facilities will almost certainly have an effect on the level of discharge in the future. This list is reproduced in table 3.4.

Table 3.4 Major new plant brought on line since 1992 or under construction at the Sellafield site

	Date Operational
Replacement sea line (for sea line 1)	1993
Enhanced actinide removal plant (EARP))
Waste packaging and encapsulation plant (WPEP))
Ancillary facilities)
THORP feed pond	March 1994
THORP head end)
Waste encapsulation plant (WEP))
Replacement low activity (LA) effluent conditioning and sentencing facilities	January 1994
THORP chemical separation	March 1994
Solvent treatment plant	May 1994
Sellafield MOX (mixed oxide fuel) plant (SMP)	July 1994
Floc retrieval facility	January 1995
Waste Vitrification Plant (WVP) line 3	1998
	1998
	2000
	2000

DISCHARGES FROM THE SELLAFIELD SITE

3.11 BNFL have recently carried out a review of discharges from the Sellafield site for the years 1951 to 1992 (Gray *et al*, 1995; Jones *et al*, In Press). BNFL have supplied us with a large volume of data which has contributed to this review. We regard this review to have been particularly relevant to our enquiries and we describe the main points in some detail in this section. Where possible we have drawn attention to the changes in the discharges which are of most importance to the new dose assessment carried out by NRPB. Finally, there has been a significant reduction in the levels of radioactive discharges from the Sellafield site over the last decade.

Liquid Discharges

3.12 Liquid discharges arise from a multitude of sources on the Sellafield site. The most important of these sources are as follows:

- i. Water from the fuel storage ponds. These ponds need to be supplied with fresh water to maintain control of the water chemistry and the levels of radioactivity at acceptable levels. The displaced water contains activity arising from fuel elements stored in the ponds.

- ii. The reprocessing plant. The majority of extracted liquid fission products are concentrated into an aqueous acid effluent stream for evaporation and storage. This material is now being converted to vitrified waste form in the Waste Vitrification Plant. However, some effluent streams cannot be treated in this way, typically because they are of high volume but low radioactivity. These process streams constitute low active liquid effluent which is discharged to the environment in accordance with authorisations. Before the evaporator plant was in operation a larger volume of low activity liquid effluent had to be discharged.

3.13 Some of the effluent arisings, including those from the reprocessing plant, are discharged batch-wise via delay tanks. These are operated in such a manner that an analysis of the effluent is available prior to discharge. Other effluents, including those from the storage ponds are discharged as a continuous flow. However, regardless of the discharge route, all liquid effluent is sampled by taking a known proportion which is then analyzed for radioactive content. This enables an estimate to be made of the cumulative amount of radioactivity discharged in any period.

3.14 Discharges of liquid waste into the sea have been made through the pipelines which extend 2.5 km from the high water mark out into the Irish Sea. Discharges started in 1952 and since that time a continuous record of liquid discharge has been kept.

3.15 Over the years, the analytical schedule for specific radionuclides has become more comprehensive. Where there are gaps in the discharge record for specific radionuclides in the earlier years of operation, BNFL have made appropriate extrapolations. However, we were told that these extrapolations could be made with reasonable confidence based on the available measurements of total alpha or total beta radioactivity, or based on available measurements of a radionuclide closely related to that for which the discharges are estimated. Some specific radionuclides, such as tritium, were estimated by other appropriate methods. This process was used and described in the NRPB reports NRPB-R171 and NRPB R-171 Addendum (Stather *et al*, 1984; Stather *et al*, 1986), which were produced for the Black Advisory Group and COMARE in 1984 and 1986 respectively.

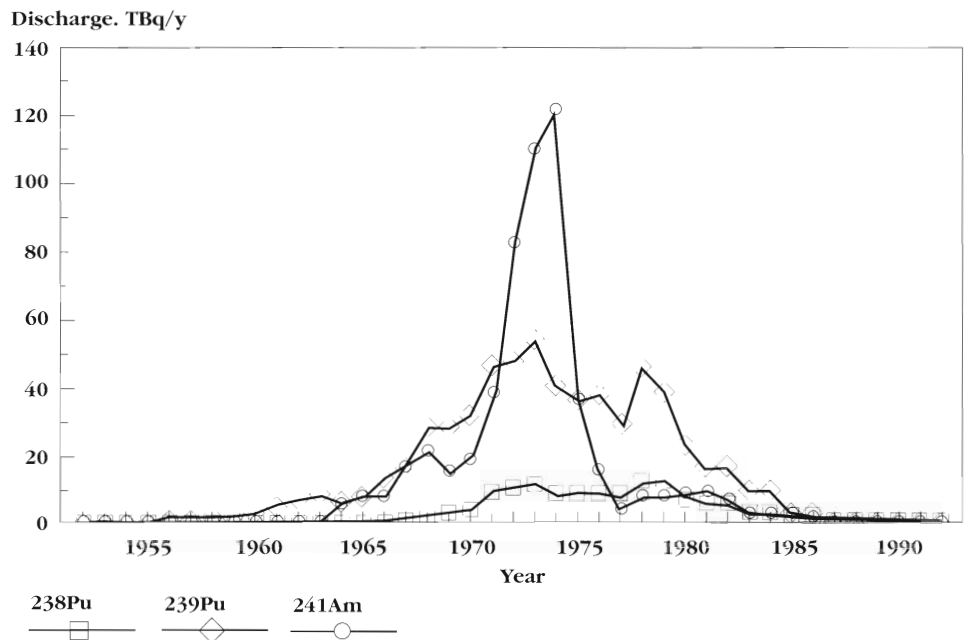
3.16 Full details of the annual liquid discharges from the Sellafield site from 1952 to 1992 are given in Gray *et al* 1995. However, graphical presentations summarising the levels of the most important radionuclides in the liquid discharges (both the main alpha and beta-emitters) during this period are given in figures 3.3 and 3.4. The main accidental releases were to atmosphere but there were some accidental liquid releases (see Table 3.2 NRPB R-276). These accidental releases were included with the routine liquid discharges if they went into the sea.

3.17 The liquid discharges of both the main alpha and beta emitters show distinct peaks in the mid 1970's, followed by a steady decline until 1992. Discharges of alpha emitters are now a small fraction of their peak value in 1973. Further reductions in discharges occurred in 1986 after the introduction of the Site Ion Exchange Effluent Plant (SIXEP) and the Salt Evaporator. Liquid discharges of one radionuclide, tritium, have not reflected the general downward trend, in that they have been fairly constant since 1976. Tritium is now the dominant beta emitter in terms of radioactivity (as opposed to dose) due to the reduction in discharges of other beta sources. Although tritium discharges are

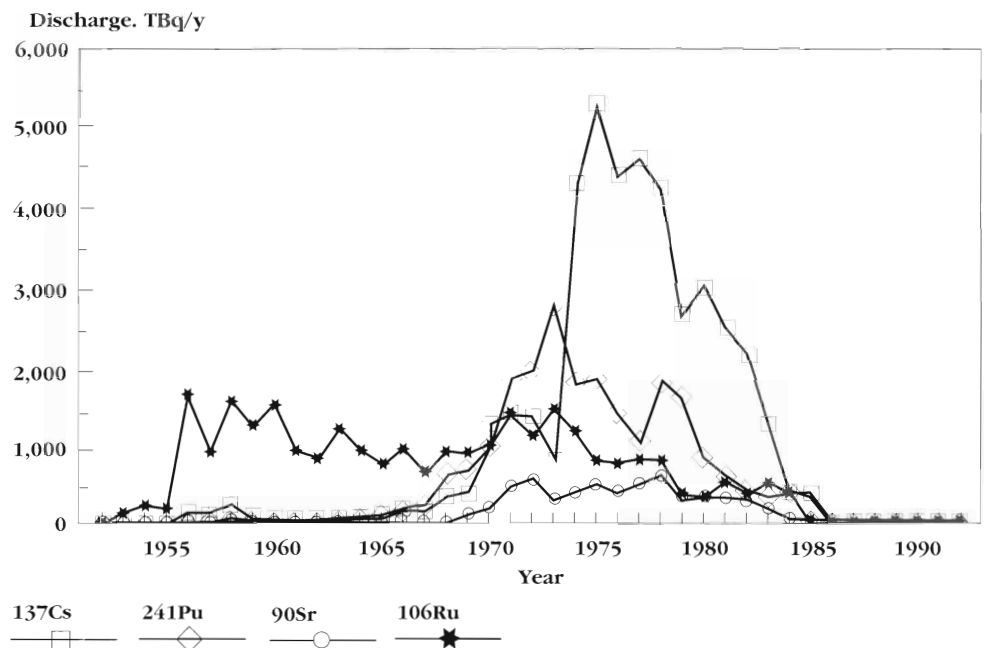
believed to cause little biological effect, the underlying assumptions of this conclusion will be kept under review. Alpha discharges continue to be dominated by Americium-241 and the plutonium isotopes.

3.18 Discharges of alpha emitters and most beta emitters fell following the start up of the Enhanced Actinide Removal Plant (EARP). However, we were advised that discharges of tritium and some other radionuclides are expected to increase

Figures 3.3 LIQUID DISCHARGES - ALPHA EMITTERS



Figures 3.4 LIQUID DISCHARGES - BETA EMITTERS



when the Thermal Oxide Reprocessing Plant (THORP) comes up to full production. Discharges of technetium-99 will also increase as backlogs of stored wastes are treated through EARP.

Atmospheric Discharges

3.19 There is considerably more uncertainty concerning the level of discharge of radionuclides to the air than there is for liquid discharges, particularly for the early years of site operation. There are essentially four main reasons for this and these are;

- i. atmospheric (or aerial) effluents are discharged from many separate points on the Sellafield site
- ii. measurement of aerial effluents is technically much more difficult than is the case for liquid discharges
- iii. records of aerial discharges were not kept in a systematic manner during the early years of site operation
- iv. aerial discharges exist in a wider variety of physicochemical forms than do liquid effluents.

The methods by which BNFL have estimated the levels of atmospheric discharges from the site are dealt with below (3.19-3.25). The actual levels as given to NRPB are reproduced in Gray *et al* 1995. The reasons for listing these discharges by stack height are also discussed below (3.27).

3.20 Atmospheric discharges from Sellafield can be characterised into three distinct physical forms.

Permanent gases: Principally radioactive “noble” or inert gases, the most important of which are argon-41 (Ar-41) and krypton-85 (Kr-85). Ar-41 is a neutron activation product of Ar-40 which is naturally present in air, thus Ar-41 was discharged in substantial quantities from the Windscale Piles which were air cooled. Smaller amounts were discharged from the Windscale Advanced Gas cooled reactor when it was in operation. However, Ar-41 is produced in lesser but still significant quantities in the air used to cool the space between the steel pressure vessel and the concrete shields of the Calder Hall Magnox reactors. Kr-85 is a fission product released from irradiated fuel when reprocessed. It is also released in smaller quantities from cooling ponds due to corrosion of Magnox fuel.

Other gases and volatiles: The most important radionuclides in this category are tritium (H-3), carbon-14 (C-14), and iodine-129 and 131 (I-129, I-131). The principal source of all these radionuclides is reprocessing plant, although smaller quantities are discharged from the reactors. Some of these radionuclides such as C-14 and the isotopes of iodine are removed, at least in part, from the aerial discharge by liquid off-gas scrubbers which means they become incorporated in the liquid discharges.

Particulates: The large air volumes used to ventilate the various parts of the process plants invariably contain particulates and fine dusts in suspension and although particulate activity is amenable to filtration, some radionuclides associated with these air streams will form part of the aerial discharges. The most important radionuclides discharged in this manner are the major fission products such as caesium-137 (Cs-137), strontium-90 (Sr-90) and ruthenium-106 (Ru-106) and also the alpha emitting actinides, the most important being the isotopes of plutonium (Pu) and americium (Am).

Problems with sampling and measuring of aerial discharges.

3.21 The flow rate of ventilation through a discharge stack is usually high, ie. millions of cubic metres per hour. The portion capable of being extracted is small and hence there are problems with ensuring that the sample is representative. The presence of particles in the air flow means that inertial forces can cause a number of problems such as deposition on surfaces, changed mix rates at interfaces such as pipe bends etc. If the sampling technique cannot overcome these problems then it may be necessary to apply corrections to the discharge data.

3.22 In the early years of operation more attention was paid to measuring and recording liquid discharges as these were numerically much greater than aerial discharges and believed to be more important environmentally. Until 1964 quantitative aerial discharges were not systematically assessed and recorded. Samples were taken and recorded but the technology available at the time was inefficient. Since 1964 continuous sampling was undertaken on the major discharge stacks with quantitative estimates of discharge being recorded. These records were mainly in the form of total alpha and total beta together with measurements of a few specific radionuclides.

3.23 In order to provide information to NRPB for their studies for the Black Advisory Group the detailed discharge records from 1964 were used by BNFL as the basis of the Aerial discharge data. Until 1964 the quantities of material discharged to atmosphere were not systematically assessed and recorded. Samples of gaseous effluent, both discrete and continuous, were taken at various times but the results were recorded as the concentration of radioactivity in the effluent and not converted into an assessment of the quantities discharged. In the period prior to 1964 most determinations were for total alpha and total beta radioactivity with few determinations of individual radionuclides. From 1964 assessments of quantities discharged were made and recorded. In addition, analytical schedules for individual radionuclides were introduced which became more comprehensive as time progressed.

Efficiency of aerial discharge sampling systems

3.24 Prior to the 1980's aerial discharge sampling systems were used primarily as process trend indicators. Although discharge results were reported to the Authorising Departments (the Department of the Environment, DoE and the Ministry of Agriculture Fisheries and Food, MAFF), environmental monitoring was considered to give the best assurance that public radiation exposure was within the recommended limits. During the 1980's there was movement toward the imposition of stringent numerical limits to aerial discharges. BNFL therefore initiated a major programme to validate and improve the quantitative performance of the aerial discharge sampling systems in use at Sellafield.

3.25 The results of this programme indicated that the stack sampling arrangements in place systematically under-estimated some discharges, especially the particulates by factors ranging between 2 and 10. Specific "stack sampling efficiency factors" (SEF's) were derived for particular radionuclides discharged from specific outlets. These factors were applied to the evaluation of discharges reported to the regulatory departments and published in annual reports from 1986 onwards.

However, these SEF's cannot be applied automatically to discharges in earlier years as the value of the sampling efficiency factor depends on the physical condition which pertained in the discharge stream at the time of measurement.

3.26 To circumvent these problems BNFL determined the most appropriate SEF's for particular radionuclides for particular plant buildings on an historical basis. This had the effect that the assumed releases are higher than those used in NRPB R171 or R171 Addendum. Because of the uncertainties involved in this

process BNFL told us that the estimates made were believed to be conservative, ie. likely to be higher than the actual discharges.

Effective heights of stacks

3.27 In addition to the quantity of material discharged, calculations of dispersions in the environment require an estimate to be made of the effective height at which the effluent is released. This will not always be the same as the physical height of the release point above the ground, because factors such as momentum and temperature of the air mass tend to increase the effective height of release. Other factors such as turbulence around buildings tend to reduce the effective release height. A measurement and wind tunnel programme was initiated in 1992 to test the release heights of stacks on the Sellafield site (Gray *et al*, 1995). The results of the study showed that the tallest stack of 120 metres had an effective stack height of 80 metres, and that no building had an effective stack height of less than 10 metres. These effective stack heights have, therefore, been used in the appropriate calculations of dispersion.

Emissions of Carbon-14 (C-14)

3.28 C-14 emissions were not specifically considered in NRPB R171 Addendum. Measurements of emissions were only available for the 1980's. However, in the 1970's Harwell researchers measured C-14 concentrations in sequences of tree rings near to the Sellafield site and produced a retrospective year by year record of C-14 concentrations in the environment for the entire period of operation of the Sellafield site. By assuming that dispersion conditions remain the same from one year to the next, these concentrations have been used to make pro rata estimates of C-14 discharges for the years when no discharge measurements were available.

Uranium Oxide discharges from the Windscale Piles

3.29 This particular discharge has been the subject of considerable discussion and recalculation and formed the topic of discussion in our first report (COMARE 1986). The Black Advisory Group were informed that this release had a value of 440 g and this value was used in the dose calculations in NRPB R171. Subsequent to the publication of this report queries were raised by Dr D Jakeman (Jakeman 1986) who had worked at the site in the 1950's, suggesting that this discharge could have been substantially larger. Discussions between Dr Jakeman, BNFL, NRPB and COMARE representatives took place and it was agreed that a figure of 20 kg would be used in the dose estimates calculated in R171 Addendum.

3.30 Since publication of our first report the Department of Health has commissioned several studies of the levels of various radionuclides in soil core samples taken from undisturbed land around the Sellafield site (Cawse and Baker, 1994). The levels measured can be back-extrapolated to the time period of interest and an estimate of the discharges calculated (Chamberlain, 1996; Jones *et al*, in press). The results of these studies suggest a discharge of uranium oxide of a value slightly lower (17 kg) than the 20 kg figure used in R171 Addendum. Having discussed the uncertainties involved in this procedure we recommended that NRPB continue to use the value of 20 kg in their new dose estimates. The uncertainties in this value and the consequences for dose variation are discussed in paragraph 3.70 below.

3.31 The other data produced by these soil monitoring studies suggested that the aerial discharges of plutonium in the early years of site operation had also been considerably underestimated. This finding was subsequently confirmed by the re-evaluation undertaken by BNFL which is discussed in paragraphs 3.19 to 3.26 above.

Aerial releases resulting from accidents and plant abnormalities

3.32 The information concerning aerial releases discussed above has related entirely to discharges which occurred on a routine or substantially continuous

basis. In addition a number of significant discharges have arisen from accidents or abnormal plant operation. The most significant of these discharges are listed below:

The fire in Pile No 1 - October 1957

Failure of plutonium evaporator leading to discharge from the Calder Hall cooling towers - June 1961

Iodine releases from reprocessing of short cooled fuel -1952, 1957, 1960, 1972, 1981

Swarf fire in Magnox decanning cave - July 1979

Release of plutonium from effluent treatment plant -September 1979

Release of americium-241 from a sludge storage tank - July 1984.

All of these releases, apart from the last, were considered by NRPB in their assessment for the Black Advisory group. BNFL informed us that quantities of activity released in these events have been retrospectively assessed from consideration of environmental measurements taken either at the time or subsequently and from relevant plant data. These data have been used in NRPB's current reassessments of doses.

Aerial discharges: Differences from NRPB R171 Addendum

3.33 In summary the aerial discharges in the current assessment which differ from those reported in NRPB R171 Addendum are as follows:

All discharges of caesium-137 and strontium-90 since 1972 were considered to be from 10 metre effective height, with a sampling efficiency factor (SEF) of 2.

Remaining particulate discharges from the reprocessing plant stacks were considered to be from an effective height of 80 metres. SEF's of 8, 4 and 3 were applied to releases of actinides, fission products and the isotopes of iodine respectively.

Discharges from B204 stack prior to 1964 have been estimated from the continuous record of initial total alpha measurements available.

Discharges of carbon-14 from reprocessing have been derived from available emission measurements and tree ring measurements.

A higher value of discharge of plutonium in 1968 because of a discharge from B230 stack.

Discharges of sulphur-35 have been reviewed.

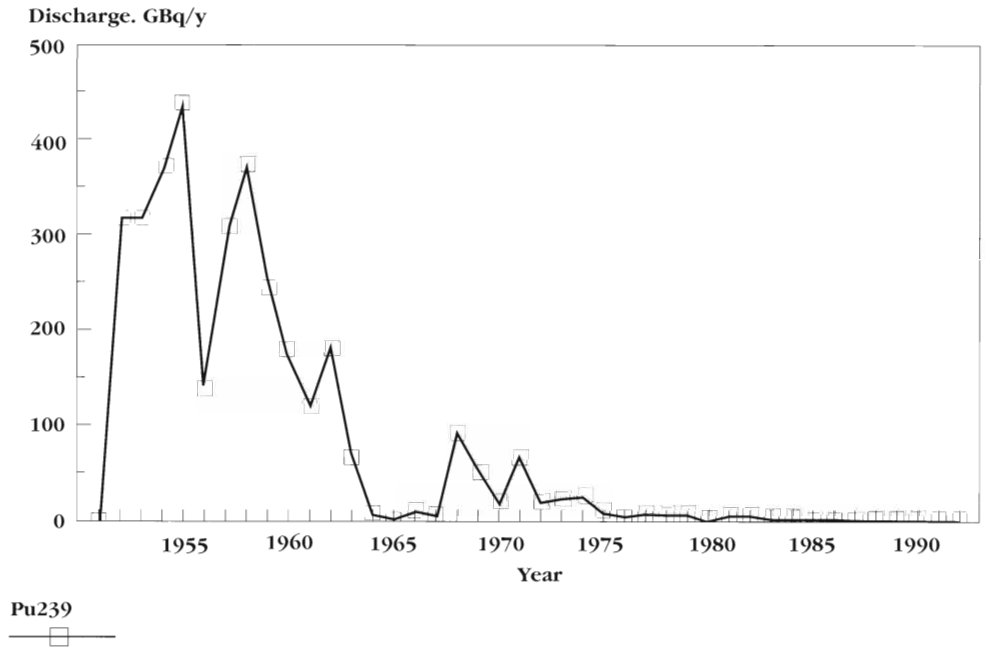
Discharges after 1982 have been added using values reported annually by BNFL.

Ground level plutonium source term of about 70 GBq with high deposition velocity (0.1 ms^{-1}) to replace figures given in R171 Addendum for Calder Cooling Towers, Piles Pond and North Group.

Changes in aerial discharges over the period of plant operation

3.34 Annual atmospheric discharges of alpha-emitters have, in general, fallen from the highest levels of discharge in the early years of site operation. There was a smaller but significant increase in the 1970's with a steady decline in discharges in the 1980's and 1990's. This is demonstrated in the graphs shown in Figure 3.5.

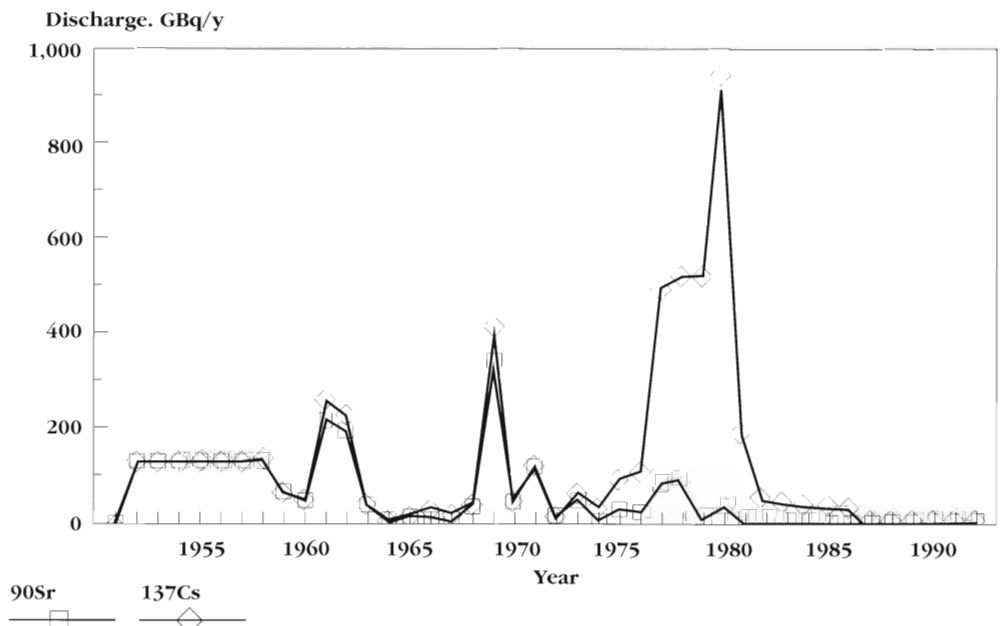
Figure 3.5 AERIAL DISCHARGES - PLUTONIUM (HIGH STACKS)



3.35 However, there was a different pattern of discharge for the principal beta-emitters, with the largest peak level of discharge occurring in the late 1970's followed by a very significant reduction in atmospheric discharges of beta-emitters since 1984 (see Figure 3.6). In particular, caesium-137 discharges have decreased due to a reduction in releases from a silo containing Magnox cladding. Similarly, discharges of ruthenium-106 declined after the introduction of new filtration systems. Discharges of zirconium/niobium-95 have also decreased considerably from 1980 onwards.

3.36 The peak in discharges of iodine-131 in 1981 was due to reprocessing of "short cool" fuel sent in error by Oldbury power station. This fuel was stored for only 27 days. Normally fuel is stored at power stations for at least 90 days, which allows short-lived isotopes such as iodine-131 ($t_{1/2}=8$ days) to decay to acceptable

Figure 3.6 AERIAL DISCHARGES - MAIN BETA EMITTERS



levels. As noted above this problem has occurred on four other occasions. HMIP told us that the company had been censured for these errors and that practices are now in place to ensure that such mistakes do not recur.

**DISCHARGES FROM
ALBRIGHT AND
WILSON LTD,
WHITEHAVEN**

3.37 Albright and Wilson Ltd extract minerals from certain ores and as part of this process discharge liquid effluents which contain significant quantities of naturally occurring radionuclides, principally uranium-238 (U-238) and its daughters, thorium-234 (Th-234), uranium-234 (U-234), thorium-230 (Th-230), radium-226 (Ra-226), lead-210 (Pb-210) and polonium-210 (Po-210). All of these radionuclides except Pb-210 are alpha emitters. We had previously noted that these discharges have contributed a significant dose to some members of the general public from the consumption of fish and shellfish caught in the Whitehaven bay area (MAFF, 1993). These members of the general public are known as the “Critical Group” for the discharges from the Albright and Wilson plant - that is they consume the largest amount of seafood which is the foodstuff containing the highest concentration of radionuclides discharged and hence receive the highest doses. The dose to the critical group is calculated as the best

Table 3.5 Estimates of discharges from Albright and Wilson

**DISCHARGES OF SIGNIFICANT DECAY-CHAIN RADIONUCLIDES
ASSUMING EQUILIBRIUM (TBq)**

YEAR	U-238	TH-234	U-234	TH-230	RA-226	PB-210	PO-210
1954	0.0423	0.0423	0.0423	0.0423	0.0423	0.0423	0.0423
1955	0.0846	0.0846	0.0846	0.0846	0.0846	0.0846	0.0846
1956	0.1164	0.1164	0.1164	0.1164	0.1164	0.1164	0.1164
1957	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587
1958	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587
1959	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587
1960	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587	0.1587
1961	0.2645	0.2645	0.2645	0.2645	0.2645	0.2645	0.2645
1962	0.3280	0.3280	0.3280	0.3280	0.3280	0.3280	0.3280
1963	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1964	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1965	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1966	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1967	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1968	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1969	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1970	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1971	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1972	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444
1973	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444
1974	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444
1975	0.4761	0.4761	0.4761	0.4761	0.4761	0.4761	0.4761
1976	0.5290	0.5290	0.5290	0.5290	0.5290	0.5290	0.5290
1977	0.4973	0.4973	0.4973	0.4973	0.4973	0.4973	0.4973
1978	0.4232	0.4232	0.4232	0.4232	0.4232	0.4232	0.4232
1979	0.2116	0.2116	0.2116	0.2116	0.2116	0.2116	0.2116
1980	0.2328	0.2328	0.2328	0.2328	0.2328	0.2328	0.2328
1981	0.1481	0.1481	0.1481	0.1481	0.1481	0.1481	0.1481
1982	0.2328	0.2328	0.2328	0.2328	0.2328	0.2328	0.2328
1983	0.4232	0.4232	0.4232	0.4232	0.4232	0.4232	0.4232
1984	0.4549	0.4549	0.4549	0.4549	0.4549	0.4549	0.4549
1985	0.4655	0.4655	0.4655	0.4655	0.4655	0.4655	0.4655
1986	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020	0.4020
1987	0.4655	0.4655	0.4655	0.4655	0.4655	0.4655	0.4655
1988	0.6771	0.6771	0.6771	0.6771	0.6771	0.6771	0.6771
1989	0.5726	0.5726	0.5726	0.5726	0.5726	0.5726	0.5726
1990	0.5726	0.5726	0.5726	0.5726	0.5726	0.5726	0.5726
1991	0.5477	0.5477	0.5477	0.5477	0.5477	0.5477	0.5477
1992	0.5477	0.5477	0.5477	0.5477	0.5477	0.5477	0.5477

estimate of the highest dose that can be received by members of the general public from radioactive discharges, from a particular site. If the Authorising Departments consider that there are no significant risks from these doses they can assume that other members of the public must also be protected as they receive lower doses than the critical group and are, therefore, also subject to an insignificant risk. Table 3.5 gives the levels of discharge used by NRPB in their dose calculations. Albright and Wilson provided NRPB with measures of the levels of natural uranium and uranium oxide discharged from 1954 to 1992. The levels of the various decay daughters were estimated by NRPB (in agreement with Albright and Wilson), by assuming that they were all in equilibrium with U-238.

ENVIRONMENTAL MONITORING DATA

3.38 Environmental monitoring is carried out by BNFL and published in annual reports. HMIP and MAFF also carry out their own monitoring of both the terrestrial and marine environments. Both HMIP and MAFF carry out or commission relevant research and MAFF undertake habit surveys and define 'critical groups' for different exposure pathways. MAFF publish annual reports of both their marine and monitoring results. Where possible NRPB have used environmental monitoring data to estimate external doses and intakes of radionuclides. When appropriate data were not available, models have been used to predict transfer through the environment. However, it is worth noting that the quantity and detail of the environmental monitoring data increased significantly in the 1970's and that there are more data available for the radionuclides and exposure routes (ie. the radionuclides of caesium, strontium, plutonium and americium and the milk and seafood pathways) which are considered to be the most important in radiological terms, that is they contribute most of the dose accrued by the general public, from discharges. In their document R276 NRPB have produced an annex containing a detailed summary of the environmental concentration data and external dose rates used in their main dose assessment. We refer those who wish to examine this data in detail to the NRPB report.

3.39 Data such as food ingestion rates and breathing rates are required in order to estimate intakes of radionuclides by people from a variety of appropriate environmental pathways. MAFF undertake surveys to determine intakes of fish, crustacea and mollusca, together with occupancy of shore areas by critical groups. National surveys provide information on the average food intakes for the population of the United Kingdom. These data have been modified to apply to the Seascale population. It was recognised that habits have changed over the years. Fish ingestion rates, for example, were higher in the 1950s and 60s than at present. This type of information was the subject of discussions of the joint COMARE and NRPB working groups. The data used in the NRPB dose assessment was agreed by these groups to be representative of average habits for the Seascale population. The implications for considering higher values on intakes etc. are discussed in the sensitivity analysis described later in this chapter.

ESTIMATION OF INTERNAL AND EXTERNAL RADIATION DOSES

Routes of Exposure

3.40 At the request of COMARE, NRPB have carried out an assessment of the risks of leukaemia and other cancers to the population of Seascale in West Cumbria from all sources of ionising radiation. The study considered the population of Seascale born between 1945 and 1992, with their radiation doses and risks followed to age 24 or 1992 inclusive, whichever is sooner. This represents a longer period than the previous study carried out for COMARE (NRPB R-171 and Addendum) which considered only risks up to the 20th birthday or the beginning of 1980. As previously, the aim was to estimate the average exposure to radiation of the population due to intakes of radionuclides into the body and external radiation. Six main sources of radiation exposure were considered:

- 1) Natural background
- 2) Medical exposures
- 3) Fallout from nuclear weapons testing
- 4) The Chernobyl nuclear power plant accident
- 5) Routine discharges from the Albright and Wilson plant at Whitehaven
- 6) Operations at the Sellafield site (including the Windscale fire)

The Chernobyl accident and discharges from Albright and Wilson had not been considered in previous assessments. Three different aspects of the Sellafield operations were considered: routine discharges, including relatively minor releases due to accidents and incidents; the Windscale fire of 1957 and the uranium oxide releases in the 1950's.

3.41 In assessing the risks to the Seascale population, the radiation doses from each of the above sources were calculated separately. Annual average doses were calculated for groups of children born in each of the study years. The first stage in the study was to estimate the intakes by inhalation and ingestion by different age groups for each year considered, together with external radiation doses. The second stage was to calculate the annual radiation doses as a function of time for each group of children. The final stage was to calculate the risks of radiation-induced leukaemia and other cancers in the study population. The number of children in each year was based on birth statistics for Seascale and so varied from year to year; this approach varies from previous assessments where the same number of children was assumed in each year. The results of the study are briefly outlined in the following sections emphasising differences between this and the previous studies.

3.42 The principles of the NRPB calculations were those adopted in the previous assessments, NRPB R-171 and Addendum. All doses are for entire organs or tissues, assuming uniformity or that mean values are appropriate to allow for non-uniformities. Microdosimetric features of dose distribution have not been considered in this assessment. In accordance with established international practice and the lack of a relevant basis for general application, children between birth and 2 years of age were treated as having the habits and intake rates of 1 year olds. Those between 3 and 7 years were treated as 5 year olds and those between 8 and 14 as 10 year olds. From 15 onwards people were considered to have the habits and intakes of adults. The levels of radionuclides in foods and air were based on environmental monitoring information wherever possible. When these were not available concentrations were predicted from the known or estimated discharges.

Changes Since the Black Assessment

(a) Intakes of radionuclides discharged to sea

3.43 Changes have been made to some of the discharge data used in the assessment and to some of the methods used to estimate intakes; the most significant of these are discussed.

There have been only minor modifications to the liquid discharges from Sellafield assumed in previous assessments. The major difference from previous studies is the inclusion of discharges of uranium and daughter radionuclides from Albright and Wilson's plant at Whitehaven. Changes have been made to the method for estimating concentrations of radionuclides in marine foods where monitoring data are not available. Generally the effects of these changes are small and the majority of concentrations were based on measurements. The intake rates of marine foods used in the assessment have changed slightly from those used in the previous studies. However, the net effect of the changes in concentrations and intakes is relatively minor. The time assumed for beach occupancy has fallen which also affects the dose from inadvertent ingestion of

sand. This has led to a slight reduction in the intake of radionuclides in sand and in the external radiation exposure but, as these are relatively minor exposure pathways, the effect on the overall assessment is small.

(b) Intakes of radionuclides discharged to atmosphere

There have been some major changes to the discharges of radionuclides from the Sellafield site to atmosphere as described above. These increases in discharges are directly reflected in the estimated intakes by inhalation. The effect overall depends on the relative contribution of the different exposure pathways and hence varies as a function of time. The intake of radionuclides through ingestion of terrestrial foods has also been considered in the NRPB assessment. Where possible measured concentrations of radionuclides in milk formed the basis of these intakes. However, when monitoring data were not available the intakes of radionuclides in other foods and in milk, were based on a model of the terrestrial food chain. These intakes are, therefore, dependent on the accuracy of the discharge data. An updated version of this model was used in the current assessment which affected the predicted intakes to some extent. However, the intake of radionuclides in terrestrial foods is a relatively minor source of exposure so these changes do not have a significant effect on the overall assessment.

(c) External Doses

External radiation doses from radionuclides on beaches and on soil have been considered in this assessment together with external radiation from radionuclides in the air. There are some changes in the way that these doses have been estimated but generally they had only a very minor effect. The only possible exception is a change in the shielding factor from 0.45 to 0.2 from exposure from radionuclides in the air, which reduces the external radiation doses from this route during the time spent indoors. This change in the shielding factor came about as a result of the considerable volume of data gathered at the time of the Chernobyl accident when actual measurements of shielding factors were made.

The most significant changes to the estimated intakes of radionuclides by the Seascale population due to operations at Sellafield are due to the amendments in the discharges of radionuclides to atmosphere, notably those of the plutonium radioisotopes. However, the effect of these and other modifications, alter as a function of time, and with the variability in the importance of different routes of exposure.

3.44 There is one further change in the way that the population doses were estimated compared with the way in which they were calculated for the Black Advisory Group. In the 1980's it was the practice to produce "conservative" estimates of dose, that is where there were uncertainties about a level of discharge or uptake the highest conceivable value for that parameter was used in any calculation, hence a conservative or upper value of dose was used as the final estimate. We were concerned that the "best" estimate should be used for the current calculations. By this we mean the value which was considered to be as close to the actual level of discharge or uptake, was used in the calculation of dose. Where there are uncertainties it was usually possible for NRPB or BNFL to estimate the probable upper and lower bounds and hence a mean figure which could be used in the calculations. The case where this does not apply is with the revised levels of aerial discharges of plutonium in the early years of plant operation. BNFL have informed us that these should be assumed to be based on "conservative" estimates of discharge.

Estimation of internal radiation doses

Models for calculating radiation doses to tissues from intakes of radionuclides

3.45 Full details of the models used to determine the doses to the population of Seascale are given in NRPB R276 and it is not necessary to duplicate these descriptions here. However, there have been quite large changes in the way the dose to the embryo, fetus and new born child were calculated compared to that

used in NRPB R171 and NRPB R171 Addendum. A brief summary of the current dose estimate procedures for these stages of life are given below.

Doses to the embryo and fetus from intakes of radionuclides by the mother

3.46 There are at present no generally accepted methods for calculating radiation doses to the developing embryo and fetus following intakes of radionuclides by the mother. A number of laboratories have developed models for a few radionuclides and recently the United States Nuclear Regulatory Commission issued for comment a draft report describing approaches to calculating doses to the embryo and fetus from internally incorporated radionuclides. Ideally, dosimetric models should be based on human data but information is available for radioisotopes of only a few elements and for most the results of animal experiments must be used, although again data are frequently very limited.

3.47 In the extrapolation of animal data to humans, care is needed. Particular problems in the development of dosimetric models for the embryo and fetus include: the varying progress of organ development in different species; the presence of several types of placenta in different species, all of which provide a selective but potentially different barrier between maternal and fetal blood; the rapidity of growth; the complex pattern of growth and differentiation with the potential for quite different distributions of radionuclides in the embryo and fetus from that of the mother; and uncertainty about the location of sensitive cells at various stages of development. Doses to the fetus from maternal deposits of radionuclides also need to be assessed.

The embryo

3.48 Because of the close apposition between the embryo and uterus wall it has been commonly assumed, in the absence of more specific information, that the dose to the embryo, up to the end of the second month of gestation, can be approximated from the dose to the uterus. This approach is adopted here.

The fetus

3.49 From the end of organogenesis a general approach has been adopted by a number of authors for calculating doses to the fetus. This considers relative concentrations of radionuclides in fetal and maternal tissues using as a basis human or animal data. Ideally, information is needed on the initial uptake of the radionuclide by the fetal and maternal tissues following its entry into maternal blood, on the extent to which activity deposited in maternal tissues is subsequently translocated to the fetus and on its retention and distribution in the developing fetus and maternal tissues (see table 3.6). For the case of the radiation dose to the fetus, being determined mainly by the activity translocated to it across the placenta, the assessment of fetal organ/tissue dose, can be derived from maternal organ/tissue dose by correcting for activity concentrations, half-lives and absorbed fractions.

3.50 In practice, published results may only give data on relative concentration ratios in the fetal and maternal tissues and details of the distribution of radionuclide in fetal tissues are often not given. A general approach adopted in this report for calculating the dose to the developing fetus, where specific information is not available, is therefore to use as a basis for dose calculations, ratios obtained shortly after administration. This is likely to be conservative as rapid growth of the fetus is expected to reduce the concentration of radionuclide in fetal tissue, although this dilution effect may, to some extent, be offset by transfer to the fetus from deposits in the maternal tissues. Radionuclides which would be expected to equilibrate rapidly between maternal and fetal tissues include isotopes of hydrogen and the alkali metals (eg, caesium) which are predominantly ionic in body fluids and have a rapid turnover in tissues. For the majority of radionuclides, activity deposited in maternal tissues will also

contribute to the dose to the fetus. In the absence of complete models for the pregnant woman, this dose may be taken to be the same as the dose to the uterus.

Intakes in the years prior to conception

3.51 There are frequently insufficient data to make realistic estimates of the radiation dose to the fetus from the intake of a radionuclide by the mother prior to conception. The results of animal studies have demonstrated, however, that for many radionuclides activity translocates to fetal tissue much more readily from the circulating blood than from deposits in maternal tissues. On the basis of the information available it is likely that this ratio will decrease with increasing time between intakes by the mother and the onset of pregnancy. As a consequence, this assumption is expected to overestimate doses from intakes of many radionuclides prior to conception. Where more specific information is available for particular radionuclides, it is used in the calculations.

Dose to the newborn child

3.52 The amount of radionuclide present in the newborn child is determined from the fetus/mother ratio at birth. This calculated body content is then used to calculate doses received after birth from intakes by the mother during pregnancy.

Table 3.6 Relative concentrations of radionuclides in fetal and maternal tissue used to calculate doses to fetal tissues

Element	Intakes in	
	Year of pregnancy	Previous years
H (HTO)	1.4	1.4
H (OBT)	1	1
C	1	1
S	1	1
Sr	0.4	0.4
Zr	0.5 ^a	0.5 ^a
Nb	0.5 ^b	0.5 ^b
Ru	0.1	0.1
Te	1	1
I	1 ^a	1 ^a
Cs	1	1
Ce	0.02 ^a	0.001 ^b
Pb	1	1
Po	0.1 ^b	0.1 ^b
Ra	0.4	0.4
Pu	0.1 ^b	0.1 ^b
Am	0.1 ^b	0.1 ^b
Np	0.1 ^b	0.1 ^b
Eu	0.02 ^a	0.001 ^b
Mn	1	1
Pm	0.02 ^a	0.001 ^b
Cm	0.1 ^b	0.1 ^b
U	1	1
Th	0.1 ^a	0.1 ^b
Fe	1	1
Co	1	1
Ni	1	1
Zn	1	1
Se	1	1
Mo	1	1
Tc	1	1
Ag	1	1
Sb	1	1
Ba	1	1

^a The relative concentration in the fetal thyroid is taken as 2; the value of 1 applies generally to other tissues

^b These relative concentration values are used to calculate fetal doses from 8-38 weeks of gestation but the *in utero* doses are doubled to allow for earlier contributions to the yolk sac

Comparisons of predicted environmental levels with measured environmental levels

3.53 A large database of measurements of radionuclide concentrations in environmental materials has been accumulated over the years of plant operation at Sellafield. These data were used directly by NRPB in their estimation of intakes and dose rates, when relevant information for Seascale was available. When these measurements were not available discharge data were used together with models of the transfer of radionuclides through the environment to estimate concentrations and dose rates. There is a large body of information of the radionuclide concentrations in marine foods, sand and gamma dose rates on beaches. As a result, estimates of radionuclide intake and external doses from the marine environment were largely based on environmental monitoring data. However, for the terrestrial pathways the database is less extensive and environmental concentrations of radionuclides have, to a greater extent than the marine environment, been derived from discharge data and models of the environment. For these pathways it is useful to compare predicted and measured data whenever possible.

3.54 There is good agreement between the measured and predicted concentrations of Pu-239 in air. The predicted data are generally higher by a factor of about 2 but with a larger overestimation (of a factor of about 5) occurring in 1985. Similar agreement has been shown for Am-241 in air, with the greatest difference being found in 1983, when the predicted values were about a factor of 2 higher than the measured values. Good agreement was found for Cs-137 except from a period starting in 1986 when the contribution from the Chernobyl accident made comparisons more difficult. Between 1987 and 1990 measured values of Cs-137 were higher than predicted values by about a factor of 2. However, NRPB have concluded that this is due to the contribution from Chernobyl and not releases from Sellafield. Measured air concentrations include a contribution from resuspension of previously deposited activity and this level of activity has been estimated. These estimates are thought to be conservative (ie. higher than actual values) and results in predicted levels having been higher than measured levels, but do not affect the predicted air concentrations for those years in which the inhalation dose was highest in the 1950's.

3.55 As a further check on the level of background radiation in Seascale we asked NRPB to look at the results of the Scottish Universities Research and Reactor Centre (SURRC) aerial survey of the vicinity of Sellafield (Sanderson *et al*, 1991) to determine if they were consistent with values used in the Seascale assessment. NRPB told us that there are two directly comparable data sets; the gamma dose rate survey and the map of caesium-137 deposited activity. The aerial survey recorded gamma dose rates at Seascale that are essentially at background levels and that are slightly lower than those used in the NRPB's dose assessment. The activity concentrations of caesium-137 recorded in the SURRC survey for the Seascale area were in the range 6.34-10.05 kBq m^{-2} . In the NRPB assessment a deposited activity concentration of 12 kBq m^{-2} was used. Thus, the NRPB assessment results are similar to, if slightly higher than, those obtained by the aerial survey.

Comparisons of predicted levels of radionuclides with measurements in human tissues

3.56 In examining the validity of the modelling procedures for the estimation of radionuclide uptake in humans the predicted values have been compared to measured values in human tissues where available. Measured levels of Pu-239/Pu-240 in skeleton, liver and lung and Cs-137 in liver for some residents of Seascale are available. Predicted levels of plutonium in liver and skeleton and of Caesium in liver are higher than measured levels, but predicted levels of plutonium in lung are lower than measured levels, these predictions being in the range 2-15 times lower in specific individuals. Fetal tissue measurements for the Seascale population are not available but the data that do exist for other parts of

the UK show good agreement between predicted and measured values. Similarly there is good agreement between predicted and measured levels of whole body caesium measurements. Radionuclide measurements in children's teeth have been carried out from samples obtained from many areas of the UK including west Cumbria. The mean measurements of concentrations of plutonium and strontium-90 for Cumbria are within the range of mean concentrations as determined for the rest of the UK.

RESULTS OF DOSE CALCULATIONS

3.57 The doses of most importance to our deliberations are summarised in Table 3.7. This table gives the doses to the red bone marrow in young people living in Seascale (up to the 25th birthday or 1992, whichever is sooner) in all cohorts. The doses from the Sellafield discharges account for less than 9% of the total dose, most of which (over 80%) is from natural sources of radiation (See figure 3.10). In accordance with ICRP recommendations the factor $W_r=20$ was used to calculate the collective dose equivalent for high LET radiation, although Table 3.6 shows the absorbed doses from high and low LET radiation separately to allow for consideration of the contributions of both types of radiation to the total dose. R276 (tables 11.2a and 11.2b) also gives some details of dose contributions from discharges of specific radionuclides and pathways, using examples of intakes by 1 and 10 year old children.

Table 3.7 Doses to red bone marrow and risks of leukaemia and non-Hodgkin lymphoma up to the 25th birthday or to 1992 (inclusive), whichever is sooner, in a cohort of 1348 persons

Source	Absorbed (man Gy)		Collective Equivalent dose * (ManSv) High + Low LET	Expected No. of radiation induced cancers	
	Collective Dose	High LET		Mortality	Incidence
Routine Discharge	3.23×10^{-2}	1.74	2.39	0.02	0.02
UO2 releases	2.3×10^{-3}	0.721	0.721	0.01	0.01
Windscale Fire	3.67×10^{-2}	0.184	0.917	0.01	0.01
Albright & Wilson	4.57×10^{-1}	5.6×10^{-4}	0.091	0.0005	0.0007
Weapons Fallout	8.7×10^{-4}	2.10	2.11	0.02	0.03
Chernobyl	-	0.079	0.079	0.0001	0.0003
Medical	-	3.07	3.07	0.02	0.02
Natural Background	0.777	23.49	39.04	0.28	0.36
Total	0.852	31.38	48.42	0.36	0.46

Expected number of cancers based on national rates;

• with $W_r = 1$ for low LET, $W_r = 20$ for alpha particles (high LET)

0.78

1.08

ESTIMATION OF RADIATION RISKS

Methodology for calculating the risk of leukaemia and other cancers

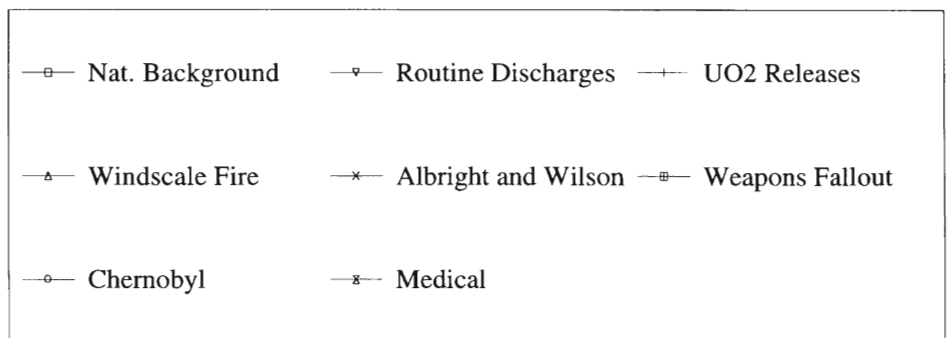
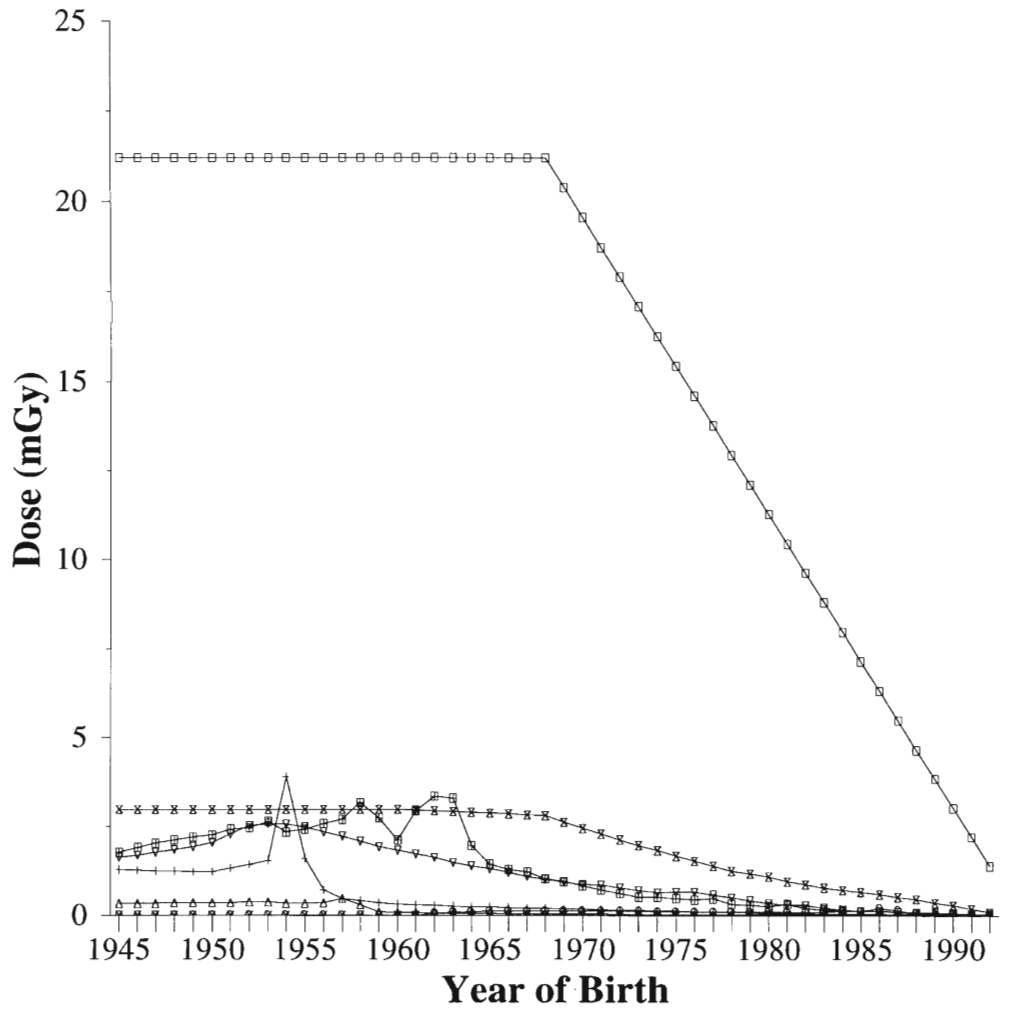
3.58 The models used to calculate the risks of radiation-induced cancer are those described in the NRPB's report on estimates of late radiation risks to the UK population (NRPB, 1993). For the majority of cancer types, including leukaemia, the models developed by the US BEIR V Committee (BEIR, 1990) are utilised. These models are based on detailed analysis of data for the Japanese atomic bomb survivors under the DS86 dosimetry. Since the models are generally of a relative risk form, they have been applied to national baseline cancer rates as part of the life table calculations. For mortality, age and calendar year-specific baseline rates for England and Wales supplied by the Office of Population Censuses and Surveys were used. Although there are statistical fluctuations in the baseline rates in successive years, the use of calendar-specific mortality rates is necessary because the underlying trend is for mortality to decrease because of improvements in therapy and hence survival rates, particularly for childhood leukaemia. For cancer incidence, the Childhood Cancer Research Group provided the national rates which are also utilised in chapter 2 of this report. To maintain consistency with that chapter and allow for the possibility that some leukaemias may be mis-diagnosed as NHL (COMARE, 1988), risks have been calculated for leukaemia and NHL by combining the relevant baseline rates with the relative risk model for leukaemia. Since it is not clear whether NHL is radiation-inducible, it should be recognised that this approach may slightly over-estimate the radiation-induced risk for leukaemia and NHL, although probably by less than 20%.

3.59 Risks have been calculated for those born from 1945 onwards and followed to the end of 1992 or age 24 years inclusive, whichever is sooner. 1945 was chosen in order to be in line with the previous assessment. Furthermore, this method will tend to overestimate the expected number of cases since it covers periods when there would not necessarily have been complete ascertainment of cases corresponding to the relevant birth cohorts. This compares with the follow-up to the end of 1979 or the 20th birthday in NRPB-R171 Addendum. In order to sum risks over cohorts born in each year, the cohort sizes quoted by Gardner *et al* (1987b) in their Seascale birth cohort study were used. Although this study and the associated schools cohort study (Gardner *et al*, 1987a) showed that many of those born in Seascale had left the village prior to commencing school, the annual population sizes for young persons of various ages in Seascale calculated on the above basis generally match closely with the recorded values, as used in the chapter 2 of this report. This indicates that the numbers of children leaving the village were approximately matched by those entering it. The only major discrepancy arises for young adults, at which ages (20-24 years) the recorded population sizes are often 60-70% of the values implied by the cohort sizes. Thus the values used do not take account of movements of young adults out of Seascale.

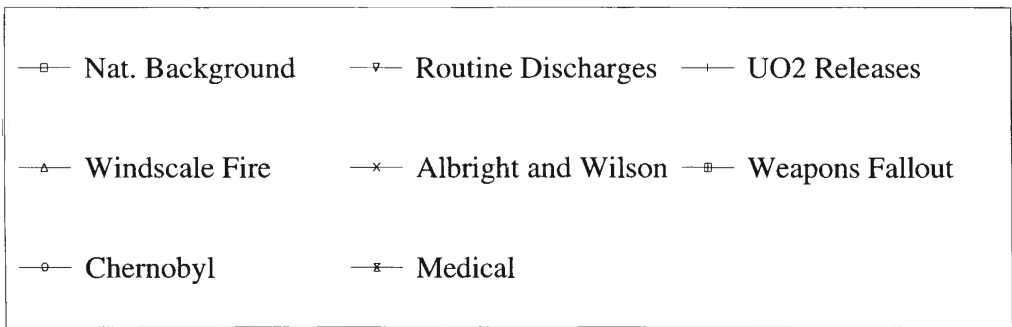
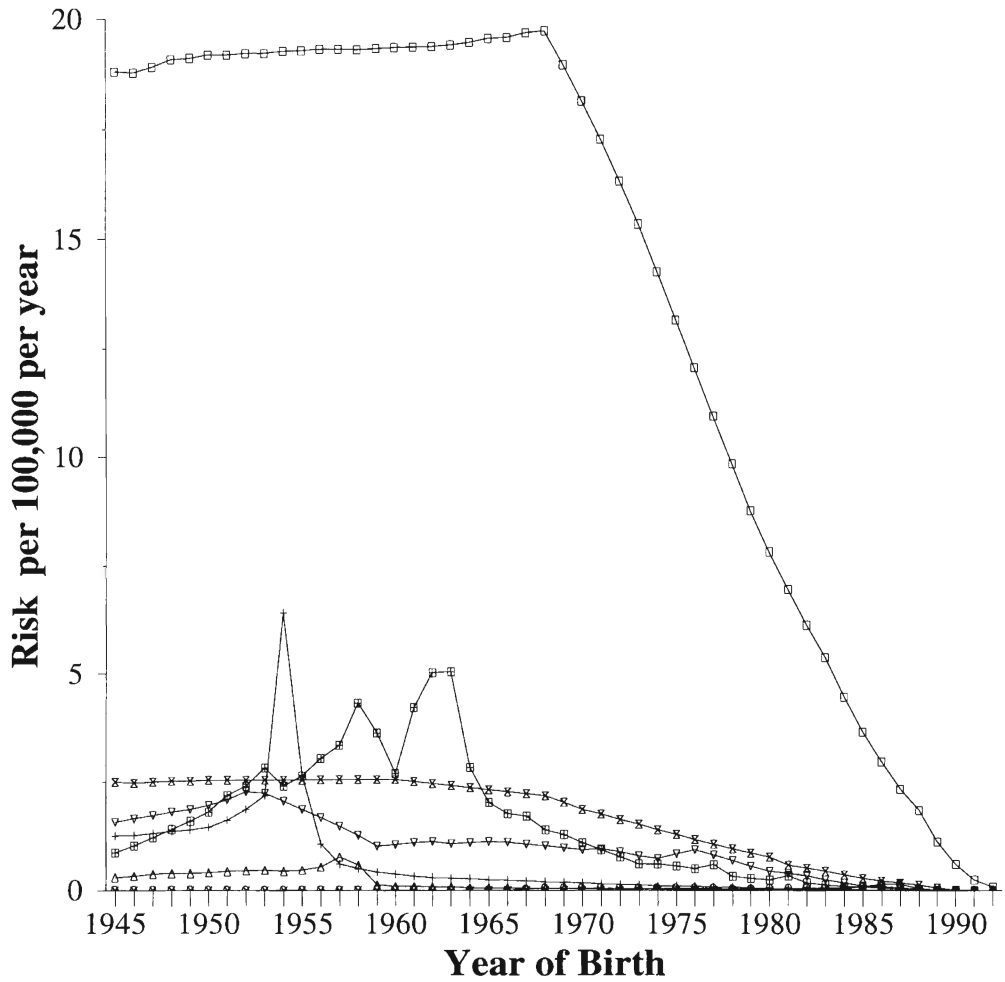
RESULTS OF RISK CALCULATIONS

3.60 Figures 3.7 and 3.8 show the individual red bone marrow low LET dose and associated risk of leukaemia or non-Hodgkin's lymphoma incidence, summed up to age 24 years or 1992 inclusive (whichever is sooner), by year of birth and source of radiation. For each birth year, the main contribution to the doses and risks is from natural radiation. As an aside, the reason for the year-by-year variation in the risks from natural radiation is the use of calendar year-specific baseline mortality rates. Among the other sources, medical exposures comprise the main component for most years of birth, although the uranium oxide releases and weapons fallout show peaks for those born in 1954 and in the late 1950s/early 1960s respectively.

Figures 3.7 INDIVIDUAL RED BONE MARROW DOSE UP TO 25TH BIRTHDAY OR 1992 INCLUSIVE, WHICHEVER IS SOONER, BY YEAR OF BIRTH AND SOURCE (LOW LET)

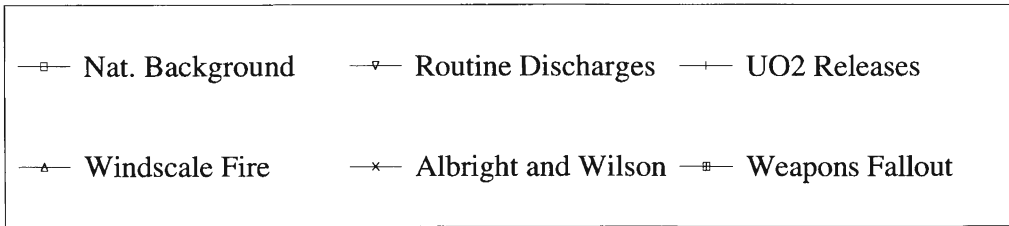
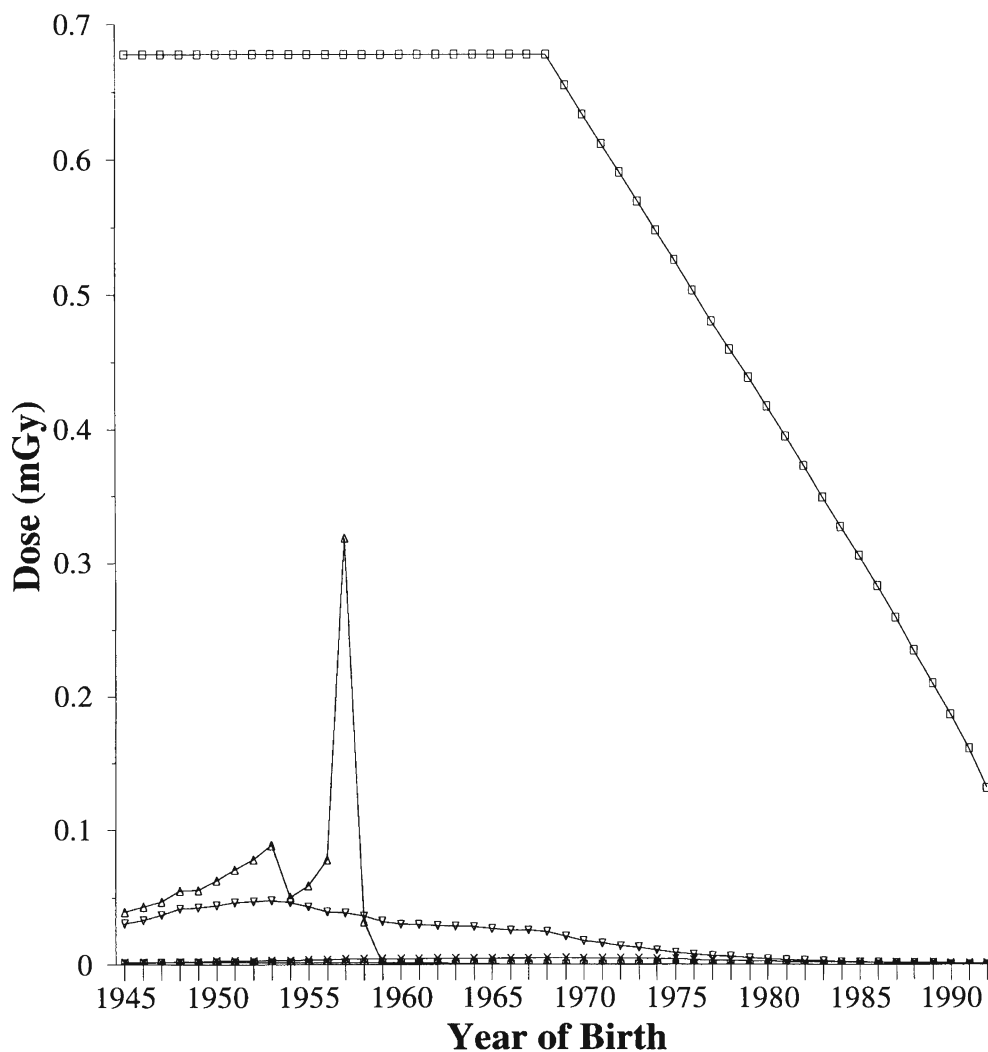


Figures 3.8 INDIVIDUAL RISK OF LEUKAEMIA/NHL INCIDENCE UP TO 25TH BIRTHDAY OR 1992 INCLUSIVE, WHICHEVER IS SOONER, BY YEAR OF BIRTH AND SOURCE (LOW LET)

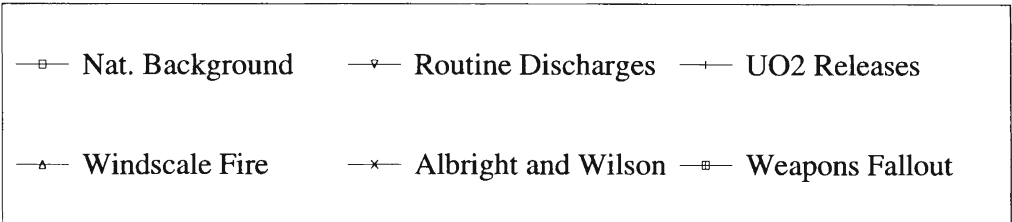
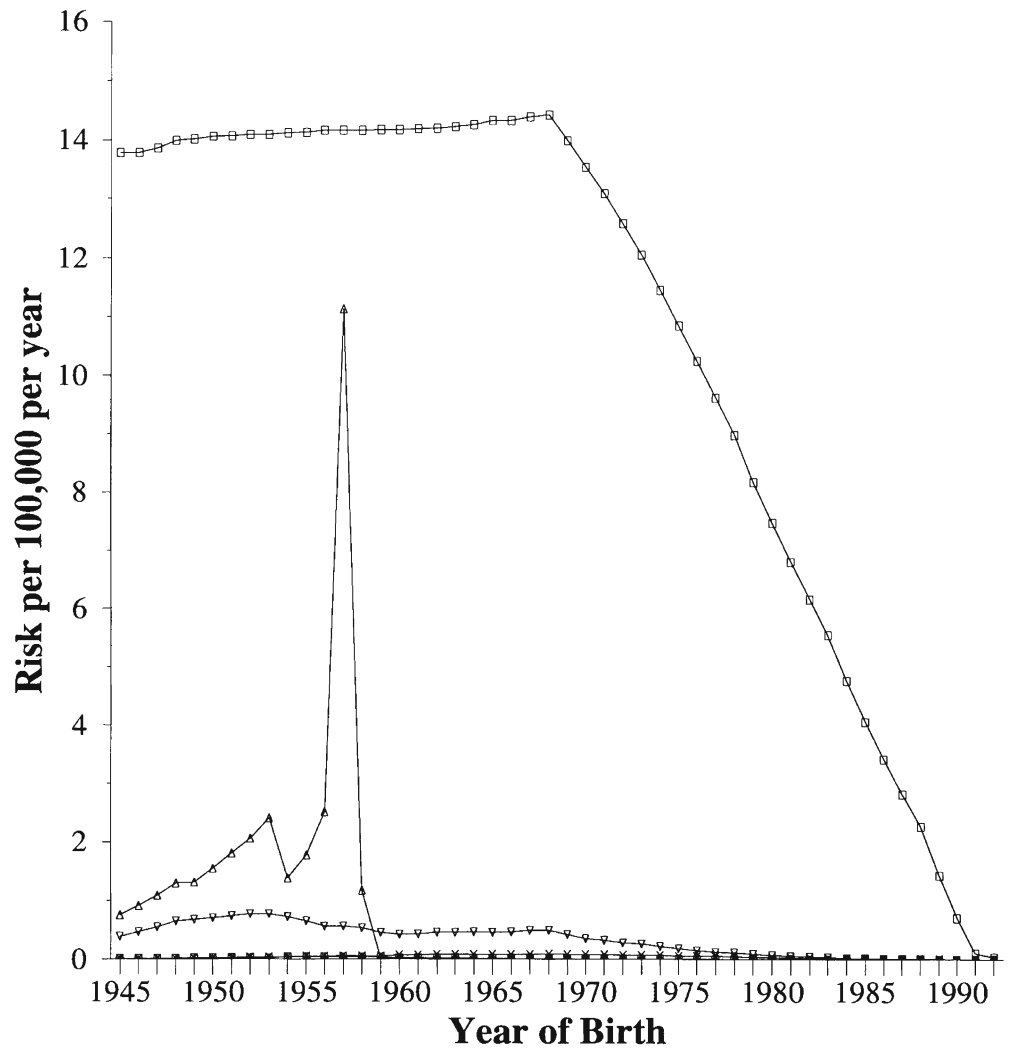


3.61 Figures 3.9 and 3.10 show doses and risks in the same format as for figures 3.6 and 3.7, but based on high LET rather than low LET radiation. Again natural radiation makes the largest contribution to the doses and risks for each year of birth. For those born in 1957, the Windscale fire makes a sizeable contribution, owing to doses from polonium-210. However, for those born in other years, the influence of the Windscale fire on doses and risks is considerably less. Of the other sources of radiation, only routine discharges give rise to values that are appreciably different from zero.

Figures 3.9 INDIVIDUAL RED BONE MARROW DOSE UP TO 25TH BIRTHDAY OR 1992 INCLUSIVE, WHICHEVER IS SOONER, BY YEAR OF BIRTH AND SOURCE (HIGH LET)



Figures 3.10 INDIVIDUAL RISK OF LEUKAEMIA/NHL INCIDENCE UP TO 25TH BIRTHDAY OR 1992 INCLUSIVE, WHICHEVER IS SOONER, BY YEAR OF BIRTH AND SOURCE (HIGH LET)



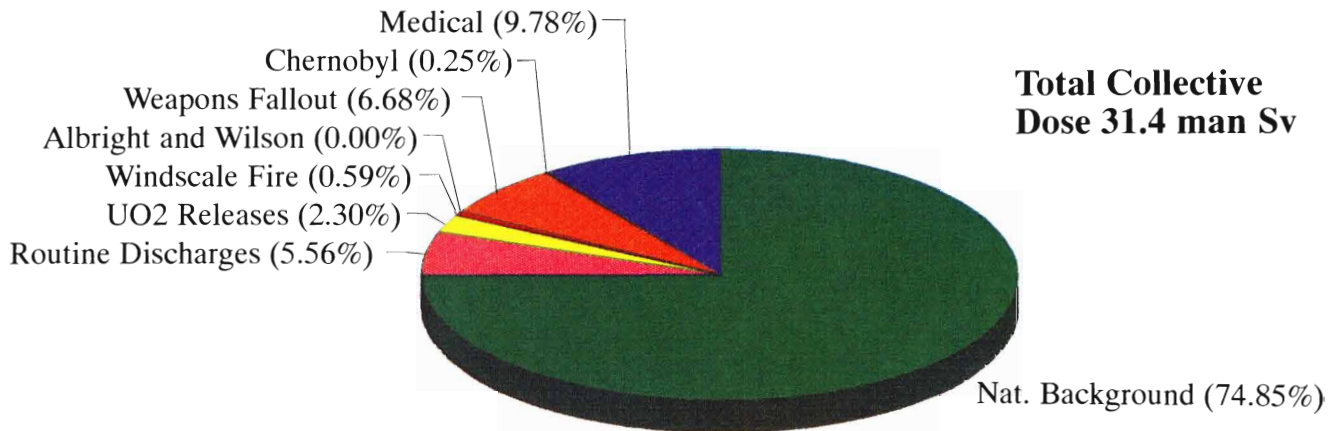
3.62 Figures 3.11 and 3.12 and Table 3.6 display the high and low LET doses and risks of leukaemia and non-Hodgkin's lymphoma for young persons in Seascale, summed over all years of birth. The calculated total number of fatal cancers (0.36) in Table 3.6 is greater than the value of 0.1 given in NRPB-R171 Addendum mainly for the following reasons:

- i. the reassessment covers a longer period of follow-up (to the end of 1992 rather than to the end of 1979) and wider age range (0-24 years rather than 0-19 years), as well as including those born from 1980 onwards. As explained in paragraph 3.59, the population size (and hence the calculated number of cancers) at ages 20-24 years may be an over estimate.
- ii. whilst the risk factor for leukaemia mortality derived from applying the revised risk models to baseline rates for recent years is similar to the NRPB R171 risk factor, applying these models to baseline rates in earlier years - when most leukaemias were fatal - yields a higher risk factor over that period. In this regard, it can be noted from Table 3.6 that the ratio of the calculated fatal to incident cases varies between sources according to whether the associated doses were received predominantly either many years ago (e.g. from the Windscale fire) or in recent years (eg. from Chernobyl) or whether they were spread more evenly over time (eg. from natural background).
- iii. NHL has been combined with leukaemia in Table 3.6; however, the calculated risks for leukaemia and NHL combined are only about 20% higher than those for leukaemia alone.
- iv. some increase is due to the raised levels of some radionuclides in the discharge reassessment
- v. high LET doses from natural background radiation, which form the majority of the total high LET dose, are higher than in NRPB-R171 addendum, owing mainly to an increase in the factor used for the dose per unit intake for polonium-210.

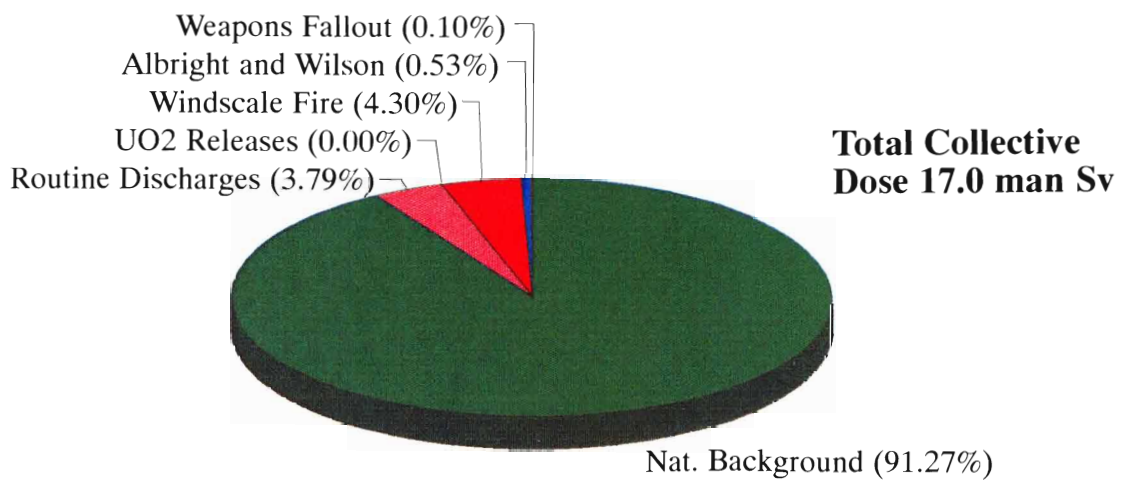
However, it should be noted that there was also an increase in high LET dose due to the higher estimate of polonium-210 released from the Windscale fire and the larger estimates of aerial plutonium discharges. As an aside, it has been calculated based on the BEIR V risk model (BEIR, 1990) used here that over 30% of leukaemia cases in the USA at ages 11-28 years may be attributable to natural radiation (Darby, 1991). This percentage is similar to that arising from Table 3.6, that is 34%, due to about 20% from natural low LET radiation and about 14% from natural high LET radiation.

Figures 3.11 PERCENTAGE CONTRIBUTION FROM DIFFERENT SOURCES TO THE COLLECTIVE RED BONE MARROW DOSE UP TO 25TH BIRTHDAY OR 1992 INCLUSIVE, WHICHEVER IS SOONER, SUMMED OVER ALL COHORTS

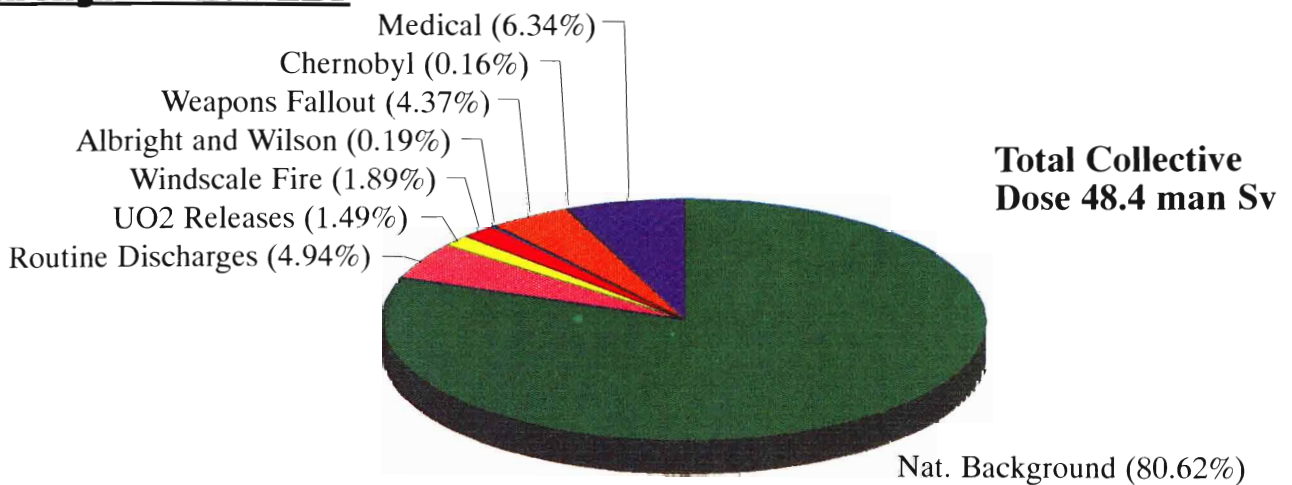
Low LET



High LET

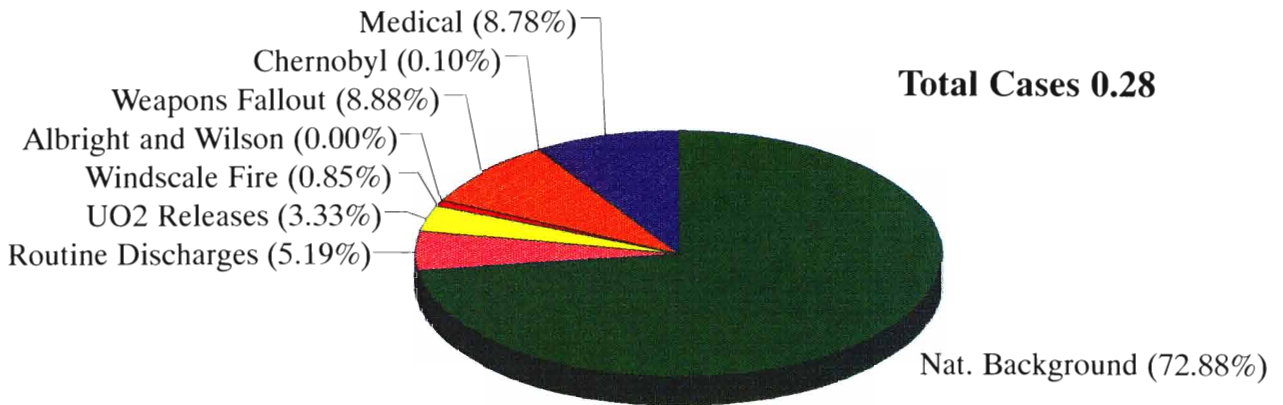


Both High and Low LET

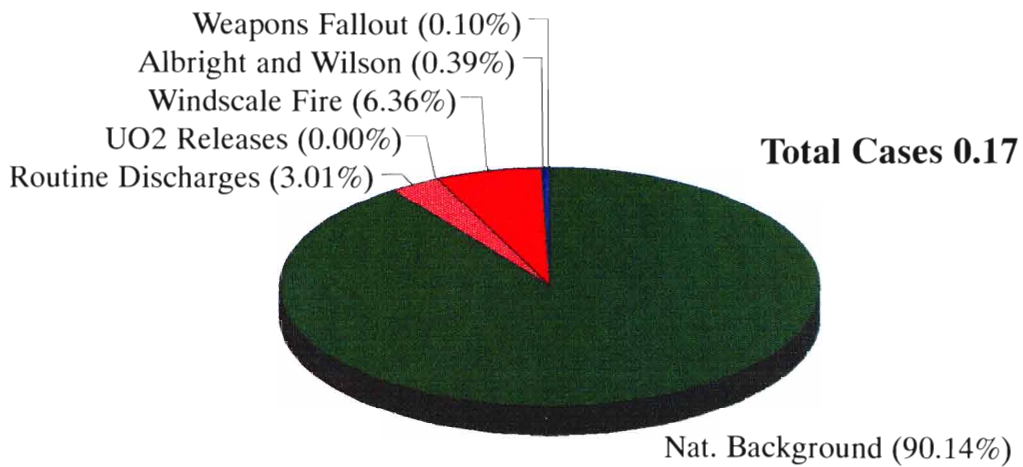


Figures 3.12 PERCENTAGE CONTRIBUTION FROM DIFFERENT SOURCES TO THE ESTIMATED NUMBER OF RADIATION-INDUCED LEUKAEMIA/NHL CANCER INCIDENCES, UP TO 25TH BIRTHDAY OR 1992 INCLUSIVE, WHICHEVER IS SOONER, SUMMED OVER ALL COHORTS

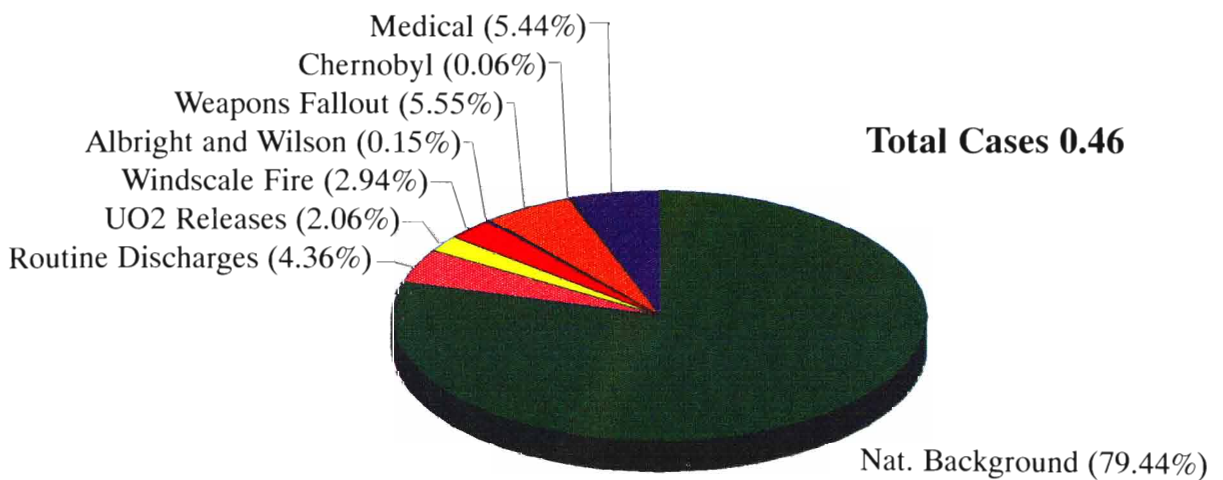
Low LET



High LET



Both High and Low LET



3.63 Figure 3.13 and Table 3.8 display the calculated risks from radiation exposure of all cancers other than leukaemia and NHL. For most sources, the main contributions to the risk are from bone cancer and from a ‘remainder’ category that includes central nervous system tumours. An exception to this pattern arises for the Windscale fire, for which most of the calculated risk is contributed by thyroid cancer. The total risk of mortality from cancers other than leukaemia and NHL in Table 3.8 is lower than the corresponding total in NRPB-R171 Addendum, namely about 0.15, mainly because the revised risk models imply low risks for solid cancers, such as those of the lung and colon, for which the baseline rates are low among young persons. In the case of cancer incidence, the main contributions to the total calculated risk are from skin and thyroid cancers, both of which are generally non-fatal.

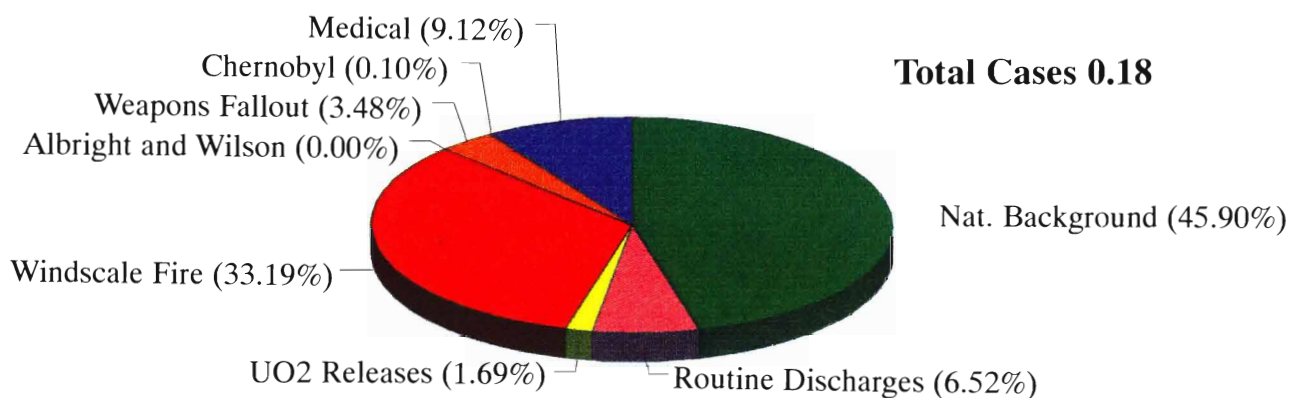
Table 3.8 Risks of all cancers other than leukaemia and non-Hodgkin’s lymphoma up to the 25th birthday or to 1992 (inclusive), whichever is sooner, in a cohort of 1348 persons

Source	Expected no. of fatal cancers LET			No. of incident cancers Both LETs
	High	Low	Both	
Routine discharges	0.002	0.002	0.004	0.01
UO ₂ release	7.1 x 10 ⁻⁷	0.001	0.001	0.003
Windscale fire	0.0004	0.006	0.007	0.06
Albright and Wilson	0.0002	1.3 x 10 ⁻⁷	0.0002	0.002
Weapons fallout	2.4 x 10 ⁻⁵	0.002	0.002	0.007
Chernobyl	-	2.7 x 10 ⁻⁵	2.7 x 10 ⁻⁵	0.0002
Medical	-	0.005	0.005	0.002
Natural background	0.02	0.02	0.04	0.12
Total	0.02	0.03	0.05	0.22

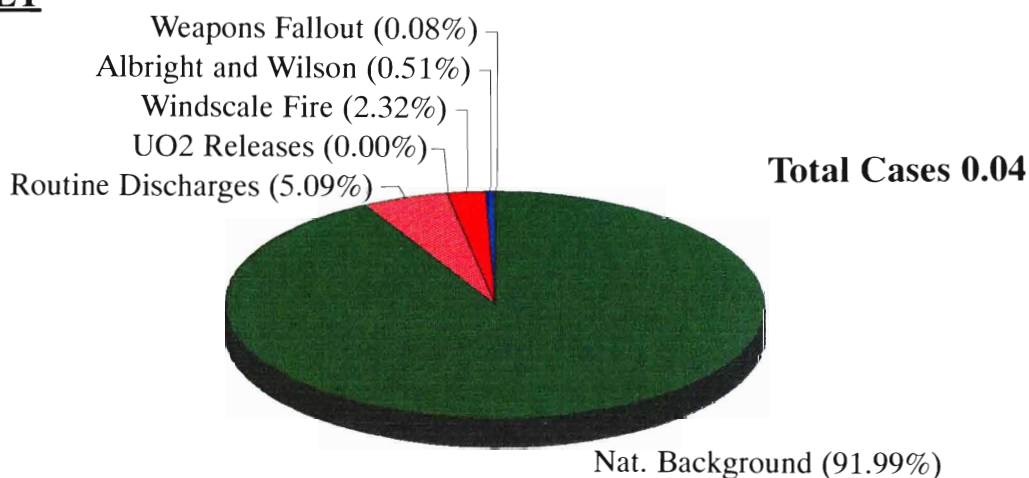
Expected number of cancers based on national rates: 1.08 2.58

Figures 3.13 PERCENTAGE CONTRIBUTION FROM DIFFERENT SOURCES TO THE ESTIMATED NUMBER OF INCIDENT RADIATION-INDUCED CANCERS OTHER THAN LEUKAEMIA/NHL, UP TO 25TH BIRTHDAY OR 1992 INCLUSIVE, WHICHEVER IS SOONER, SUMMED OVER ALL COHORTS

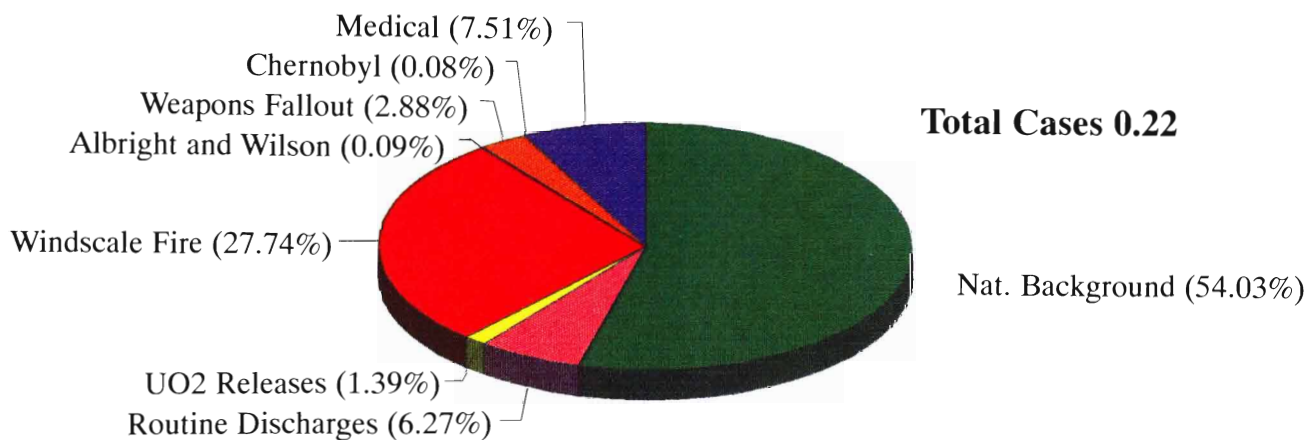
Low LET



High LET



Both High and Low LET



SENSITIVITY ANALYSIS

3.64 The paragraphs above describe the main assessment of the doses and risks to the population of Seascale as carried out by NRPB. They also undertook a sensitivity analysis concerning certain radionuclides and pathways previously agreed with COMARE, to investigate factors which could lead to an increase in doses from Sellafield operations. The results of this sensitivity analysis are given below.

3.65 There are many thousands of input parameters included in the main assessment. It is, therefore, important to limit the sensitivity study to the most important parameters. NRPB have performed scoping calculations of the radiation doses to determine the changing profile of dose with time and the key years which warrant further study. The most important pathways and parameters contributing to dose have been identified by a detailed analysis of the results for specific years. This process has identified a number of parameters which are likely to have a particular impact on the dose and consequent assessment of risk. These factors are discussed together with additional parameters identified during the course of the assessment.

Routine Discharges from Sellafield

Discharges in the 1950s

3.66 NRPB calculated that the highest inhalation and external doses from routine discharges from Sellafield occurred during the early 1950s, with a peak in 1955. NRPB was informed that the plutonium-239 discharges were upper estimates based on immediate counting of filter papers which would include a contribution from radon progeny. The discharges were, in addition, increased by a factor of 8 from the levels predicted by sampling to take account of the efficiency of sampling. The effect of different assumptions regarding the magnitude of the discharge were considered. For plutonium-239 the implications of a different particle size and lung class were also considered.

3.67 BNFL were consulted about the likely range of plutonium-239 and argon-41 discharges during the 1950s. NRPB were informed that the plutonium-239 discharges were upper estimates. The discharges have been increased by a factor of 8 from the levels predicted from sampling data, to take account of the low efficiency of sampling at that period in time. However, although the sampling techniques were likely to sample smaller particles most effectively, the sampling efficiency factor also takes account of larger particle sizes discharged. The intakes were calculated on the basis that all of the material discharged was respirable. As a result, the actual intakes may be as much as a factor of 10 smaller than those estimated for the main assessment. It would, therefore, seem to be unreasonable to increase these intakes further. The assumed particle size is also unlikely to be a sensitive parameter. For the main assessment, an aerodynamic diameter of 1 μm Activity Median Aerodynamic Diameter (AMAD) has been assumed. This is consistent with a relatively high absorption of material from the lung. The actual discharges are likely to have contained a larger fraction of large particles than was assumed and these particles would have lower absorption rate than the smaller particles.

3.68 The argon-41 discharges have been estimated on the basis of a known power loading in the reactors and a relationship between power and argon-41 discharge derived by UKAEA. BNFL estimate that the discharge data used in the main assessment are likely to be correct to within 25%. The external dose predicted for 1955 in the main assessment and a maximum predicted value are given in table 3.9.

Table 3.9 Predicted external doses in 1955 from release of argon-41

	Main assessment dose (Sv)	Maximum predicted dose (Sv)
All age groups	1.8×10^{-4}	2.3×10^{-4}

3.69 It should be noted that the NRPB assessment of doses from argon-41 discharges assumed a stack height of 80 metres; however, the chimneys of the Windscale piles were much taller. The temperature of the release also added to the physical height giving an effective release height of about 200 m. This would have led to external doses to Seascale residents from argon-41 which were approximately 40% of the dose in the main NRPB assessment. In order to put these data into context the doses from inhalation and ingestion, integrated to the age of 25 for this year are given below.

Table 3.10 Predicted doses resulting from routine discharges in 1955

	Ingestion dose (Sv)	Inhalation dose (Sv)	Total dose (Sv)
Infant	1.2 10 ⁻⁵	7.1 10 ⁻⁵	2.7 10 ⁻⁴
5 Year old	9.3 10 ⁻⁶	1.3 10 ⁻⁴	3.2 10 ⁻⁴
10 Year old	1.5 10 ⁻⁵	8.2 10 ⁻⁵	2.8 10 ⁻⁴
Adult	1.3 10 ⁻⁵	5.4 10 ⁻⁵	2.5 10 ⁻⁴

Discharges of Tritium - Effect of Varying Biological Activity

3.70 BNFL were consulted about the magnitude of tritium discharges to the atmosphere and to the marine environment. The estimated discharges have been revised to take account of additional tritium sources identified by BNFL. The data presented here take account of both these revised discharges and the inclusion of the ingestion pathway. In the main assessment, the contribution of tritium was considered for inhalation only. For the purposes of this study, ingestion doses have been estimated on the basis of a specific activity model. This implicitly assumes that tritium is present as tritiated water and freely exchanges with the environment. The ingestion of organically bound tritium has been taken into account by increasing the predicted intake by 25%. This factor is based on experimental evidence on the build up of organically bound tritium in materials and predictions from a dynamic model developed at NRPB (Higgins *et al*, 1996). The organically bound fraction has a dose per unit intake factor two times greater than tritium present as tritiated water.

3.71 The highest doses from tritium occurred during the 1950s. The predicted dose to the red bone marrow of an infant, from routine discharges of tritium in 1955 is 1.7 µSv. For comparison purposes, the dose estimate corresponding to the inhalation pathway, based on assumptions in the main assessment, is 0.003 µSv. It is possible to make maximising assumptions about the proportion of tritium intake assumed to be organically bound. If the total estimated intake of tritium at equilibrium were assumed to be organically bound, the predicted dose would be 2.4 µSv.

3.72 The possibility of the attachment of tritium to DNA in cells leading to more localised irradiation of specific cells has been discussed. There is contradictory evidence on the impact of this on the dosimetry. *In vitro* experiments have suggested that doses may be increased by a factor of 8. However, studies conducted over longer periods have suggested that the doses from tritiated water may be of a similar order. Other evidence suggests an enhanced dose factor of between 2 and 6. Thus, the most pessimistic (and unrealistic) scenario would be to assume that available tritium is entirely organically bound and attached to DNA. This would result in an increase in the estimated dose of a factor of 16, giving a dose of 19 µSv. This should be compared with 270 µSv received from other routine exposure pathways during this year.

3.73 The intakes of tritium may also be compared with intakes from natural sources and fallout. The intakes of tritium during the peak period of discharge represented by 1955 are as follows.

Table 3.11 Intakes of tritium (kBq) from routine, natural and fallout sources in 1955 and from the Windscale Fire in 1957

	Routine	Natural	Fallout	Windscale Fire
Infant	25	0.2	1.3	120
5 Year old	31	0.3	1.9	380
10 Year old	34	0.4	2.2	430
Adult	41	0.5	2.8	650

Note: Intakes from fallout were a factor of 33 higher in the peak year (1962)

3.74 It is useful to note that the difference in the infant and adult intakes of tritium from the Windscale Fire is the result of a combination of two factors. Inhalation was the most important intake route and the adult inhalation rate is the higher. (The importance of the inhalation pathway here is due to the accident situation and single release scenario). Moreover, the consumption of locally produced milk was banned in the three months following the fire, which significantly reduced the predicted infant intake from ingestion.

**Uranium oxide
Discharges - Effect of
Magnitude of Release
and Respirable
Fraction**

3.75 The inhalation and ingestion doses based on the main assessment assumptions are presented for comparison purposes. The ingestion doses are based on monitoring results, and therefore are not sensitive to changes in the assumed discharge. The inhalation doses, however, are dependent upon both the assumed magnitude of the release and the particle size and lung class. The inhalation dose is dominated by the intake of plutonium-239, the dose from which is unlikely to be significantly affected by changing assumptions regarding particle size and lung type, as discussed above.

3.76 As a result, the only parameters which need to be considered further in this study are the magnitude of material released and the proportion assumed to be respirable. BNFL were approached to provide ranges on these data. BNFL indicated that the highest reasonable estimate of the discharge may be up to a factor of 1.5 times higher than the 20 kg release assumed in the main assessment. Higher estimates have been made in the past, but these are not supported by environmental monitoring information. In the main assessment, 5 per cent of the activity released is assumed to be within the respirable range. BNFL confirmed that this is the most reasonable estimate, but gave an upper value of 15 per cent for the purposes of this study. This gives a maximum predicted inhalation dose of 4.5 times the value presented in the main assessment as given in table 3.12. This dose is still two orders of magnitude lower than the ingestion dose predicted for this source.

Table 3.12 The inhalation and ingestion doses received during 1954 based on a discharge of 20kg uranium oxide

	Ingestion Dose (Sv)	Inhalation Dose (Sv)
Infant	$5.0 \cdot 10^{-4}$	$2.9 \cdot 10^{-7}$
5 year old	$2.3 \cdot 10^{-4}$	$5.1 \cdot 10^{-7}$
10 year old	$2.8 \cdot 10^{-4}$	$3.9 \cdot 10^{-7}$
Adult	$1.9 \cdot 10^{-4}$	$3.0 \cdot 10^{-7}$

Additional Radionuclides

3.77 The marine discharges of two radionuclides, not considered in the main assessment, have been considered as part of the sensitivity study. The nuclides of particular interest are tritium and polonium-210. The doses from tritium were addressed above. The marine pathways do not contribute significantly to the doses from tritium. The impact of routine discharges is dominated by terrestrial foods.

3.78 The peak marine discharge of polonium-210, of $4.2 \cdot 10^{11}$ Bq, occurred in 1957. This includes a contribution from the Windscale Fire of around $1.1 \cdot 10^{11}$ Bq. The discharge in 1956 and 1958 was of a similar order ($3.5 \cdot 10^{11}$ and $2.6 \cdot 10^{11}$ Bq respectively). The doses resulting from these discharges are therefore considered in the context of the routine doses received in the same years.

3.79 The infant ingestion dose from polonium-210 in 1957 was calculated to be $1.6 \cdot 10^{-7}$ Sv. This value may be compared with the main assessment ingestion dose from routine discharge of $1.3 \cdot 10^{-5}$ and the total dose of $2.4 \cdot 10^{-4}$ Sv. The inclusion of this radionuclide does not, therefore, significantly affect the results.

Releases in 1975 - Effect of varying intake pathways on dose

3.80 A number of additional intake pathways were considered for the representative year of 1975, which constitutes the year of highest ingestion dose. The following additional pathways were taken into account:

1. High intakes of marine foods
2. Deliberate ingestion of soil and sand by infants (*pica*)
3. Inhalation and ingestion of house dust
4. The transfer of activity to infants through breast milk

3.81 The influence of different gut transfer factors was also considered, as described below. These additional doses should be considered in the context of the doses estimated from the assumptions of the main assessment, summarized in Table 3.13.

Table 3.13 Predicted red bone marrow doses from routine releases from Sellafield in 1975

	Ingestion dose (Sv)	Inhalation dose (Sv)	External dose (Sv)	Total dose (Sv)
Infant	$3.5 \cdot 10^{-5}$	$6.3 \cdot 10^{-6}$	$1.2 \cdot 10^{-5}$	$5.2 \cdot 10^{-5}$
5 year old	$9.1 \cdot 10^{-5}$	$1.1 \cdot 10^{-5}$	$1.2 \cdot 10^{-5}$	$1.1 \cdot 10^{-4}$
10 year old	$1.3 \cdot 10^{-4}$	$7.2 \cdot 10^{-6}$	$1.2 \cdot 10^{-5}$	$1.5 \cdot 10^{-4}$
Adult	$2.7 \cdot 10^{-4}$	$4.3 \cdot 10^{-6}$	$1.2 \cdot 10^{-5}$	$2.9 \cdot 10^{-4}$

High intakes of marine foods

3.82 The maximum intake rates of marine foods presented in NRPB-R171 were used to estimate the maximum doses from this source to each age group. These intake rates are higher than the MAFF critical group intake rates for the 1970s. They have been enhanced to take account of the possibility of higher intakes of marine foods during earlier years. The concentrations of activity in foods was lower in earlier years, and thus the data presented in table 3.14 below are representative of the maximum likely dose.

Table 3.14 Maximum red bone marrow dose estimated for marine foods ingestion using activity concentration data for 1975

Age group	Ingestion dose (Sv in one year)
Infant	$1.1 \cdot 10^{-3}$
5 year old	$5.3 \cdot 10^{-3}$
10 year old	$6.5 \cdot 10^{-3}$
Adult	$1.0 \cdot 10^{-2}$

Ingestion of soil and sand by infants

3.83 The main assessment takes account of inadvertent ingestion of soil. The deliberate ingestion of soil by children was not considered in the main assessment because this pathway affects only a few children. Moreover, it is a recognised medical condition which lasts for a relatively short time. The concentrations of activity in soil were calculated from the source-specific soil concentrations calculated for the main assessment. The sand concentrations were directly available from the main assessment. The deliberate ingestion of soil and sand is a medical condition known as *pica* (for the calculations given here, *pica* was assumed to last 6 months). An intake rate of 20 g d^{-1} was assumed to apply for a period of 6 months (Healy, 1977). Information available from BBC surveys indicates that children generally spend around 10% of their time outdoors. It was assumed that soil ingestion will occur only during this period, implying an ingestion rate of 8.3 g h^{-1} during the 15 hours spent on the beach during the six month period when *pica* occurred.

Table 3.15 Doses to the red bone marrow from the deliberate ingestion of soil and sand during 1975

	Dose from ingestion of soil (Sv)	Dose from ingestion of sand (Sv)
Infant with pica	$5.2 \cdot 10^{-5}$	$1.8 \cdot 10^{-4}$

The total dose from deliberate ingestion of soil and sand of 2.3×10^{-4} Sv should be compared with the infant dose in the main assessment of 5.2×10^{-5} Sv. The inclusion of this pathway would, therefore, increase the total infant dose by a factor of 5. The possibility of the ingestion of silt has also been considered. This pathway would lead to a dose of around 1.9×10^{-3} Sv. However, there is little silt available on the beaches around Seascale and this dose should be viewed with caution as a maximum value.

Inhalation and ingestion of house dust

3.84 During 1984/85 Imperial College, London undertook a survey of the concentration of plutonium-239 and plutonium-240 in house dust and garden soil in a number of communities in Cumbria (Goddard *et al*, 1986). This information has been used to derive a ratio between the activity concentration in house dust to that in soil for 1985 and then to extrapolate this ratio to estimate levels of radionuclides in house dust in earlier years. The most conservative case was used to estimate a house dust concentration based on the soil concentration in 1975. These results imply doses which are extremely small (Table 3.16). In fact two further house dust surveys have been carried out in 1989 by ICI (Heslop and Reed, 1994) and in 1985 by NRPB (Fry *et al*, 1985). The earliest survey by Imperial College showed the highest level of house dust contamination and thus these data were used for the dose calculations. We have reviewed the evidence from these studies for worker and non-worker homes in Seascale and noted that low levels of some radionuclides not normally detected in the general environment have been found in some houses. However, it is not clear whether these findings can be attributed to transfer from the general environment or whether some component was transferred by workers to their homes.

Table 3.16 Maximum doses from inhalation and ingestion of house dust in 1975

	Inhalation dose to an adult (Sv)	ingestion dose to an infant (Sv)
Strontium-90	3.4×10^{-8}	3.1×10^{-6}
Caesium-137	3.5×10^{-9}	3.5×10^{-7}
Plutonium-238	1.8×10^{-7}	3.8×10^{-7}
Plutonium-239	1.7×10^{-6}	3.7×10^{-6}
Americium-241	5.8×10^{-7}	1.6×10^{-6}
Total	2.6×10^{-6}	9.3×10^{-6}

Transfer of activity through breast milk

3.85 The potential of an infant receiving an enhanced intake of radionuclides through breast milk has been considered. The highest intake is likely to arise from a mother who is a high consumer of local marine foods. The Ministry of Agriculture, Fisheries and Food have undertaken surveys of the population around Sellafield for a number of years. This information has been used to specify a high intake rate representative of the 1970s. An intake of 41 kg y^{-1} for both cod and plaice and of 15 kg y^{-1} of crab was assumed for the mother. Concentrations in fish and shellfish estimated for the main assessment were used to estimate the intake of the mother. Information on the transfer of activity to milk was reviewed. The most recent information is contained in a report to the

International Union of Radioecologists (Gall, 1990). This suggests a mean transfer, expressed as the fraction of the mother's uptake transferred to each litre of milk per day, for caesium-137 of 0.8 d l^{-1} . However, the caesium body content also affects the transfer to milk. Assuming equilibrium, a transfer factor of 0.37 d l^{-1} was used. A value of 0.4 d l^{-1} was used for transfer of strontium-90 and $5.8 \cdot 10^{-5} \text{ d l}^{-1}$ and 10^{-5} d l^{-1} for plutonium and americium isotopes. The intake of breast milk was assumed to be 200 kg during the first year of life, based on information in a paper by Paul (1988).

3.86 In table 3.17 the predicted doses to the infant consuming breast milk from a high rate consumer of marine foods is compared with the dose to an infant from milk from an average consumer of marine foods, and from intake from a cow.

Table 3.17 Doses to an infant from breast milk and cows milk during 1975

Dose from milk from high rate consumer of marine foods (Sv)	Dose from milk from average consumer of marine foods (Sv)	dose from cows milk (Sv)
$3.8 \cdot 10^{-4}$	$4.4 \cdot 10^{-5}$	$1.4 \cdot 10^{-6}$

Implications of different gut transfer factors

3.87 The most important radionuclides contributing to the ingestion doses from routine releases from Sellafield in 1975, were identified as caesium-137 and caesium-134, strontium-90, plutonium-239 and americium-241. Together these radionuclides represent 97% of the infant ingestion dose during the year in question. A maximum value for the gut transfer of each of these radionuclides was determined. For each of these radionuclides, the red bone marrow dose was found to vary linearly with the gut transfer factor. Therefore, the variation of dose with change in f_i may be assessed by simple scaling. For the purposes of this study, gut transfer factors of 1 for all ages (as opposed to 0.6 for infant and 0.4 for children and 0.3 for adults) for strontium-90 and $3 \cdot 10^{-3}$ and $1 \cdot 10^{-2}$ for adults and infants respectively (as opposed to $5 \cdot 10^{-4}$ and $5 \cdot 10^{-3}$) were assumed to apply for both plutonium-239 and americium-241 respectively. The caesium isotopes are assumed to have a gut transfer factor of 1 in the main assessment and cannot be increased further. Therefore, the data presented for caesium radionuclides in table 3.18 below are consistent with the main assessment.

Table 3.18 Red bone marrow doses from ingestion in 1975 assuming enhanced gut transfer factors (Sv)

	Sr-90	Cs-134	Cs-137	Pu-239	Am-241
Infant	$5.3 \cdot 10^{-6}$	$4.7 \cdot 10^{-6}$	$2.2 \cdot 10^{-5}$	$2.1 \cdot 10^{-6}$	$5.8 \cdot 10^{-6}$
5 year old	$2.3 \cdot 10^{-5}$	$9.7 \cdot 10^{-6}$	$4.2 \cdot 10^{-5}$	$4.2 \cdot 10^{-5}$	$1.1 \cdot 10^{-4}$
10 year old	$6.3 \cdot 10^{-5}$	$1.4 \cdot 10^{-5}$	$5.7 \cdot 10^{-5}$	$4.6 \cdot 10^{-5}$	$1.2 \cdot 10^{-4}$
Adult	$1.0 \cdot 10^{-4}$	$4.1 \cdot 10^{-5}$	$1.7 \cdot 10^{-4}$	$4.3 \cdot 10^{-4}$	$9.2 \cdot 10^{-5}$
Infant dose from these 5 radionuclides = $4.0 \cdot 10^{-5}$ Sv (compared with $3.4 \cdot 10^{-5}$ Sv in main assessment)					

Note: The gut transfer factor of 1 for caesium is assumed, as in the main assessment

The use of enhanced gut transfer factors results in an increase in the ingestion dose of less than 20% for infants, due to the relatively high contribution from caesium radionuclides to the predicted dose. For adults, the predicted increase is greater due to the relatively greater importance of intakes of other radionuclides.

Thoracic lymph node doses due to Sellafield discharges and natural radiation

3.88 It is generally believed that leukaemic cells originate from damaged stem cells in bone marrow (except possibly in the embryo). This is the reason for focusing attention on this organ in the main dose and risk calculations carried out by NRPB. Both the Black Advisory Group and COMARE had previously looked at the doses to the tracheo-bronchial lymph nodes as it was known that these lymph nodes could be the sites of origin for leukaemia and lymphoma in laboratory animals and they are sites which could be subject to exposure of inhaled radionuclides. For this report COMARE asked NRPB to estimate radiation doses to the thoracic lymph tissue for Sellafield discharges and natural background radiation sources.

3.89 Carrying out a full calculation of thoracic lymph node doses for each year, age group and radiation source would have been very time consuming; thus, the doses were calculated for children aged 1 year (integrated to the 25th birthday) for the most important discharge source of irradiation of the thoracic lymph glands, the actinides. The doses from this source peaked in 1955, hence this year was chosen for comparative purposes, along with 1975 a year when discharges from all sources were at or near a maximum. These doses needed to be compared with the doses from the natural alpha emitters polonium-210, lead-210 and radium-226 as well as doses from uranium and thorium, beryllium-7 and sodium-22. Red bone marrow doses from the same radionuclides for the same years were also included as comparators.

3.90 The results are given in Table 3.19. In 1955 plutonium discharges were at their peak and table 3.19 gives the doses from plutonium in both its insoluble form (type S, slow clearance from lung) or moderately soluble form (type M faster clearance from lung). BNFL informed us that in the early years of site operation most plutonium discharged would have been in the type M form but in later years an increasing proportion would have been discharged in the insoluble form (S form). If a worst case scenario is assumed, where all the material was in the S form, in 1955 the doses from plutonium are over 7 times greater than the high LET component of doses from natural sources. However, the doses are less than half the total equivalent dose to the organ from low and high LET components of natural background radiation. In 1975, the high LET and total equivalent doses to the lymph nodes due to natural background are respectively 3 times and 10 times greater than those from plutonium (amounting to 19 µSv).

Table 3.19 Thoracic Lymph Node (TLN) and Red Bone Marrow (RBM) doses from both inhalation and ingestion intakes for a 1 year old, integrated to age 25 years (µSv)

Radionuclide (s)/ (inhalation type)	1955		1975	
	TLN	RBM	TLN	RBM
Pu-239 (M)	12	70	0.6	4.1
Pu-239 (S)	430	5.1	19	1.3
Naturals	56	660	56	660

DISCUSSION

3.91 In their report R276 the NRPB have concluded that the number of cases of leukaemia and NHL expected to have occurred in young people up to their 25th birthday, born in and resident in Seascale, over the time period 1945 to 1992 and attributable to all sources of radiation (natural and man-made) would be 0.46. This estimate has to be compared with the 12 cases of leukaemia and NHL in the Seascale population of young people, identified by the epidemiological studies described in chapter two of this report.

3.92 For the study population, natural background radiation contributes the largest proportion of the risk (79%), whereas the discharges from the Sellafield plant, both authorised and accidental, contribute less than 10 %. Medical exposures are estimated to contribute about 5% and weapons fallout about 6 %. The crucial question is whether the excess of cases of leukaemia and NHL at Seascale as compared to the national average can be accounted for by the discharges. The observed number of cases of leukaemia and NHL occurring among the group of young persons born between 1945 and 1992 and living in Seascale in that same time period is 12. As explained in NRPB R276, this group is taken to be equivalent to the cohort of children born in Seascale between 1945 and 1992, some of whom will have moved away and been replaced by incomers. The expected number of cases of leukaemia and NHL in this group, based on national rates, is 0.49 for 1963-83, 0.16 for 1984-92 and may be approximately estimated as 0.5 for 1945-62. This total of 1.15 expected cases is similar to the total of 1.08 given on page 100 of R276. On either basis, only about one case would be expected in the whole 48 year period and the excess of 11 cases may be compared with approximate estimate of 0.05 cases expected from Sellafield discharges. The risk from the Sellafield discharges (based on the number of excess cases would have to be about 200 times greater than that calculated, if it were to account for this excess of 11 cases. The figure of approximately 200 is subject to considerable uncertainty. First, the observed number of cases (12) should be regarded as an estimate of the occurrence of cases in Seascale which reflects the underlying, unknown risk of ALL/NHL in young people and which is subject to statistical fluctuation; as such it has 95% confidence limits of 6.20 and 20.96. Correspondingly the excess as compared with the expected number is approximately 5 to 20 cases and the confidence limits for the measure of the discrepancy between the excess and what would be expected from the Sellafield discharges are then approximately 100 and 400 respectively. Secondly, the expected number (0.05) is itself subject to uncertainties associated with the estimation of radiation doses and risks as discussed below. On the basis of national rates the expected number of cancers other than leukaemia and NHL is 2.58 (Table 3.8); four cases were observed within the period 1945-1992. This excess of 1.42 may be compared with the 0.07 expected from Sellafield discharges (Table 3.8). However, in this case no useful comparison can be made between these figures since the observed excess of 1.42 for these cancers could easily be explained by chance.

3.93 A further conclusion drawn from the data presented in R-276 and the comparison of the observed and expected numbers of cases of leukaemia and NHL, is that the dose received by the Seascale population from all sources, both natural and man-made, is approximately 25 times too low to account for the observed number of cases.

3.94 Similar comparisons are quoted in the report R171 Addendum and at that time it was considered that the doses from the Sellafield discharges were approximately 250 times too low to account for the observed number of cases. The present value is very similar despite the fact that it is now appreciated that the airborne discharges of plutonium were underestimated during the early years

of site operation and that there have been 3 more cases of leukaemia and NHL diagnosed since the that time. There has also been a variety of other changes to the discharges, dose calculations and risk assessment.

Uncertainties in the estimation of radiation doses and risks

3.95 Both the Black Advisory Group and COMARE have previously emphasised the uncertainties involved in the procedures for estimating doses and risks. For this report we were concerned to discuss the uncertainties remaining in these procedures in the current assessment which takes into account recently acquired additional relevant data. We therefore asked NRPB to undertake various sensitivity analyses of some of the critical or uncertain steps in the assessment. Below we describe the importance of these factors as they relate to each element of the dose and risk assessment.

Measurement or estimate of radioactive discharges to air and sea

3.96 The main points of new information regarding discharge data have been summarised in this chapter. As there is considerably more uncertainty concerning the level of discharge of radionuclides to the air than there is for liquid discharges we have concentrated our discussion and analysis of the uncertainties on the former.

3.97 The main differences from NRPB's assessment for the Black report are due to:-

- changes in effective stack height and sampling efficiency factors of caesium-137 and, strontium-90 discharges
- changes in sampling efficiency factors for remaining particulate discharges for the releases of actinides, fission products and iodine isotopes
- discharges from the B204 building prior to 1964 now estimated from the continuous record of initial total alpha measurements available.
- discharges of carbon-14 (C-14) from reprocessing have been derived from available emission measurements and tree ring measurements.
- a higher value of discharge of plutonium in 1968 because of a discharge from B230.
- review of discharges of sulphur-35 (S-35)
- discharges after 1982 have been added using values reported annually by BNFL
- discharges to sea and predicted air concentrations,

3.98 The estimate of atmospheric discharges are based to some extent on measurements of radionuclides in the environment, particularly in soil cores. We note that these are in good agreement with the revised estimates of plutonium discharges provided by BNFL.

3.99 We asked NRPB to estimate the effect of different assumptions regarding the magnitude of the discharges for the years of highest estimated doses in the early 1950s with a peak in 1955. The inhalation dose was almost entirely due to plutonium 239 and the external dose from argon-41. This resulted in a maximum

predicted external dose for all age groups of 1.25 times the main assessment dose (see table 3.8).

3.100 We also considered possible changes in the uranium oxide discharges up to 1.5 times the 20 kg released assumed in the main assessment. If the respirable range is increased from 5% to 15% the maximum predicted inhalation dose becomes 4.5 times the value presented in the main assessment for the year 1954 (see table 3.17). This value is still two orders of magnitude lower than the ingestion dose predicted for this source.

3.101 One of the possibilities raised by Black was that there might have been undetected discharges that have given rise to doses to the public greatly different to those believed to have occurred. In this assessment, for example, we have found that airborne release of plutonium in the early years were underestimated by a factor of 3 which, as noted previously, was reflected by a similar increase found in measurements of caesium-137 in soil monitoring studies. However, we still consider that it is very unlikely that the Seascale findings can be explained solely on the basis of undetected discharges because the dose estimation procedure relies mainly on measured levels of radioactivity in the environment, rather than on modelling from discharge data.

Improved environmental modelling.

3.102 The most important progress since R171 and Addendum on Environmental Models is the revised polonium-210 (Po-210) uptake in the gut from seafood. As Po-210 is a naturally occurring alpha emitter from the radon decay series this has increased the estimated natural high LET doses to the population.

Historic environmental radionuclide levels on which the dosimetry analysis is based.

3.103 We have reviewed past radionuclide monitoring practices and in particular we note that the soil monitoring studies commissioned by the Department of Health have shown that the levels of Cs-137 in soil samples were approximately 3 times higher than previously expected on the basis of early discharge data. This caesium would be expected to be associated with plutonium releases and this expectation was confirmed when the re-assessment of early plutonium discharges to atmosphere found levels to be about 3 times higher than previously thought.

3.104 The most recent measurements of strontium levels in soil confirmed previous estimates. As strontium would be associated with uranium discharges, these data indicate that the uranium discharges from the Windscale piles were of the same level as those discussed in our first report and NRPB R171 Addendum, as opposed to those in Black and R171. There is no evidence from recent soil sampling to indicate they could have been still higher. These more recent soil core measurements suggest that reliance on environmental monitoring data is more robust than estimates based on discharge data, at least for the long-lived radionuclides such as strontium, caesium, uranium, plutonium and americium, which we have noted are the most important in radiological terms. However, soil core measurement carried out at the present time cannot provide data on short-lived radionuclides, released in the early years of plant operation and which will have decayed to undetectable levels by the present time.

Discharges of tritium

3.105 In the main assessment the contribution from tritium was considered for inhalation only. In the sensitivity analysis, ingestion doses were also considered. The assumptions made were that tritium was present as tritiated water and freely exchanging in the environment. The ingestion of organically bound tritium was accounted for by increasing the predicted uptake by 25%. The possibility of the attachment of tritium to DNA in cells leading to localised irradiation of specific cell has been discussed. There is contradicting evidence as to the impact of this

on dosimetry. The most pessimistic scenario that all available tritium is organically bound and attached to DNA, produces an increase in dose by a factor of 16. However, for the year of highest discharge of tritium 1955, this assumption still only results in an estimated dose of 19 μ Sv. This gives us some assurance that the doses from tritium have not been grossly underestimated.

Specific hypotheses relating to environmental radiation considered previously by COMARE

3.106 Having considered the main advances in knowledge and the remaining uncertainties in the dose and risk estimate procedure, we addressed specific issues previously raised by Black and COMARE which have now been the subject of further research, these being;

- uncertainties in lifestyle data and environmental pathways,
- uncertainties in metabolic models,
- the appropriate RBE for high LET radiation
- varying sensitivities of different tissues.

i Lifestyle and environmental pathways

3.107 A remote possibility discussed by Black which we have addressed is that ingestion and or inhalation of radionuclides has been grossly underestimated as a result of inaccurate lifestyle data. We have considered this possibility in the sensitivity analysis, which has examined pathways by which uptake of certain radionuclides could be maximised, such as high intakes of marine foods, deliberate ingestion of soil and sand by infants, ingestion and inhalation of house dusts and transfer of activity through breast milk. The results of these analyses all implied doses which are extremely small. We conclude that the new data suggest that a gross underestimation of dose, as a result of inaccurate lifestyle data, is extremely unlikely to have occurred.

3.108 An example of such a pathway is transfer of radionuclides in dust from soil and sand to the home where normal habits, especially of children, might lead to inhalation or ingestion. However, from the evidence provided by the household dust surveys, we consider that this now seems highly unlikely, although we can be less confident regarding short-lived radionuclides discharged in earlier years.

ii Uncertainties in metabolic models

3.109 Both the Black Advisory Group and COMARE recognised the inevitable uncertainties involved in estimating the radiation doses attributable to the intake of radionuclides. However, reasonable confidence is provided by the comprehensive reviews and updates of this subject by the International Commission on Radiological Protection (ICRP). The NRPB, in its review of radiation doses reported in R-276, took account of these advances in knowledge since its previous reports R171 and R171 Addendum.

3.110 Nevertheless, to ensure as far as we reasonably could that foreseeable uncertainties would not result in substantial underestimations of dose, the NRPB undertook a Sensitivity Analysis for the major or potentially significant contributors to dose. The results provided additional reassurance that collective doses were most unlikely to have been grossly underestimated.

3.111 It is possible that radionuclides could be distributed in an unexpected way within the body and thus deliver their dose to important biological targets in such a way as to increase the risk of leukaemogenesis above that assumed from use in current biokinetic models. Current models are based on average doses to individual organs or tissues and do not include microdosimetric aspects of non-uniformities of dose or target cells within the tissues. However, we have seen no evidence so far to suggest that such uncertainties are of sufficient magnitude for the Sellafield discharge radionuclides so as to materially affect the assessment,

nor would such an effect be specific to the Seascale population alone.

3.112 In their report, the Black Advisory Group made a calculation of the risks of leukaemia induction up to the age of 20 in Seascale, assuming that all childhood leukaemias in England and Wales were due to background radiation. This produced an estimate of risk approximately 4-6 times greater than that calculated by NRPB, but was still far too small to explain the excess of childhood leukaemias in Seascale. This calculation also assumed that natural and man-made radiation interacts with biological material in the same physical manner. We have considered whether this calculation could be too generalised in assuming that all radiation behaves in the same way and can be equally well represented by tissue equivalent doses. We have also posed the question; could radiation from artificial sources behave in a different way and have different effects from natural radiation? Could some radionuclides or their physicochemical forms, in discharges but not present in either natural background or fallout, behave sufficiently differently on a microscopic scale? However, we have seen no evidence that those radionuclides characteristic of the Seascale environment deviate significantly in the ways just described.

i

ii High LET radiation

3.113 We have in the past drawn attention to the greater uncertainties in estimating doses and risks for high LET radiations than for low LET radiations. The evolution of dose estimates from the time of the Black Advisory Group to the present assessment is illustrated in Table 3.20, using the example of a child born in Seascale in 1950 up to and including age 24. The previous assessment was to the 20th birthday; thus the current assessment represents an extra five years. The table shows a breakdown of the contributions made, from the different sources of radiation, to the equivalent dose to red bone marrow, which is further broken down into high LET and low LET radiation. The changes in dose estimates are attributed to increasing information on radionuclide exposures and biokinetics.

Table 3.20 Contributions to equivalent dose (μSv) to red bone marrow of child born in Seascale in 1950 up to the 20th or 25th birthday, from all radiation sources

	Low LET (μSv)			High LET (μSv)		
	Black Report 1950 + 20 yrs	COMARE 1 1950 + 20 yrs	R276[1995] 1950 + 25 yrs	Black Report 1950 + 20 yrs	COMARE 1 1950 + 20 yrs	R276[1995] 1950 + 25 yrs
Natural Background	20,000	20,000	21,220	940	1,900	13,550
Fallout	2,200	2,300	2,256	34	44	28
Medical	3,900	3,900	2,975	0	0	0
Albright & Wilson	-	-	0.4	-	-	47
Sellafield Discharges	2,600	5,100	3,277	74	320	880
Windscale Fire	560	560	356	280	280	1,246
TOTAL	29,000 μSv	32,000 μSv	30,000 μSv	1,340 μSv	2,600 μSv	16,000 μSv
Discharges+Fire as a % Natural Background	15.8%	28.8%	17.1%	37.0%	31.6%	15.7%

3.114 The most outstanding revisions since the Black Advisory Report have been a 6 fold increase in the estimate of doses from high LET radiation from the Sellafield discharges (including those from the Windscale fire). The estimates of high LET doses from these same sources have increased by a factor of 3.6 since the time of the reassessment carried out for COMARE's First Report. Also, there has been a 14 fold increase in the estimated high LET doses from natural background radiation since the doses reported in the Black Advisory Group report and a seven times increase since the doses reported in COMARE's First Report.

3.115 Contributions to the high LET component of the natural background radiation dose come from lead-210, polonium-210, Radium-226, uranium, thorium, radon and thoron. Estimates of most of these have increased since the Black Advisory Group, particularly the dose from polonium-210 due to an increase in the gut transfer factor and more importantly to improvements in the metabolic models. The estimate of high LET dose from natural background radiation has also been elevated due to further information on radon and thoron.

3.116 Thus, the ratio of doses from Sellafield discharges to those from natural background sources for high LET radiation has decreased since the time of the Black Advisory group report and COMARE's First report. There are also slight general increases in doses shown in table 3.19 because the most recent assessment included individuals aged up to their 25th birthday, compared with individuals aged up to their 20th birthday in the previous assessment.

3.117 Whilst the risk coefficients for low LET radiation are based on a large body of data derived from human populations, the estimated risks from high LET radiation are much less certain, with much more reliance on animal data. Therefore, the potential exists for greater uncertainties in the risks from high LET radiation than for low LET radiation risks.

3.118 The NRPB estimates of risk for leukaemia and NHL have assumed that the ICRP-specified radiation weighting factor (W_R) of 20 for high LET radiation is directly applicable as the RBE for leukaemias in particular. Conversely, the NRPB have also calculated the value of RBE for high LET radiation (alpha particles) which would be needed to explain the excess number of cases in Seascale. This required RBE factor would be approximately 1000.

3.119 However, if we assumed an RBE factor of 100 or more, applied equally to all components of the alpha particle absorbed dose to red bone marrow, then it can be estimated that doses to the population from natural background sources would be predicted to induce more cases of leukaemia and NHL than have actually been found in the UK population. Such a large value of RBE of 1000 is clearly untenable using these arguments, unless there were very large discrepancies in the currently accepted methods of estimating dose to the leukaemogenic target cells (assumed to be uniformly distributed in the red bone marrow) from the artificial alpha emitting radionuclides (Pu & Am) as compared with the natural alpha emitting radionuclides (Po, Rn and short-lived daughters). Such large dosimetric discrepancies are unlikely and would be contrary to evidence for whole organisms (man and animals), cited by NRPB, which indicate an RBE of less than 20.

**iv Different tissues:
Thoracic lymph node
doses**

3.120 The studies carried out by NRPB show that the estimated doses to the thoracic lymph nodes from discharges of plutonium, during the early years of plant operation, could have exceeded those estimated for the high LET component of natural background radiation. This is the only organ site we have

been able to identify where discharge doses may have exceeded background doses. However, even in the most pessimistic case in 1955, the total equivalent dose to the thoracic lymph nodes from natural background radiation is greater than that estimated from plutonium. We know of no human data which clearly identifies human leukaemic cells originating from the thoracic lymph nodes, although it is recognised that many human lymphomas arise from lymph node tissue and these could include thoracic nodes. The doses involved are far too low to be a contributory factor to the Seascale cases. Nevertheless, these dose calculations suggest that thoracic lymph nodes deserve to be included in future dosimetric studies, particularly if any changes were to be made to present assumptions or data regarding the inhalation pathway.

Possible variations in the sources of radiation dose which might be specific to the Seascale population

3.121 We have identified possible pathways of exposure which could lead to higher doses, or routes of exposure liable to high levels of uncertainty, which might allow resulting doses to be considerably underestimated. NRPB have addressed these situations in their sensitivity analysis. None of the estimated doses from these sources and pathways are remotely near the size of the doses which would be required to explain the excess cases.

3.122 The background doses used for comparison with the doses from discharges, fallout and medical exposures in the NRPB dose assessment are for average exposures in the UK. Given the unusual level of childhood leukaemia in Seascale we asked NRPB to examine the data on levels of background radiation in the village, eg. external gamma, radon levels in buildings. NRPB have examined the available data and assured us that the levels are all very similar to the national average and that there are many other places which considerably exceed these levels, for example, considerably higher levels of radon are found in some houses in Cornwall and Devon than in Seascale. These data show that Seascale is not an area of abnormally high background radiation.

3.123 BNFL have examined their records to establish whether any unusual medical procedures or experimental investigations were carried out during the relevant period. We have been assured that no procedures have been undertaken that would produce doses outside the normal clinical range. BNFL have provided intake data from a procedure carried out at UKAEA Windscale in the early 1960s to study, in human volunteers, the effect of sodium alginate in inhibiting the oral uptake of Strontium-85. We asked NRPB to estimate the doses from this procedure. NRPB calculated that the committed equivalent dose to the gonads was approximately 13 μSv , the committed equivalent dose to the bone marrow from participation in the study was approximately 12 μSv and the committed effective dose (ie. whole body dose) approximately 11 μSv . As a result of a proposal made at the Windscale Inquiry in 1977, a study was carried out by BNFL to assess the internal doses arising from ingestion of Caesium-137 present in locally caught fish. Volunteers ate locally caught fish over a period of 4 weeks and their caesium-137 levels were measured. At our request NRPB estimated the doses that would have arisen from these intakes. NRPB calculated that the committed equivalent doses to the gonads and the bone marrow did not exceed 20 μSv and the committed effective doses did not exceed 22 μSv , for any of the volunteers in the study. These are all very low doses and of no radiological significance.

CONCLUSION

3.124 We conclude that the current best estimate of the radiation doses to the Seascale population is far too small to account for the observed numbers of cases of leukaemia and NHL that have occurred in the young people of the village during the period of time studied.

CHAPTER 4

POSSIBLE EFFECTS OF PATERNAL PRECONCEPTION IRRADIATION IN CANCER

INTRODUCTION

4.1 The Black Advisory Group made various recommendations for research to resolve questions that they had identified. These included a recommendation for a case control study to investigate relevant features of the records on cases of leukaemia and lymphoma in the area.

4.2 The Department of Health and the Medical Research Council subsequently funded a study undertaken by Professor Martin Gardner and his colleagues to investigate factors that could be relevant to the development of leukaemia and lymphoma in young children (Gardner *et al.*, 1990a).

4.3 While this study was under way, we noted in our Second Report that many of the people who live near Sellafield and Dounreay were workers at the nearby installations. This raised the possibility that the excess of childhood leukaemia could be related to parental occupation at these nuclear installations. There was no direct evidence for this but we postulated two mechanisms by which such an effect could theoretically be mediated. One of these was unrecognised pathways of radiation exposure, for example by radioactive materials being brought home via workers and this is discussed elsewhere in this report. The second was the possibility of a preconception effect.

4.4 In our Second Report we pointed out that some animal experiments suggested that preconception parental exposure could (in some circumstances) lead to malignancy in offspring by inducing some sort of heritable change. At that time there was no evidence of this from the limited data available in humans, but we drew attention to the possibility that parents occupationally exposed to radiation might be at above average risk of having children with leukaemia and that this needed to be explored.

4.5 This hypothesis was emphasised by Professor Gardner when he discussed the results of his case control study published in 1990.

Gardner case-control study

4.6 From the results of this study Professor Gardner and his colleagues concluded that:

“The raised incidence of leukaemia, particularly, and NHL among children near Sellafield was associated with paternal employment and recorded external dose of whole body penetrating radiation during work at the plant before conception. The association can explain statistically the observed geographical excess. This result suggests an effect of ionising radiation on fathers that may be leukaemogenic in their offspring, though other, less likely, explanations are possible.”

4.7 This result was dominated by four case fathers with exposure of more than 100mSv total preconception dose or estimated by Professor Gardner to be more than 10mSv during the 6 months before conception. A dose-response effect was

also seen in that the highest risk was associated with the highest accumulated radiation doses before conception.

4.8 The authors speculated that:

“Since radiation badge recordings will reflect gonadal dose we interpret this finding to suggest an effect of the radiation exposure on germ cells producing a mutation in sperm that may be leukaemogenic in subsequent offspring”.

However they also pointed out:

“ Other explanations may be possible, such as exposure to internally incorporated radionuclides or other concomitant exposures in the workplace: it has not been possible to examine the first of these so far, and the second seems unlikely...Additionally contamination of the home with radioactive or other material through occupational exposure may be relevant”.

HSE study

4.9 The Health and Safety Executive (HSE), in a subsequent case-control study (HSE, 1993,1994), also found a statistical association between the incidence of childhood leukaemia and NHL and the fathers' total external preconception radiation dose, largely based on the same cases as Gardner *et al.* The controls in this study were children born in West Cumbria between 1950 and 1990 who had not been diagnosed with cancer before the age of 25 and whose fathers had worked at Sellafield. The association, however, was confined to the population of Sellafield workers who started work at the plant before 1965 and who were resident in Seascale at the time of their child's birth. The HSE were provided with more detailed dosimetric data than were available to Professor Gardner. From these data they showed that there was no evidence of any association between father's preconception radiation dose and the incidence of childhood leukaemia and NHL for fathers resident outside Seascale when their child was born. Also, while an association was reported for children born in Seascale between the incidence of these diseases and the father's external radiation dose in the 12-week period before conception, this was not statistically significant. No positive association was found for cancers other than leukaemia and NHL (taken together) nor for any other factors studied such as internal radiation dose, chemical exposures or involvement in contamination incidents.

Paternal Preconception Irradiation (PPI)

4.10 The suggestion that preconception exposure to a mutagen may lead to an increased risk of cancer in the offspring was first made in a study of the outcome of diagnostic X-rays (Graham *et al.*, 1966) and has been the subject of numerous experimental and epidemiological studies. It has become known as the paternal preconception irradiation (PPI) hypothesis and if it were true would imply that radiation-induced mutations occur in the male germ line and cause a predisposition to cancer in the next generation.

4.11 In this chapter we have specifically addressed the possible effects of PPI from either external or internal radiation as an explanation of high incidence of childhood leukaemia in Seascale but we have not discussed the other speculative mechanisms involving workers, namely other occupational exposures or transfer of radioactive or other material to the home via workers. These are addressed in Chapter 3 and Chapter 8.

HUMAN EPIDEMIOLOGY

Paternal radiation exposure

Atomic bomb survivor data

Nuclear workers

4.12 The most substantial body of data regarding preconception radiation effects is derived from studies of the atomic bomb survivors, particularly the work of Yoshimoto and colleagues at the Radiation Effects Research Foundation (RERF) (Yoshimoto, 1990).

4.13 Registration during the period 1948-1953 gave women access to special rations, thus encouraging what is believed to be virtually complete registration. Details of exposure history were obtained, either by interview or mailed questionnaire. There was a wide range of doses (0-6Sv), although over 50% received less than 5mSv. The average doses were 0.07Sv paternal, 0.08Sv maternal. Eight categories of cancer were analysed by Yoshimoto *et al* (1990) and others (Little *et al*, 1994).

4.14 Significant positive trends for cancer in offspring with parental dose were seen only for (a) NHL in the post 1950 births as a function of paternal gonadal dose (this trend was largely attributable to a single case and must therefore be regarded as unreliable) (b) cancers other than leukaemia and NHL in the births up to 1950 as a function of maternal dose. The general applicability of the findings is suspect because in both instances the trends were confined to a single city.

4.15 Several case-control studies carried out before Gardner *et al* used estimated or reported worker exposure (recall-based, which is likely to be less reliable than film badge data). Hicks *et al* (1984) found no link for 'all cancer' in offspring of male workers potentially exposed to ionising radiation. After the publication of the Gardner study McKinney *et al* (1991) found non-significant indications of an excess risk of leukaemia (odds ratio = 2.35, 95% CI 0.92 - 6.22) associated with reported pre-conceptional ionising radiation exposure. There was, however, considerable overlap of cases with those in the Gardner study.

4.16 More recent case-control studies have used recorded worker radiation exposures, which are more likely to give valid results. Urquhart *et al* (1991) in a study (of childhood leukaemia and NHL in Caithness near the Dounreay nuclear installation) which included only 13 cases, found no indication of a positive association with preconception exposure, although the small numbers in each exposure category inevitably limit the confidence in this result. Roman *et al* (1993) in the Berkshire and North Hampshire (the area which includes the Aldermaston and Burghfield nuclear weapons establishment) case-control study of 54 cases of childhood leukaemia and NHL (0-4yrs) found no convincing association with external recorded dose. Kinlen *et al* (1993) in a study of 1369 cases of leukaemia and NHL in Scotland and 4107 matched controls found 11 case fathers and 30 control fathers with preconception radiation exposure and hence no indication of an association with PPI.

4.17 The Ontario case-control study of McLaughlin *et al* (1992, 1993), whose methodology can perhaps be more directly compared with the Gardner report, included 112 cases and 890 controls with 59 fathers (6 of cases, 53 of controls) exposed. They found no increased risk of leukaemia in the children of fathers working in these facilities. In particular, although the numbers of cases and the prevalence of exposures in the highest doses categories were similar for the control fathers in both the Ontario and West Cumbria studies, the Ontario study found no evidence of a risk associated with such doses. Differences between the studies include the fact that Canadian workers "receive a substantial proportion (20-40%) of their total exposure as an internal dose (largely due to tritium)" (McLaughlin *et al*, 1993), that workers in Ontario did not have the types of chemical exposure received by the Sellafield workers, and that some of the control fathers with high doses were uranium miners.

4.18 The HSE case-control study (1993) referred to in para 4.9 found an association with total paternal external (but not internal) paternal radiation dose and this association was limited not only to the offspring of Sellafield employees resident in Seascale but also to those who started work at the site before 1965.

4.19 Parker *et al* (1993) have suggested that if leukaemia is associated with paternal preconception exposure, geographical leukaemia distribution should reflect that of collective dose. 92% of the births to Sellafield employees occurred outside Seascale during the relevant period (1950-1989) and the fathers of these children had received 93% of the total preconception dose. Parker *et al* noted that the numbers are large; 774 births to Seascale residents and 8,174 in West Cumbria, with a total collective dose of 38 and 490.4 man Sv respectively. They made the point that if the four Seascale cases associated with PPI could be attributed to the 38 man Sv collective dose, some 52 additional cases would have been expected in West Cumbria where Gardner *et al* (1990) found four cases with preconception irradiation.

4.20 A statistical comparison (Little *et al*, 1993) of several relevant datasets revealed that the leukaemia risks observed in the Gardner study were incompatible with those derived from the Japanese, Canadian and Scottish data sets, whether for six months or total preconception dose, although the incompatibility with the Canadian and Scottish datasets is statistically non-significant ($p \approx 0.1$, two sided). The leukaemia relative risk coefficients for paternal exposure in the preconception periods for children in the Canadian and Scottish groups were found to be statistically compatible with the coefficients derived from studies in the offspring of the Japanese bomb survivors.

4.21 There is a highly significant discrepancy (Little *et al*, 1994) between the risks of leukaemia and NHL statistically associated with paternal pre-conception dose in those children of the Sellafield workforce born in Seascale and the risks in the children born outside Seascale (and also with the Japanese, Ontario and Scottish datasets). See Table 4.1 below. The preconception exposure leukaemia and NHL risks in the non-Seascale born children of the Sellafield workforce are consistent with the leukaemia risks observed in the Japanese, Scottish and Canadian datasets.

Table 4.1

Relative risks of leukaemia and Non-Hodgkin's lymphoma in offspring of Sellafield workers and of leukaemia in all other datasets for 100mSv total paternal preconception dose.

Risk estimates for 100mSv exposures calculated using a linear relative risk model fitted to each dataset.

	<i>Relative Risk</i>	<i>95% CI</i>
1. Sellafield workers: offspring born in Seascale	36.04	(14.34-73.01)
2. Sellafield workers: Offspring born in W. Cumbria but not in Seascale	1.27	(0.51-3.36)
3. Japanese A bomb survivors: (mothers and fathers whole body dose)	1.01	(<0.99-1.19)
4. Japanese A bomb survivors: (fathers gonadal dose)	<0.98	(<0.98-1.10)
5. Ontario nuclear workers:	0.63	(<0.27-3.40)
6. Scottish nuclear workers:	<0.51	(<0.51-2.95)
Modified with kind permission from Little <i>et al.</i> , J. Radiol. Prot. 1994; 14: 187-201.		

4.22 These observations reinforce the conclusion that the Seascale cluster is highly unusual but that the observed risk in Seascale is not applicable generally to the offspring of radiation-exposed fathers.

Ambient radiation levels

4.23 Many studies have been undertaken in which the background environmental radiation levels have been compared with a range of outcomes including the childhood leukaemias. In summary we have found it impossible to draw firm conclusions largely owing to confounding factors and methodological problems in the available data. Overall we found no substantial evidence to suggest that background radiation to parents could be shown to cause childhood leukaemia in their offspring.

Cancer treatment including radiotherapy

4.24 Many children of both sexes, are now successfully treated for cancer (Stillier, 1994) and although some become infertile or more prone to miscarriage or stillbirth as a result of treatment received, a large proportion will have children (Byrne *et al.*, 1987). The health of offspring may be related to genetic factors associated with the cancer in survivors or to germ cell mutagenesis resulting from treatment by radiation or cytotoxic drugs. Survivors of cancer occurring in childhood or early adulthood form one of the largest groups exposed before reproducing to high doses of therapies that are potentially germ cell mutagenic. Moreover, relatively accurate radiation dosimetry, excepting gonadal doses, and cytotoxic drug dosages are possible because of the existence of detailed clinical records. In the present context we are concerned specifically with outcome in children of treated male patients.

4.25 Draper (1989) reviewed earlier studies of the occurrence of cancer in the offspring of patients who had themselves been treated for cancer. Such 'multigeneration carcinogenesis' might occur as a result of genetic transmission, the mutagenic effects of either radiotherapy or chemotherapy, or simply by chance. A total of around 4000 offspring were included, mainly from two large US cohorts (Li *et al*, 1979; Mulvihill *et al*, 1987) and one British study (Hawkins *et al*, 1989). About 1700-1800 children are estimated to have been born to male cancer survivors. About 60% of these might have received radiotherapy. Among this group of offspring followed up for an average of about 10 years, the only tumours observed were retinoblastomas, which could be accounted for by the well-recognised heritable component in this disease, and one case each of leukaemia and Burkitt's lymphoma, both born to fathers treated only by surgery. There does not appear to be an excess of malignant disease in the offspring of these fathers. A further seven cases, including three of leukaemia, were diagnosed among approximately 2000 offspring of female survivors; the observed number of cases is greater than that expected in the general population of children (ie about 3 cases). This excess can probably be accounted for by the fact that a small proportion of all cases of childhood cancer is associated with inherited genetic predisposition syndromes.

4.26 Two large series and a number of smaller ones have subsequently been published. Among the latter, no malignant neoplasms were observed in the offspring. The former were concerned with offspring born to survivors of Wilms' tumours (Hawkins *et al*, 1995a) and leukaemia/NHL (Hawkins *et al*, 1995b). Three cases of Wilms' tumour were observed in the offspring of Wilms' tumour survivors. No cases of leukaemia or of any other malignant disease were found among the offspring of survivors of leukaemia/NHL. These 382 offspring (of which 157 were born to male survivors) were followed up for a median of 5.8 years; the expected number of cases of malignant disease based on standard population rates was 0.36.

4.27 We therefore find no evidence from the offspring of cancer patients treated with radiation and/or cytotoxic drugs for the existence of PPI. It should be emphasised that even had there been a detectable increase in childhood cancer among these offspring, the most likely explanation would have been a heritable predisposition to early cancer (known to exist) rather than PPI.

External diagnostic radiation

4.28 Another potential source of evidence considered by the committee was the offspring of patients who had undergone diagnostic x-ray examination prior to conception. In the USA-based "Tri-State study" (Graham *et al*, 1966), patient x-ray exposure was assessed from medical reports rather than self-reports (a validation study on a sample of the data collected had shown that only 65% of x-rays were accounted for by self-report). A significant positive association of leukaemia was noted with the mothers' preconception radiation dose (RR=1.6, p=0.006, two-sided) but not with the fathers'. Selection of controls, however, was less than ideal: it was noted, for example, that the percentage of first-born babies among controls was higher than in New York State, one of the States from which the cases were drawn.

4.29 The Oxford Survey investigated 4542 children who died from cancer at age 10 or less (Kneale and Stewart, 1980). Information about pre-conception x-ray exposure was collected at interview (usually with the child's mother). No associations were evident.

4.30 Using data collected as part of the Collaborative Perinatal Project of the National Cancer Institute, 40 children with cancer were compared with 80

children who were cancer-free at age 7 (Shiono *et al*, 1980). The exposure data, which were collected prior to diagnosis, related only to mothers. A significant association of leukaemia was reported for mothers (Odds Ratio (OR)=2.61, $p=0.021$, one-sided), but there was no evidence of a dose response from the estimated medium gonadal to high gonadal dose category. Supplementary data supplied by one of the authors of the study (C S Chung, personal communication) for the nine cases of leukaemia and NHL showed a much weaker association (OR=2.17, $p=0.33$, one-sided).

4.31 The US Children's Cancer Study Group (Bunin *et al*, 1989) compared 182 cases of non-familial retinoblastoma with matched controls. For the 67 sporadic heritable cases (where it is likely that a new parental germ cell mutation had occurred) they found non-significant raised relative risks for preconception paternal x-rays of the lower abdomen or back (OR=1.8, $p=0.42$) and for preconception maternal x-rays of the lower abdomen or pelvis (odds ratio = 2.0, $p=0.30$). Since this study is based on very small numbers, and many cases had been excluded for various reasons, it is difficult to evaluate these findings.

4.32 In a Chinese study (Shu *et al*, 1988), the authors reported a significant trend of leukaemia with fathers' x-ray dose, as indicated by the number of diagnostic x-ray films ($p<0.01$, two-sided). A follow-on study (Shu *et al*, 1994a) which used similar methods but collected data from both parents by interview has, however, failed to confirm these findings. We have some reservations about the fact that this study relied on self-reporting and especially about "surrogate reporting" ie mothers reporting the fathers' radiation dose. A further recent paper by the same group (Shu *et al*, 1994b) has claimed a positive association between fathers' diagnostic x-ray exposure and childhood leukaemia. We note again the difficulties with the recall element which were likely to lead to over-reporting in some situations but under-reporting in others.

4.33 So far we have considered the Gardner data relating to external radiation doses alone. As Gardner stated in his paper, it had not been possible to examine other possible explanations for his findings such as exposure to internally incorporated radionuclides. These were, however, included in the studies of offspring of patients given Thorotrast and the HSE study and we now consider them together.

Implications of internal radiation dose for PPI hypothesis

4.34 Andersson *et al* (1995) found six cases of cancer during a follow-up period ranging from 0 to 50 years (median 40 years) of 226 offspring of men injected with Thorotrast. The expected number of cases was 4.5, a non-significant relative risk of 1.3. The estimated average preconception dose to the testis from alpha particle irradiation was 62.7mGy, 941mSv. A non-significant excess of 4 cases compared with 2.9 expected was also found among the 143 offspring of mothers given Thorotrast. There were no cases of leukaemia/non-Hodgkin's lymphoma. Little *et al* (1996) have calculated that the risks of leukaemia/NHL in the offspring in the Thorotrast study are statistically compatible with those observed in the offspring of the Sellafield workforce born outside Seascale, in the Japanese atomic bomb survivors, and in the offspring of the Ontario and the Scottish radiation workforces, but not with those in the children of the Sellafield workforce born in Seascale.

4.35 Overall, the studies of diagnostic radiation do not appear to have supported Gardner's findings, but we note that, in general, the studies have been hampered by a lack of reliable dose information, by small size of estimated diagnostic doses inevitably dwarfed by background and the limitations of the self reporting approach. Only in the case of the offspring of fathers treated with Thorotrast was

the testis dose (of internally emitted alpha particles) large enough to allow reasonable power. There were no cases of leukaemia/NHL and the statistical incompatibility of the data with those of the Seascale-born offspring of the Sellafield workforce argue that it is most unlikely that the Seascale childhood leukaemia cases are attributable to paternal exposures to alpha particle emitters such as plutonium.

4.36 Internal radiation exposures were studied by McLaughlin *et al* (1993) and no association was found with tritium or radon. There was however, a suggestion in the HSE report (1993) of an association with working where exposure to tritium and exposure to trichloroethylene might have occurred, although this association was with assessed potential exposure to tritium and was not supported by the limited data on recorded tritium exposure.

4.37 It is accepted that although methods of radiation dose assessment have changed over the years, recorded external dose estimates are known for Sellafield workers with reasonable accuracy. There is less certainty about internal radiation dose but the HSE study has now produced independent assessments of each individual internal dose to the gonads from records of intakes, which we believe are the best assessments of internal dose to date and they show no association with subsequent childhood leukaemia (or other cancers) (HSE, 1993). We have also noted in paragraph 4.17 that the Ontario workers study found no association of childhood leukaemia with paternal exposure and that 20-40% of the estimated paternal exposure was internal, largely from tritium.

4.38 Under the conditions prevailing at the Sellafield plant, internal doses to gonads are conventionally considered to be very small compared with the external doses recorded by film badge (HSE, personal communication). Internal doses are, however, notoriously difficult to determine and it is therefore possible that recorded doses have underestimated total gonadal doses from radionuclides. In particular, it remains possible that short range Auger emitters might give high doses to testicular germ cells by virtue of their short electron ranges if they were concentrated in germ cells or bound to gonadal DNA. Rao *et al* (1985), have suggested that doses and damage to testicular germ cells could be far higher for some radionuclides and chemical forms than conventional organ dosimetry would predict. Nevertheless, we know of no reason why the nuclides to which the Seascale population of workers might be exposed should be any different to those in other West Cumbrian locations.

4.39 We understand that estimates of neutron doses to workers form a relatively small component of the total paternal preconception doses and, moreover, a larger proportion of collective neutron dose will be associated with the children born outside Seascale, (BNFL, personal communication). We therefore believe that they are most unlikely to be responsible for the apparent association with recorded external film badge readings. Furthermore, the HSE considered neutron dose, qualitatively, and found no association.

Mechanisms affecting internal radiation dose

4.40 Work on possible mechanisms by which radionuclides could deliver a higher dose to the testis than previously thought has been carried out by Hoyes *et al* (1994) investigating the uptake of iron, indium and ruthenium in the rat testis. The micro-dosimetric aspects appear to depend largely on the ability of these nuclides to bind to transferrin and thus be transferred across the blood-testes barrier. Germ cell damage in the male primarily depends not only on the proximity of the radiation to the seminiferous tubules, but also on a long biological half life and not necessarily the rate of uptake.

4.41 Laboratory work with indium 114m has demonstrated that di-ferric plasma transferrin can carry the indium across the blood-testes barrier (Hoyes, 1995). Systemic administration of indium 114m results in reduced rat testicular weight. Breeding studies in the same laboratory have shown reduced litter size and increased dominant lethal mutations following indium administration. Preliminary findings from the same laboratory suggest that plutonium crosses the blood testes barrier by transferrin binding. In addition, indium compounds vary in their concentration in the cell nucleus (30-90%) versus the cytoplasm, and in the proportion of the nuclear fraction bound to DNA (4-10%), (Rao *et al*, 1988). Specifically, significant exposure of the Sellafield workforce to indium-114m would not be expected and has not been reported. More generally, any exposure to transferrin binding radionuclides and their putative effects would not be unique to Sellafield workers living in Seascale.

4.42 Another pathway not associated with transferrin leads to zinc-65 being localised in the testes and possibly giving rise to an unexpectedly high dose (Tucker, 1995). Although zinc-65 exposure occurs in the Sellafield working environment it is more commonly associated with CANDU/Winfrith type reactors; the McLaughlin study (1993) did not show any evidence of transgenerational carcinogenesis in the Canadian workforce.

4.43 Lord *et al* (1995) have shown that an injection of 128Bq/g plutonium-239 to male mice 3 to 6 months pre-conception produced offspring which had abnormal haemopoiesis and an abnormal microenvironment. The content of haemopoietic progenitor cells was reduced, probably as a result of a deficient regulatory stroma, but there were compensatory increases in proliferation and differentiation resulting in normal levels of mature haemopoietic cells. The relevance of these observations for leukaemia induction is unclear. However, the findings do suggest that marrow abnormalities in mice can occur in offspring as a result of irradiation of the father, and if such abnormalities do occur they might act as promoters or make the marrow more susceptible to further injury.

4.44 In summary, there remain some important questions about the microdosimetric and biological aspects of germ cell response to radiation regarding the recent data on concentration of some nuclide species in the testes and high testicular dose from Auger emitters. It would seem that doses to critical cells might be higher than conventionally predicted and hence quantitative conclusions should not be too dogmatic. However, none of the postulated dosimetric theories offers a coherent biological explanation as to why excess leukaemia incidence should be confined to Seascale when the worker population potentially exposed is widely spread throughout West Cumbria.

HERITABILITY AND PREDISPOSITION

4.45 The principle that a predisposition to human leukaemia and lymphatic lymphoma can be inherited is not in doubt. Children with certain genetically determined disorders such as Down's syndrome, neurofibromatosis type 1 (NF1), ataxia telangiectasia, Fanconi's anaemia, Bloom's syndrome and some other immunodeficiency disorders are known to have a higher than average risk of developing leukaemia or lymphatic lymphoma. There is also evidence from family, twin and consanguinity studies strongly supporting a degree of heritable predisposition. (Taylor and Birch, 1995; Lynch and Marcus, 1995).

4.46 Certain other types of cancer, such as retinoblastoma and familial non-polyposis colon cancer (FNCC), are known to be subject to a genetic predisposition that can lead to an incidence approaching 100%. For leukaemia and lymphoma, however, such strong predisposition conferred by a single mutation transmitted through the germ line to otherwise normal individuals is not

known to occur. The hereditary disorders mentioned in the previous paragraph are associated in some instances with a strong predisposition to leukaemia/lymphoma but taken together do not account for more than a few per cent of childhood cancer patients. Any other genetic predisposition in the general population is likely to be associated with a multitude of genes each of relatively small effect (see eg paragraph 4.63).

4.47 There is evidence from the artificial context of transgenic mice that activation of proto-oncogenes such as c-abl or loss of the p53 tumour suppressor gene, which are associated with predisposition to cancer, are not so disabling as to be incompatible with live birth. (Donehower *et al*, 1992; Kempetal, 1989; Hanahan, 1989). There is also a rare mouse mutant (“min”), susceptible to intestinal tumours because of a mutation in the Apc gene, that was identified after paternal exposure to ethyl nitroso-urea (ENU), (Moser *et al*, 1995).

4.48 We hold the view therefore, that there is no *a priori* reason why a mutation conferring predisposition to leukaemia/lymphoma should not be induced and transmitted to the offspring of an exposed person. The questions that need to be addressed, therefore, are (i) whether or not the radiation doses to which Sellafield workers were exposed would have been sufficient to induce mutations at a frequency that would be necessary to account for the incidence of leukaemia/lymphoma in their children, and (ii) whether or not the predisposition conferred by any such mutation would be strong enough to result in the disease in a sufficiently high proportion of cases.

EXPERIMENTAL and ANIMAL MODELS

4.49 We now consider some experimental animal data from investigation of PPI effects and possible carcinogenic outcomes. We note that non-carcinogenic transgenerational effects are well known. For example, congenital malformations in offspring following preconception irradiation have been clearly demonstrated by Nomura (1975) and confirmed by others (Russel, 1982; Lyon and Renshaw, 1986). In the work of Lyon, the total malformations in the first generation offspring (F1) was 12% and in the second generation (F2) 2.6%.

Carcinogenesis in the mouse following preconception irradiation

4.50 A substantial body of experimental work has been built up by Nomura which lends some support to the PPI hypothesis (Nomura, 1992). Table 4.2 from Nomura summarises a number of studies showing the doubling dose, increase in mutation rate and dose received for leukaemia incidence in male and female mice following external x-irradiation of the male parent in comparison with calculated doses for the Sellafield (Gardner) and Japanese studies.

TABLE 4.2
Leukaemia in the first generation (F1) offspring after paternal exposure to radiation in men and mice (from Nomura, 1994)

		Dose (mSv)	Relative risk	Doubling Dose (mSv)	Induced Rate mSv (x10 ⁶)
Sellafield (Gardner et al, 1990)	All stages	≥100	6.24 (1.5-25.8)	11.9 (2.5-126)	22.2 (2.1-105)
	Postgonia ^a	5-9	3.54 (0.3-38.9)	1.5 (0.1-)	179 (0-2680)
		≥10	7.17 (1.7-30.5)	1.0 (0.2-8.8)	260 (30-1250)
Hiroshima and Nagasaki (Yoshimoto & Mabuchi, 1991)	Spermatogonia	435	1.24	900	0.23
ICR (Nomura, 1978, 1982)	Spermatogonia	360-5040	1	-	0
	Postgonia	360-5040	1.9-3.2	950 ^b	1.9 ^b
LT (Nomura, 1986, 1991) ^c	Spermatogonia	3600	1	-	0
	Spermatogonia	3600-5040	4.5-7.4	450	9.0
N5 (Nomura, 1986, 1991) ^c	Spermatogonia	5040	9.6	300	6.9
	Spermatogonia	5040	18.1	150	13.8

Doubling doses in mice and men were calculated as uniparental exposure in contrast to the previous paper (Nomura,1990) because fathers and males were exposed to radiation in the Sellafield and mouse studies and conjoint parental gonad doses were used for the F₁ study of the atom-bomb survivors. Induced rate of leukaemia per mSv in the Sellafield study was calculated by the formula: (background incidence of leukaemia relevant to Sellafield study, 53 x 10⁻⁵)(Gardner, pers comm) x (excess risk value) /(paternal dose, mSv). External doses to employees were in the range of 100-150 mSv for all stages, 5-9 and 10-15 mSv for post'gonia (Gardner, pers comm). Average doses used for the calculation in this table were 125, 7.5 and 12.5 mSv, respectively.

^aFathers exposure during 6 months before conception indicates post-spermatogonial exposure for the most part, but includes spermatogonial exposure in part.

^bAverage value at 2160-5040 mSv.

^cIncludes some unpublished data.

Note: In the 2nd line of col. headed 'Doubling dose' the upper confidence level is absent in the original publication.

References used in Table 4.2:

Yoshimoto, Y. and Mabuchi, K. (1991) Mortality and cancer risk among the offspring (F₁) of atomic bomb survivors. *J Radiat Res.* **32**, 294-300.

Nomura, T. (1978) Changed urethan and radiation response of the mouse germ cell to tumour induction. In: *Tumours of early life in man and animals*. Ed: Severi, L. pp 873-897. Perugia Univ Press.

Nomura, T. (1982) Parental exposure to x-rays and chemicals induces heritable tumours and anomalies in mice. *Nature*, **296**, 575-577

Nomura, T. (1986) Further studies on x-ray and chemically induced germ-line alterations causing tumours and malformations in mice. In: *Genetic toxicology of environmental chemicals, Part B Genetic effects and applied mutagenesis*. Ed: Ramel, C. pp 13-20, Alan R Liss, New York.

Nomura, T. (1990) Of mice and Men? *Nature*, **435**, 671

Nomura, T. (1991) Paternal exposure to radiation and offspring cancer in mice: reanalysis and new evidences. *J Radiat Res.* **2**, 64-72.

4.51 If mutations predisposing to the appearance of a malignant disease in the next (F1) generation can be induced in paternal germ cells it would, on the basis of what is known about radiation induced mutation rates, be fairly difficult to demonstrate in experimental animals because of the low frequency expected. Nomura has reported the incidence of leukaemia in the offspring of three strains of irradiated mice, (see Table 4.2). The numbers of leukaemias were small and there was considerable variation between the three strains and between the various germ cell stages. Even so, the calculated mutation rates (0 to 6.9 x 10⁻⁶

per mSv for treatment of spermatogonia and 1.9 to 13.8 x 10⁻⁶ per mSv for spermatozoa) are of an order of magnitude higher than those of recessive specific locus, dominant cataract and enzyme activity mutations in mice which involve 7 to 15 gene loci. They are, however, close to the rates for major skeletal mutations in mice where the number of loci is unknown.

4.52 Even higher rates were reported for tumours of the lung in Nomura's work (Nomura, 1983). It is known, however, that concurrent controls were not always employed in those studies carried out before 1980 and also that Cattanaach *et al* (1995), have found an apparent seasonal variation in tumour incidence which casts a degree of uncertainty on the interpretation of Nomura's data.

4.53 No studies are known to have confirmed Nomura's finding definitively. In a project commissioned after Gardner's 1990 publication, Cattanaach and colleagues effectively repeated one of Nomura's experiments using inbred strains of mice (approximately 1800 mice in total) with well-established lung tumour propensity, (Cattanaach *et al*, 1995). The paternal radiation exposures and end points were chosen to match optimum selected components of Nomura's protocol. These results did not support those of Nomura in that the rate of tumour incidence was not related to paternal radiation dose, nor did the incidence vary significantly between germ cell stages irradiated (week of mating) or sex of offspring. An important finding arose from the experimental procedure which involved irradiating the mice in sequential batches. It was noted that tumour rates varied in both experimental and concurrent control groups in a progressive and cyclic way suggesting a seasonal effect on tumour incidence. This result emphasises the necessity of concurrent controls to enable valid interpretation of studies of this type.

4.54 Selby (1993) has suggested that one of the results of preconception radiation experiments in the mouse is to increase the number of dominant lethal effects, thus decreasing litter size and leading to better nourished and thereby larger surviving offspring; the assumption being that the greater number of target somatic cells in such animals increases the chance of malignant transformation. This is supported only by indirect evidence from some experiments designed with other end points in mind. It appears that there have been no specific experiments to refute Selby's proposition but the study of Cattanaach *et al* did not find any effect related to body size suggesting that this hypothesis cannot have general application.

4.55 Takahashi has reported work in progress which seems to show a marked increase in liver tumours in male, but not in female, mice following irradiation by 50cGy californium-252 neutrons to the male parents (Takahashi *et al*, 1992). These unusual results have yet to be fully repeated in the originating laboratory and cannot at present be evaluated, and the possibility that a viral mechanism may be confounding the results also needs to be examined (Kohn *et al*, 1965; Cosgrove *et al*, 1993).

Transgenerational effects of chemicals with radiation

4.56 In addition to the above reports involving paternal irradiation there have been a number of reports of excess tumours appearing in the offspring of animals treated with various chemicals (Tomatis, 1994). In 1988 Vorobtsova and Kitaev reported multiple lung tumours in urethane-treated F1 generation after male parents had been subjected to 4.2 Gy of external irradiation.

4.57 Luz and colleagues (1994) have treated male mice with ethyl nitroso-urea (ENU) which were then mated at five months. Offspring were given the bone-seeking radionuclide thorium-227; the end point was the rate of development of

bone sarcomas. Results provided some support for the observation that an earlier onset of tumours had been seen with ENU plus thorium-227, than with radiation alone, although this observation was seen only in female offspring; lifetime risk of sarcoma was independent of ENU exposure. No correlation of tumour incidence (at eight months) with body size was noted arguing against the Selby hypothesis (see para 4.55).

4.58 These more carefully conducted studies with concurrent controls provide an example of a chemical mechanism whereby transgenerational effects in mice may be produced. The possibility must be acknowledged that irradiation could influence bone tumours resulting from chemically-induced germ-line mutations at a later, promotional, stage in their development. The observed effect is, however, likely to be small.

4.59 In experimental animals, however, a notable feature of all the reports of paternal radiation exposure and tumour incidence in offspring is the degree of inconsistency between strains, between endpoints, and between germ cell stages. If normal mutation rates are involved the frequencies of tumours expected in the first generation would be below the detection level of practicable experiments. Those studies where positive results have been obtained are therefore not easily explained by the operation of conventional mutational processes.

Further radiation effects

4.60 Conventional mutations are not the only changes elicited in cells by ionising radiation. Some changes occur with a much higher frequency. For example, an early observation was that x-irradiation of C₃H10T^{1/2} mouse cells induced, at a high rate, the tendency to undergo a second mutation to morphological transformation many generations later (Kennedy *et al*, 1980). This phenomenon has been ascribed to radiation-induced genetic instability at high frequencies effectively amplifying the effect of the single initial changes. Other examples following exposure to ionising radiation include the strong persistent mutational response in GRS1 mouse lymphoma cells (Simons and Niericker, 1994), Chinese hamster ovary cells (Chang and Little, 1994), and in mouse and human bone marrow cells (Kadhim *et al*, 1992, 1994, Kronenberg, 1994). These have been reviewed by Little (1994).

4.61 In addition to these “instability” or “amplification” phenomena, other radiation induced changes may occur at high frequency. Kamiguchi (1987), for example, has reported that about one per cent of human spermatozoa with visible chromosome aberrations were seen after 20mSv low-LET irradiation *in vitro*. Martin *et al* (1986) have published data on chromosome abnormalities in sperm of men who had previously received radiotherapy. Abnormalities were still observable in their spermatozoa 2-5 years later and at moderately high frequencies. These included data on late structural aberrations that should be free of the methodological problems associated with quantifying numerical abnormalities. Martin observed 6% of sperm with unstable (un-rejoined) chromosome abnormalities. These types of aberrations are conventionally regarded as not being transmissible through spermatogenesis, their presence may, thus, be suggestive of a radiation-induced instability leading to new aberrations at later times.

4.62 A further line of inquiry which has challenged conventional mutational expectations concerns radiation induced mini-satellite mutations after paternal irradiation. Dubrova *et al* (1993) have shown a very high frequency of induced mutations in offspring of mice, especially after spermatid irradiation and this has been confirmed by Sadamoto (1994). No significant effect has been found in offspring of human A-bomb survivors or at a human locus in transgenic mouse,

but in both cases the statistics may have been too limited. Further results are expected from the children of “liquidators” after the Chernobyl explosion and other irradiated parents, but these may not be available for several years. From the very high frequencies of the induced mini-satellite mutations in the mice it appears that they must occur by an untargetted (trans-acting) mechanism rather than by DNA damage to the mini-satellite loci.

4.63 The role of mini-satellite mutations in the causation of human disease is not yet clear. It seems possible that mini-satellite DNA is ‘junk’ DNA with little or no role in normal cellular function. Mini-satellites may nevertheless act as sensitive markers of genetic instability or other events which could themselves be related to disease. However, evidence exists that in some cases at least mini-satellites could be linked more directly to human diseases including cancer. Krontiris *et al* (1993) have reported an association between mutations in a mini-satellite adjacent to the *HRAS1* oncogene and the occurrence of several human malignancies, including leukaemias and lymphomas. The relative risk for these alleles, which are present in about six percent of the population, are modest (2 to 3-fold) and it is not known whether the association reflects causality (Krontiris *et al*, 1993). Krontiris (1995) has proposed that some mini-satellites may have a regulatory function and that mini-satellite mutations could lead to altered gene expression and a propensity to malignant transformation. Further investigation of mini-satellite mutations in both germ cells and somatic cells is necessary.

4.64 Despite these observations, there is no real evidence that the highly radiosensitive processes leading to unconventional changes in germ cells (including mini-satellites) are responsible for childhood leukaemia. If there was a general association between paternal radiation exposure and childhood leukaemia, it should have been apparent in the offspring of the survivors of the Hiroshima and Nagasaki explosions and in those of the Ontario nuclear workers. The possibility that an “unconventional” change might interact synergistically with some unknown factor specific to Seascale is considered in Chapter 8.

DISCUSSION

Genetic implications of Gardner results

4.65 We recognise that predisposition to leukaemia has a heritable component, although in humans strong predisposition appears to be almost entirely associated with certain clear cut genetic diseases. In laboratory animals there is some evidence that offspring of irradiated fathers may have a raised incidence of leukaemia and other cancers, but we have reservations about some aspects of these studies. It is clear, moreover, that these effects, even if real, are specific to certain strains of laboratory animals and are not generally applicable. In addition, the mutation rates that they would imply are too low to account for the Seascale cluster.

4.66 The spontaneous mutation rates for most human tumour susceptibility genes is believed not to differ markedly from those responsible for conventional heritable disorders. Whilst it is known that high spontaneous mutation rates apply to certain DNA repeat sequences in the human genome (Jeffreys *et al*, 1985), if human genes capable of giving rise to leukaemia were more highly radio-sensitive than has been assumed, then an observed excess of leukaemia in the offspring should have been expected in all the studies. This was not the case although it should be noted that the dose rate differences in Japan and Sellafield are considerable and that germ cell killing may have affected the incidence in Japan.

4.67 Wakeford *et al* (1994a), in a study of the collective occupational dose distribution in West Cumbria have demonstrated that only 7% of the collective paternal preconception dose attributable to the Sellafield workforce for children

born during 1950-1989 is associated with maternal residency in Seascale at the time of their offsprings' birth. The collective paternal dose associated with Seascale for these children is 38 person Sv; given that there were 5 leukaemias in Seascale, the calculated mutation rate would be 13.2×10^{-2} mutations per person Sv. This is about 70 times higher than the ICRP estimated rate of 0.18×10^{-2} excess cases of Mendelian and chromosomal disorders per person Sv. The leukaemia-related mutation rate in Seascale would therefore be too high to be explained in this way by some orders of magnitude, assuming conventional genetic mechanisms.

4.68 The excess cases of leukaemia/lymphoma in the offspring of Sellafield employees is not associated with any of the hereditary disorders known to cause a strong predisposition. Any hypothetical mutations occurring in the paternal germ cells must therefore have been in genes conferring a modest degree of predisposition. Many such mutations would be needed among the exposed group in order to result in even a single case. The data we have seen suggest that preconception doses to the West Cumbrian population (and to the Sellafield workforce) are too small by some orders of magnitude to have caused the observed leukaemias/lymphomas by any human genetic mechanism as currently understood.

CONCLUSIONS

4.69 Gardner *et al* (1990a), concluded that the observed geographical excess of leukaemia and NHL among children near Sellafield could be explained by the statistical association with paternal employment and external recorded radiation dose. We have not found any epidemiological study elsewhere to support Gardner's findings in Seascale in relation to preconception radiation effects. This study was superseded by studies which had access to more accurate data and these showed that the excess in Seascale was not confined to those born there (Kinlen, 1993) and that there was no significant dose-response relationship based on the six month preconception dose, although there was for total external dose for male workers who started work at Sellafield before about 1965 and whose children were born in Seascale (HSE, 1993,1994).

4.70 The Gardner report's finding led the authors to suggest that although they recognised that other mechanisms were possible, radiation-mutated germ cells might give rise to leukaemia in subsequent offspring. In examining this hypothesis we have looked not only at the mechanisms whereby such an effect might occur but also at the likelihood of the germ line mutation rates being high enough to give rise to the observed leukaemia incidence.

4.71 We conclude that while there is no doubt that the hypothesis of paternal preconception irradiation causing cancer in offspring can be sustained in principle, the implied level of risk of leukaemia/NHL at Seascale when compared to known radiation-induced mutation rates for other specific genetic effects is inconsistent with the accepted dosimetry. It has been suggested that the measured dose of external radiation may be a surrogate measure for internal exposure to radionuclides or to chemicals. However, the HSE study found no association between internal dose to fathers and the risk of leukaemia in their offspring. Furthermore, there is no evidence for any relevant radionuclide or chemical exposure that has been unique to those Sellafield workers resident in Seascale. In summary, quantitative considerations have led us to conclude that the size of those PPI effects expected on theoretical grounds or demonstrated in animals is too small by at least an order of magnitude to explain the Seascale phenomenon. We consider that PPI cannot account for the Seascale childhood leukaemia excess.

CHAPTER 5

EXPOSURE TO CHEMICALS USED AT OR DISCHARGED FROM THE SELLAFIELD SITE: CONSIDERATION OF THE RISK OF CANCER AND LEUKAEMIA INDUCTION IN THE GENERAL POPULATION AND THE OFFSPRING OF SITE WORKERS

INTRODUCTION

5.1 In their report, the Black Advisory Committee considered some environmental aspects of the Sellafield site and in West Cumbria generally. These included the major non-radioactive contaminants discharged into the environment by BNFL and the discharges from Albright and Wilson (Marchon Works) in Whitehaven. The committee also considered other inorganic and organic chemicals that might be present in the environment. They found no convincing evidence of any unexpected environmental carcinogen or agent peculiar to the area around Sellafield.

5.2 However, when we were considering the increased incidence of childhood leukaemia near Dounreay we returned to the issue of chemical exposures as a possible factor and in our second report on Dounreay, we recommended (Recommendation 5) “that if possible a study be made of the chemicals used both at Dounreay and Sellafield and in the immediate neighbourhood identifying the time pattern of their use, the extent of worker exposure and the disposal routes employed.” In response to this recommendation BNFL provided lists of chemicals, both current and historic, used at the Sellafield Plant and also details of the manner by which they were discharged. In addition, lists of chemicals used in the Research and Development Section which may give rise to concern regarding mutagenic and carcinogenic potential, were provided (See Table 5.1).

5.3 On receipt of the information on chemicals handled and discharged at Sellafield and Dounreay in 1990, the Government advisory Committee on Mutagenicity of Chemicals in Food, Consumer products and the Environment (COM) were asked by the COMARE Secretariat to consider the information provided by BNFL and to comment on the mutagenic potential of any of the chemicals which might give rise to some concern.

5.4 Their initial considerations led COM to request and receive further information from BNFL. [The principal data sources consulted by COM are starred in the references] Following their discussions, COM reached the following conclusions:

- i. The lists of process chemicals used currently at Sellafield as provided by BNFL do not give rise to concern regarding mutagenic potential.*
- ii. However, the Committee noted that in the past chemicals that do give rise to concern were used, namely benzene, dichromates and hydrazine. The Committee also noted that the methods used to dispose of the stock of benzene over the period 1952-59 are unclear.*
- iii. Regarding the chemicals handled by the Research and Development Section at Sellafield these clearly include many compounds that have mutagenic and carcinogenic potential and should be handled accordingly.”*

CONSIDERATION OF CHEMICAL EXPOSURES

General

Risk from Paternal Exposure to chemicals

5.5 In addition to the specific consideration of the chemicals used at Sellafield COM were also asked by the COMARE Secretariat to provide advice on whether there was any evidence that paternal exposure to chemicals could result in malignancies in the offspring. This request formed part of our consideration of the potential of paternal exposure to radiation or chemicals to induce malignancies in the offspring discussed in Chapter 4.

5.6 The COM considered the available data on chemicals from the published literature, covering both animal studies and from human exposure, relevant to this question. This involved the assessment of a considerable number of studies.

5.7 Results from a limited number of studies in laboratory animals did suggest that paternal exposure to certain mutagenic chemicals could result in malignancies in their first generation offspring. It was noted that limited data from humans exposed to cytotoxic agents used therapeutically had not indicated such an effect. It was felt prudent, however, to assume that a chemical shown to be mutagenic in germ cells in laboratory animals had the potential to induce malignancies on the offspring.

5.8 The Committee on Mutagenicity gave further consideration to this issue, concentrating particularly on the mechanisms involved and how this related to the Sellafield data. Conclusions were reached regarding the mechanisms by which paternal exposure to relatively low levels of chemicals may result in malignancies on the F-1 (first generation) offspring and on further research work needed in this area. A summary of these conclusions has been published [Hansard 16 July 1991 vol 195 cols 145-6]

5.9 The full conclusions reached by the Committee on Mutagenicity in 1991 are given below:-

Evidence that paternal exposure to chemicals may result in malignancies in the F1 offspring.

- “i) Radiation and chemical mutagens have been shown to produce the types of mutations at the gene and chromosome level that are known to be associated in humans with predisposition to the development of malignancies in offspring.*
- ii) Only very limited data are available from animal studies on paternal exposure to mutagens and the development of tumours in offspring. These suggest that with ionizing radiation and certain chemicals paternal exposure results in the induction of malignancies in the offspring.*
- iii) The data available on the effect of chemicals in humans do not allow any firm conclusions to be drawn. The limited data available on paternal exposure to cytotoxic agents used therapeutically have not indicated that there is any increased incidence of malignancies in the offspring of such patients.*
- iv) It would be prudent to assume in principle that a mutagen capable of affecting both somatic cells and germ cells *in vivo*, has the potential to induce malignancies in offspring, following paternal exposure.*

Environmental mechanisms by which paternal exposure to relatively low levels of chemicals may result in malignancies in the F1 offspring

- v) *Whether or not the excess childhood leukaemia reported in the vicinity of the sellafield plant is a consequence of paternal exposure (either to radiation or some other mutagen) the data are not readily reconcilable with what is known about the genetics of childhood leukaemia. The data are, therefore, worthy of further consideration.*
- vi) *If the predisposition to these leukaemias is a consequence of induced heritable mutations, then, both on theoretical grounds and from animal experiments, one might, making certain assumptions, expect to see a higher level of congenital abnormalities in any population sufficiently mutagenized to show such a level of carcinogenic gene mutation; although it has not been properly investigated, we know of no evidence for this in the Sellafield area.*
- vii) *If the 6-7 fold excess incidence of childhood leukaemia reported among the offspring of some male Sellafield workers having received over 100 mSv is a consequence of induced inherited mutation, this would imply a germ line mutation frequency of at least 1 in 300. This is many orders of magnitude greater than most spontaneous mutation rates for single genes and considerably greater than the expected mutation frequency increases following exposure to low doses of radiation. The only classical mutations that could be expected to give rise to such large increases are chromosomal deletions which would be detectable cytologically. The majority of such deletions would, however, not be viable and those that were would also be associated with other, and often gross, phenotypic abnormalities. A genetic basis may be able to accommodate the results if there were a large number of genes (say 20-100) that could influence childhood leukaemias. If so, however, one would expect many of these to be general neoplastic genes and their effects would not be confined to childhood leukaemias. Nevertheless, even on such a model it is not possible to explain the apparently extremely low mutation doubling dose.*
- viii) *Extremely high frequencies of neoplasia among the offspring of male mice exposed to either radiation or the chemical carcinogens N-ethyl-N-nitrosourea (ENU) and particularly urethane have been reported by Nomura in a series of publications. Although these are mostly lung adenomas, leukaemias were apparently increased in some strains. In any case the genetic problem remains whatever the neoplastic endpoint. Nomura has argued that the mutations in his mouse model are unlikely to be chromosomal on the grounds that:-*

“(i) urethane produces tumours but not translocations or dominant lethals and

(ii) that tumours occurred no more frequently in mice with X-ray induced translocations than in those without translocation”.

However urethane is an established in vivo clastogen in the mouse and the latter argument is statistically invalid. On the other hand it should also be noted that in one of the two strains of mice studied by Nomura, no increased incidence of leukaemia was observed in F1 progeny from irradiated spermatogonia, but a two-fold increase was seen in offspring from irradiated sperm and spermatids - a pattern which could imply an involvement of chromosomal mutations as opposed to more subtle gene alterations.

- ix) *It is clearly important that a better understanding be gained of the mechanistic basis of tumour induction following paternal exposure. If the Seascale cluster is an example of such an effect it is likely that there will be others resulting from chemical exposure; the increase in West Cumbria of leukaemia among the offspring of fathers working in the chemical, iron and steel, and agricultural industries for instance was just as great as that found among the offspring of Sellafield workers. Chemicals capable of causing such an effect may not necessarily be recognised as conventional mutagens (although both ionizing radiation and urethane are). Moreover one may speculate about the possible involvement of other agents such as viruses. The Committee, however, would find it difficult to advise on these possibilities on the basis of current knowledge.*
- x) *The Committee therefore strongly recommends:*
- a) *That work be carried out in this country to confirm the observations of Nomura and to establish a similar experimental model that can be used for mechanistic studies.*
- b) *That in such work, the emphasis should not be exclusively upon ionizing radiation but should include chemicals, in particular urethane”.*

5.10 COM's recommendation concerning the need for further work to produce confirmation of the Nomura observation was accepted by Government. Appropriate research to examine the preconceptual effects of ionising radiation was funded by CCHARR. Details of this work and its relevance to the current report are discussed in detail in Chapter 4 of this report.

THE HSE STUDY

5.11 In addition to the evidence considered by COM, we took note of the report published by the Health and Safety Executive in October 1993 on their investigation of leukaemia and other cancers in the children of male workers at Sellafield (HSE, 1993). The results of this study are considered further in Chapter 4. However, in addition to the main study of radiation doses to members of the workforce, HSE undertook a study of the chemicals in use on the site in the past. The study covered all areas of the site.

5.12 The starting point in identifying the chemicals in use was the list provided by BNFL to COMARE and subsequently considered by COM. An HSE toxicologist reviewed this list and added a number of chemicals used on site which were regarded as meriting further examination. An attempt was made to link the potential for exposure to chemicals by determining the locations and methods of usage of each of the chemicals on the list, as a function of time between 1949 and 1991.

5.13 Records of the location of chemicals and of how and where they were used were available from the mid 1970's until the present time. However, further back in time fewer data are available. Since its inception the nuclear industry has monitored and recorded radiation doses and levels of radioactivity in working areas; however, in common with other industries there has been little or no quantitative monitoring of the levels of chemicals in the working environment. Consequently, the statistical power to detect any real effects of chemical exposures is less than if accurate measurement of these factors were available.

5.14 The potential exposure of male workers in the study to the chemicals of interest was assessed in terms of the job title of the subject, the area in which they

had worked and the period of work. Where more detailed information was available on the work activities of the subjects (eg. from annual staff reports) this was used. For each period of work by a subject a seven point scale was used to score his potential exposure to each chemical of interest. This assessment was made by a team of inspectors from the Nuclear Installations Inspectorate (NII) after interviewing representatives from the workforce (including ex-employees) with knowledge of the working environment at the relevant times.

5.15 None of the chemicals examined showed positive, statistically significant associations consistently across the various analyses performed with the data. In some analyses, statistically significant associations were found between the incidence of leukaemia or NHL and the father's potential exposure to chromates/dichromates, formaldehyde/formalin, hydrofluoric acid, picric acid, trichloroethylene (TCE) and thiophenyltrifluoroacetone (TTA). The strongest of these associations were for chromates/dichromates (4 cases) and for TCE (9 cases). Three of the four chromate/dichromate cases were resident in Seascale at birth and the report notes that the association with Seascale accounts for the association with chromates/dichromates but not vice versa.

5.16 When a comparison was made between the fathers with the longest potential exposure to TCE (8 cases) and other subjects, the statistical association with leukaemia and NHL in offspring was quite strong. However, five of these case fathers were also potentially exposed to tritium (see Chapter 6) and the associations between these two types of potential exposure and the incidence of leukaemia and NHL in offspring could not be distinguished. In view of this finding and the absence of strong independent supporting data, the authors of the report considered that the evidence of a causal effect between exposure of fathers to TCE and the incidence of leukaemia and NHL in the offspring was weak.

5.17 The authors also noted that any of the possible associations outlined above were relevant only to the early years of plant operation (up to 1965) as were associations relating to exposure of workers to radiation.

DISCUSSION

5.18 We have noted COM's comments and recommendation and have further considered the results from the HSE study as to whether exposure to chemicals could account for the excess of childhood cancer and leukaemia in the area around Sellafield.

5.19 We are aware that the types and quantities of chemicals used at Sellafield, both now and in the past, are similar to those used in other chemical industries. In the Gardner study (1990) the increase in West Cumbria of leukaemia and NHL in the offspring of fathers working in the chemical, steel and agricultural industries was as great as that found amongst the Sellafield workers.

5.20 We note the concerns expressed by COM as to exposures to various chemicals in the early period (pre 1960) of the operation of the Sellafield plant, which are to some extent mirrored by the findings and conclusions of the HSE report. However, it is difficult to estimate the size of any possible biological effects because of the relative paucity of quantitative data available for this time period and further work is unlikely to clarify details of exposures to chemicals before 1960. We also note that COM have said that process chemicals used at the plant since 1988 do not give rise to concern regarding mutagenic potential.

5.21 Bracken has long been suspected of being carcinogenic in man (Evans and Mason, 1965). It was noted in the Black report (1984) that many areas of Cumbria including Seascale were supplied with water from bracken-infested

hills. Evans & Galpin (1990) have shown that bracken spores can produce leukaemia in weanling mice. However, there is no evidence that bracken fern is implicated in human leukaemia. Since bracken is ubiquitous it cannot explain the unique situation in Seascale.

SUMMARY

5.22 Whilst there is evidence that some adult leukaemias may be associated with occupational exposure to certain chemicals such as benzene, of which there were very large quantities discharged in the early years of plant operation, there are currently no data showing a link with environmental exposure and subsequent cases of childhood leukaemia. Any hypothesis to explain the Seascale cluster as being due to exposure to chemical discharges from the Sellafield site would need to take into account that adult (data available for 25 to 74 years old from 1984 onwards) leukaemia rates in Seascale are not elevated and that the leukaemia rate is not similarly raised in other nearby villages subjected to the same levels of discharge.

5.23 Notwithstanding the paucity of data on both environmental exposure to chemicals and occupational exposure to parents, we have been unable to find any evidence of exposure to chemicals which is unique to the population of Seascale and does not affect other populations in West Cumbria. We conclude that exposure to chemicals is unlikely to explain the observed excess of childhood leukaemia in Seascale.

TABLE 5.1 LIST OF MAIN CHEMICALS CONSIDERED BY THE COMMITTEE ON MUTAGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COM)

Acetone	Ammonia and compounds
Aniline and compounds	Arsenic and compounds
Benzene and derivatives	Beryllium
Benzidene and compounds	Butex
Cadmium and compounds	Carbon tetrachloride
Chlorine	Chloroform
Chromium, Chromates/Dichromates	Clinoptilolite
Dichloroethane	Dichloromethane
Ethylene Glycol	EDTA
Formaldehyde/formalin	Freons
Graphite	Gadoline compounds
Hydrazine	Hydrogen chloride
Hydrogen fluoride	Kerosene
Lead and compounds	Mercury
Methanol and derivatives	Nitric acid
Naphthylene	Nickel and compounds
Oxalic acid	Phosphoric acid
Potassium compounds	Sodium compounds
Sulphamic acid	Sulphuric acid
Styrene	Tetrachloroethane
Tetrachloroethylene	Triethylamine
Tributyl phosphate	Trichloroethane
Trichloroethylene	Toluene
Toluidenes (ortho)	Zinc compounds

Note: British Nuclear Fuels provided a list of chemicals which covered many pages. They also provided details on chemical use, quantity used, disposal routes, and details of the plant building/section in which the chemicals were used. The list above covers the main chemicals considered by COM but it is not a definitive list of all of the chemicals appraised.

CHAPTER 6

INFECTIOUS AETIOLOGY OF CHILDHOOD LEUKAEMIA: POSSIBLE ASSOCIATIONS WITH THE INCIDENCE OF CHILDHOOD LEUKAEMIA WITH REFERENCE TO THE SEASCALE POPULATION

INTRODUCTION

6.1 The Report of the Black Advisory Group (Black, 1984) looked briefly at the possibility of the increased incidence of childhood leukaemia in West Cumbria being due to factors other than ionising radiation. The report found no evidence for any unexpected environmental carcinogen or agent peculiar to the area around Sellafield. In our second (1988) and third (1989) reports we suggested hypotheses for the observed excess leukaemia incidence which were not directly related to exposure to ionising radiation. These hypotheses primarily concerned chemicals, viruses and demographic phenomena. We have noted that there are two principal hypotheses which have been developed; one which is biological and the other which is suggested by epidemiological studies. We review these hypotheses below, together with the current evidence. In this chapter we will focus on the possible relationship of childhood leukaemia to infectious agents and the role of population mixing.

6.2 The causes of leukaemia are probably multifactorial, resulting from more than a single agent or pathway: for instance, a combination of an inherited genetic predisposition and environmental factors may be involved. In common with other malignant diseases, leukaemogenesis requires more than one mutation (Greaves and Chan, 1986). Initiation, which could be *in utero*, is thought to be followed by a latent sub-clinical pre-leukaemic phase which may progress to leukaemia following exposure to promoting factors. If an infectious agent is involved in the aetiology of leukaemia it could act as either an initiating or a promoting agent.

6.3 The clinical forms of leukaemia in children display great heterogeneity. [See chapter 2 for discussion of subtypes]. Because the different subtypes may have different aetiologies, it is desirable on biological grounds to analyse subtypes separately. However, in the past, epidemiological studies often have had small numbers of cases involved in each sub-category and information on subtyping is frequently not available.

6.4 Leukaemogenic agents may be selective in the type of disease they induce. In several species of domesticated animals virally induced leukaemias are of the lymphoid type. In hens and in laboratory rodents, however, viruses that cause myeloid leukaemia have been described. In adult humans, chemicals such as benzene and alkylating agents induce acute myeloid leukaemia (AML) and acute lymphoid leukaemia (ALL) but not chronic lymphocytic leukaemia (Kaldor *et al* 1990a,b); ionising radiation at high doses is known to induce predominantly myeloid leukaemia in adults and also ALL at all ages.

6.5 Viruses are known to be co-factors in the generation of certain solid cancers in adult humans; for instance liver cancer is associated with hepatitis B and C infection, as is cervical cancer with certain papilloma viruses. In laboratory and domestic animals, several retroviruses have been described that cause leukaemia and, largely because of this, the role of viruses in the aetiology of childhood

Viral and Chemical Aetiology

leukaemia has been the subject of speculation for many decades. Thus far only Epstein Barr virus (EBV) has been identified in childhood leukaemias (2-3% of B-cell leukaemias) and the only known examples of viruses as contributory causes of haematopoietic diseases in man are the human T-lymphotropic virus type 1 (HTLV-1) and EBV in Burkitt's lymphoma. HTLV-1 is believed to be responsible for an aggressive form of T-cell leukaemia/lymphoma in adults and is endemic in certain parts of Africa, South West Japan, South East USA, the Caribbean basin, Alaska and Papua New Guinea.

Epidemiological evidence relating to an infectious aetiology for leukaemia.

6.6 The possibility that an infection may influence the risk of leukaemia is given indirect support by a number of observations:

6.7 Childhood Peak: The early childhood peak in incidence of leukaemia, seen in most developed countries, was first noted in the UK in the 1920s and is not present in Black Africans. Before 1945 this peak was also missing for Black Americans, but it has now appeared. One hypothesis is that the appearance of the peak in childhood is associated with the acquisition of a more affluent lifestyle (Greaves and Alexander, 1993) which brings with it a relative isolation from infections that would otherwise occur in early childhood.

6.8 Place of residence: The distance of place of residence from built-up areas has been reported to be positively associated with the risk of childhood ALL (Alexander *et al*, 1990). Infections tend to occur in children at an older age if they live in rural areas (Anderson and May, 1982).

6.9 Socio-economic status: Some reports suggest that the incidence of childhood leukaemia is higher in geographical areas of higher socio-economic status. For instance Draper *et al* (1991) found that children living in the top 20% of areas as ranked by socio-economic status had a risk of leukaemia about 10-20% higher than those in the lowest 20%. However, it is not known if the cases of leukaemia in these areas are *themselves* of higher social class and socio-economic status can be confounded with environmental exposures.

6.10 Space-time Clustering: Cases of infectious diseases which are transmitted from person to person often show evidence of clustering in space and time. A review of a large number of epidemiological studies of children with leukaemia concluded that there was absence of consistent evidence of space-time clustering. This suggests that if the disease is infective in origin, children with leukaemia cannot be important in spreading the underlying infection (Smith, 1982). However, a long and variable latent period for leukaemia induction could obscure clear evidence of space-time clustering (Grufferman and Delzell, 1984). Some examples of a chromosomal abnormality subject to space-time clustering have recently been reported in some human populations which have not been exposed to radiation above background levels and this has led to the speculation that an infective agent may be responsible (Neel *et al*, 1992).

6.11 Social contact in infancy: Attendance at creches has been reported to be associated with a reduced risk of childhood leukaemia in a study in Greece. Children in creches may be younger when first exposed to a range of infectious agents (Petridou *et al* 1993). MacMahon (1992) reviewed studies showing an inverse association between birth order and childhood leukaemia and suggested that this was consistent with children in later birth orders being more likely to be exposed to viruses at an earlier age than their older siblings.

6.12 Infections during pregnancy: An increased risk of leukaemia has been reported among children whose mothers had a viral infection during pregnancy

(Fedrick & Alberman, 1972; Adelstein & Donovan, 1972). Gilman *et al* (1989) found an increased risk of leukaemia in children whose mothers had acute respiratory infections or were vaccinated during pregnancy. However, Leck and Steward (1972) found no association between maternal influenza in pregnancy and the risk of haemopoietic neoplasia. Several large case-control studies have reported associations between childhood leukaemia/ALL and a family history of autoimmune, immune dysfunction and related diseases. Alexander (1993) suggested that these findings were consistent with chronic infection in the mothers being a causative factor in the subsequent development of leukaemia in their offspring.

6.13 Infections during first year of life: Viral infections in infants under the age of 6 months have been associated with increased risk of ALL (McKinney *et al*, 1987). In this study there was also some evidence that routine immunisation may be protective against leukaemia but because of the small numbers involved, no firm conclusions could be drawn. A protective effect of routine childhood immunisation has been shown, for childhood malignant disease generally (Kneale *et al*, 1986; Hartley *et al*, 1988).

6.14 Some of the epidemiological data described above are consistent with the causal mechanism postulated by Greaves but none provides strong support for the hypothesis. We conclude that the role of infectious agents in the aetiology of childhood leukaemia is unproven but plausible.

Kinlen Hypothesis.

6.15 Further evidence for an infectious aetiology of childhood leukaemia has come from studies that were developed to test a hypothesis which was proposed by Kinlen in 1988 of a role for population mixing in the aetiology of childhood leukaemia .

6.16 The lack of marked space-time clustering in childhood leukaemia indicates that, if infective in origin, it may result from an uncommon response to an infection. Cases caused in this way would not necessarily cluster in space and time if the agent was mainly spread by infected individuals who were not ill and did not themselves develop neoplastic disease as a result of infection.

6.17 Feline leukaemia provides an example of an uncommon haematological malignancy which results from a widespread infection. A high proportion of urban cats can be infected with *feline leukaemia virus* but few contract leukaemia. However, in households in which large numbers of cats are kept in close proximity, more than a hundred times greater risk of feline leukaemia occurs, which may be attributed to the increased viral exposures.

6.18 Kinlen has postulated that higher than normal levels of new infections are likely to occur in populations following extensive mixing of individuals from different areas, bringing together infectious and susceptible individuals. He suggests that the phenomenon is likely to be particularly marked when the mixing involves persons from urban and rural backgrounds.

6.19 The severity of an illness due to an infectious agent may be influenced both by the age at infection and the dose of the agent. Examples in which a more severe outcome is associated with infection in adolescence rather than in infancy include paralysis from polio and infectious mononucleosis from Epstein-Barr virus infection.

6.20 If infection was a contributing factor in the development of leukaemia in children, Kinlen argued that this might provide the explanation for the excesses of

childhood leukaemia near the two nuclear sites at Sellafield and Dounreay (Kinlen, 1988). The large initial influx of both professional and other workers, combined with an unusual level of migration and job turnover, has given these geographically isolated areas a highly unusual demographic pattern. In such situations, children may have been exposed to infections at a higher intensity and at a later age than might otherwise have been the case.

6.21 A summary of data relating to this theory has recently been published by Kinlen (1995), on which Table 6.1 is based. Seven of these nine studies were conducted by Kinlen and his colleagues. They sought situations where population mixing had occurred to an exceptional extent. Some studies include NHL under the definition of 'leukaemia', while others do not, depending on the form in which data were available. For completeness, a recent study by Kinlen *et al* (1995) has also been included in the table. We note that the results support Kinlen's hypothesis.

Table 6.1 Childhood leukaemia and population mixing in mainly rural residential and occupational situations: Ratios of observed numbers of cases to those expected (on basis of general population rates) in the highest exposure category of population mixing. (Observed numbers in parentheses)

Based on Kinlen 1995

TYPE OF AREA	COUNTRY	0 - 4 yrs	5 - 14 yrs	0 - 14 yrs ^a	Reference
Rural Local Authorities #	Scotland	4.70 ** (7)	1.39 (1)	2.79 ** (8)	Kinlen (1988)
Rural New Towns	England, Wales & Scotland	2.75 ** (20)	0.41 (3)	1.58 * (23)	Kinlen et al (1990)
Rural 'military'	England & Wales	1.92 ** (43)	1.34 (28)	1.65 ** (71)	Kinlen & Hudson (1991)
Local Authority (Growth) ^b	England & Wales	1.29 (30)	1.48 ** (51)	1.40 ** (81)	Langford (1991) Langford & Bentham (1990)
Rural 'oil' ^c	Scotland	1.87 ** (31)	1.15 (17)	1.53 ** (48)	Kinlen et al (1993)
'Commuting increase' ^b	England & Wales	1.76 ** (46)	1.32 (33)	1.50 ** (79)	Kinlen et al (1991)
Rural reception for wartime evacuees ^b	England & Wales	1.24 (49)	1.91 (41)	1.47 * (90)	Kinlen & John (1994)
Growth communes ^d	France	0.52 (1)	1.46 (7)	1.19 (8)	Laplanche & de Vathaire (1994a,b)
Rural Construction Sites ^c	England, Wales & Scotland	1.39 ** (63)	1.35 * (67)	1.37*** (130)	Kinlen et al (1995)
TOTAL (except #)		1.55 *** (283)	1.39 *** (247)	1.47 *** (530)	

^a In the case of the French growth communes, the data include the 15-24 age group.

^b Ratios to the reference category rather than national rates; ^c Includes NHL.

^d French growth communes are mainly close to population centres and therefore may not be relevant. If growth communes *outside* the highest category are included, the corresponding values are: 1.47***(236); 1.28**(227) and 1.37***(463), respectively.

* P < 0.05; ** P < 0.01; *** P < 0.0001 (2-sided p values)

Data from the *rural local authority* study is largely included within the *rural new towns* study.

6.22 All of the studies showed an increased risk of leukaemia among children aged 0-14 years old when children in localities subject to an unusually high amount of population mixing were compared with a relevant control group. Summarising the results of these studies, the author reported an overall increased relative risk of childhood leukaemia associated with population mixing which was highly statistically significant (Relative Risk = 1.47; $p < 0.0001$). A similar highly significant risk was reported for both the 0-4 and 5-14 years age groups.

6.23 We note that the results are consistent with the view that children in rural situations are relatively protected from infectious agents, low population density or geographic isolation effectively limiting contact with infective agents. This results in a higher than average prevalence of susceptible individuals and makes such groups vulnerable to an epidemic, if there is a large population influx.

6.24 Other evidence supportive of the Kinlen hypothesis comes from Langford and Bentham (1990) and Langford (1991) who found that mortality rates for childhood leukaemia in local authority areas in England and Wales between 1969 and 1973 were significantly higher in those areas with the highest rate of population growth, irrespective of whether they were new towns which Kinlen had studied.

Studies which do not support the Kinlen hypothesis.

6.25 We have also considered several published studies which have not supported the Kinlen hypothesis. However we note that these other studies have involved different kinds of population mixing from the type investigated by Kinlen.

6.26 Laplanche and de Vathaire (1994a) examined leukaemia mortality rates among persons under 25 years of age resident in French communes (administrative units) which had exhibited a large and rapid population increase between 1968 and 1990. No increase in childhood leukaemia was observed. This study was not strictly analogous to the Kinlen *et al* 1990 study since the communes were not in rural areas but near to population centres (ie. overspill type); however their population increase exceeded 100% between two consecutive censuses (Laplanche and de Vathaire 1994b).

6.27 Wolff (1991) reported that the large scale evacuation of children during World War II had not affected overall mortality from childhood leukaemia. However, national mortality rates are inevitably rather insensitive to increases among indigenous rural children given the small fraction they represent of the country's children.

6.28 Petridou *et al* (1991) found no evidence of an increased risk of death from childhood leukaemia associated with the massive influx of tourists to Greek Islands. However, Kinlen has pointed out that mortality could not be examined for the first 15 years following the rise in modern tourism, which was the only period in which excesses were found in all the British studies of population mixing.

Greaves hypothesis

6.29 Greaves (1989) has suggested that it is the immune response to infection, rather than any specific infection, which plays a critical role in the development of certain types of leukaemia. An infection may induce proliferative stress in the bone marrow lymphocyte precursors, so increasing the risk of mutations in an already vulnerable cell population. Greaves argued that the significance of infections with viruses, bacteria or other pathogenic micro-organisms (eg. fungi, mycoplasma) may lie in their antigenicity and associated ability to stimulate proliferative activity in lymphocyte precursor cells or modify normal immune surveillance of malignant cells.

6.30 Greaves (1988) suggested that the majority of common ALL (cALL) are initiated in proliferating B-cell progenitor cells *in utero* but require an additional post-natal event for full expression as acute leukaemias. This model is supported by Steenbergen *et al* (1994) who reported that for many ALL patients the initial genetic events leading to transformation may have taken place in early fetal life.

6.31 Greaves *et al* (1993) postulated that the observed increased risk for cALL in developed countries may result from a rare, pathological response to delayed exposure to one or more types of micro-organism that, in less developed countries, are transmitted neonatally or in infancy. Such a response is most likely to occur if the age at which the infection is acquired is later than normal, the delayed immunological challenge resulting in a pronounced or less regulated proliferative stress (Greaves 1988). A parallel might be drawn between Epstein-Barr virus causing clinically apparent infectious mononucleosis much more commonly in young adults than in children (Linder and Purtillo, 1984).

6.32 Greaves' original hypothesis proposed a non-specific antigenic challenge or infection by a specific agent which was involved in the late events leading to cALL. Alexander (1993) has postulated that this hypothesis, taken in conjunction with the work of Kinlen and epidemiological studies on clustering, may favour a specific transmissible agent which is implicated during gestation and subsequently during the time period leading up to diagnosis.

Sewage Discharges

6.33 The possibility that the discharge of untreated sewage might be a contributory factor in the aetiology of childhood leukaemia in Seascale was drawn to the attention of the Black Advisory Group (Black 1984, para 2.46). At that time there was no reason to consider this seriously as a likely explanation; a situation which has been changed by the more recent hypotheses of Kinlen and Greaves dealt with in this chapter.

6.34 BNFL informed us that in the early years of operation of the Sellafield site there was a substantial amount of temporary accommodation on the site for migrant construction workers. During this period and subsequently, raw untreated sewage from the whole Sellafield site was discharged directly to the River Ehen and allowed to flow out to sea less than a mile from Seascale beach. A sewage treatment plant was commissioned in 1984 on the Sellafield site. For most of the post-war period the sewage from Seascale itself was also discharged close to the beach but we understand that the pipeline is now further out to sea. If infectious agents were implicated in the Seascale leukaemia cluster, a rather more direct route for some types of infectious agent could therefore be envisaged for their transmission in the case of Seascale than for other communities in West Cumbria. Anecdotal reports suggest that the beach, which Seascale village itself directly abuts, was a common place for children to play twenty years or more ago until the early part of the 1980s. If the postulated infectious agents persisted in sewage there would have been a possibility of local residents, perhaps particularly children, being exposed to them either through direct contact with sewage on the Seascale beach or via seaspray. This represents another unique feature of Seascale since it is the only village close enough to Sellafield to be exposed in this way.

DISCUSSION

Relevance to Seascale

6.35 If we suppose that Kinlen's hypothesis concerning the aetiology of childhood leukaemia is correct, then we need to consider the features of Seascale that may enhance the risk for childhood leukaemia. These include its remote location and the high socioeconomic status of the residents up to 1971. We consider these factors in more detail below.

6.36 The demographic profile of Seascale has been highly unusual in several ways. A marked population influx occurred in the years 1948-51 and further increases occurred during the 1950s so that its population trebled in a dozen years. In addition, it had a higher proportion(43%) of residents classified as social class I(SCI) than any other parish in the country (Gardner *et al*, 1987a,b); the parish with the next highest proportion of SCI residents had only 11%. The social class distribution was much the same at the 1971 census but the proportion of SCI residents decreased considerably over the following 20 years, though these conclusions are based on only a 10% sample of residents.

6.37 The HSE Study(1993) which investigated leukaemia and other cancers in the children of male workers at Sellafield addressed population mixing. They defined migration index as the ratio of births to non-Cumbrian born fathers to births to Cumbrian born fathers. The migration index was determined within each of 11 population bands, one of which was Seascale. They found a strong correlation with rate for leukaemia/NHL and migration index ($p = 0.0005$). However, if the analysis is restricted to the population centres other than Seascale, there is no significant association ($p = 0.48$). The study showed that in Seascale there were 4.5 times as many births to non-Cumbrian born fathers as to Cumbrian born fathers. Outside of Seascale the average ratio is 1:4 in the other direction.

6.38 Seascale is also close to a unique industrial site, Sellafield, which is the largest rural worksite in the UK, and is also notable in having on the site a large (often mobile) contractors' workforce during most of its 40 year history. Seascale has had a continual influx of workers since around 1940; between June and December 1940 there were 4000 imported workers on the Drigg site; then in 1941, Sellafield imported a similar number. The site was partly demolished between 1945 and 1946 by Courtaulds; then it became a nuclear site. If an excess of childhood leukaemia in the Sellafield area preceded 1946/7 then this would support the Kinlen hypothesis. If there was no excess then this would provide evidence against the Kinlen hypothesis, however the numbers involved may be inadequate to make this judgement. We therefore asked for further details of the activities around Seascale prior to commissioning the Sellafield nuclear site and on the childhood cancer rate in Seascale during that period. No childhood leukaemias were observed in Seascale prior to commissioning the Sellafield nuclear site, but the expected number in the period 1900-1945 was only 0.27 in those aged 0-24 years. This is discussed in more detail in Chapter 7.

6.39 Seascale has received a constant reintroduction of 'susceptibles', as a result of the unusually high level of inward and outward migration of high social class scientists and executives with their families in the early years. Continued population flux may explain why the incidence of leukaemia in Seascale has been raised for a long time. In summary, Seascale is extreme in terms of the length of time in which a high level of population mixing has occurred.

6.40 Kinlen (1993) observed that the excess incidence of childhood leukaemia in Seascale occurred in both those born in Seascale and in those who moved into the area. This feature is still consistent with the population mixing hypothesis as those moving into Seascale may have come from a rural area (Kinlen, 1995a).

6.41 Kinlen (1995b) has noted that of the leukaemia and NHL cases in Seascale, the youngest affected children were born in the village, whereas most of the older children were incomers to the parish. He compares this to observations in tropical Africa on Burkitt's lymphoma, the first human malignancy to be firmly linked to a virus, where the mean age at onset was lowest in areas of highest incidence and

most of the older affected people were immigrants from low incidence areas (Burkitt and Wright, 1966). Kinlen (1995b) suggested that this finding pointed to a high degree of immunity at those older ages among the locally-born as a result of their earlier exposure to infection.

6.42 An increased incidence of childhood leukaemia/NHL in Seascale is compatible with the Kinlen hypothesis and also with that of Greaves, both of which relate to haematological malignancy. It should be noted that of the 17 Seascale cases shown in table 2.3, 8 are of leukaemia, 4 of NHL and 5 of other cancers.

6.43 Although it is probable that population mixing could account for some instances of an increase in haematopoietic malignancies in Seascale, it remains unclear whether the hypothesis can explain the whole of the excess. The risk of childhood leukaemia is increased around two-fold for 0-14 year olds in parishes within 10km of major construction sites (Kinlen *et al* 1995). Consequently, if Seascale had no more extraordinary features than these areas, population mixing would at best seem to offer only a partial explanation. Although a number of unusual features have been identified with respect to Seascale we cannot quantify these.

6.44 Interpretation of some of the epidemiological studies by Kinlen is complicated by the potential for denominator errors in the circumstances of a mobile population. Nevertheless, the magnitude of the excesses and the large number of positive studies point to a genuine phenomenon.

6.45 Most of the published reports have identified circumstances in which there was a *transient* increase in the risk of childhood leukaemia, but in only one reported study, in addition to Seascale, has there been an excess of childhood leukaemia/lymphoma over an extended period. This study of a construction site was notable for a prolonged period of construction work (Kinlen *et al*, 1995).

CONCLUSIONS

6.46 The evidence cited in this chapter provides reasons to believe that some kinds of infective processes may be associated with childhood leukaemia. However, there are several hypotheses dealing with infectious aetiology; these are not wholly compatible with each other or with all the available data. The Greaves hypothesis was formulated for common (B-lineage) acute lymphoblastic leukaemia; it may not be obvious that it is applicable to other sub-types. The characteristic feature of this concept is the leukaemogenic risk of *delayed* infections (of general type). The absence of infections at a young age leads to an accumulation of B-lineage stem cells, which would otherwise die or mature. If common infections occur late they may stimulate proliferation, and mutation, in an enlarged stem cell pool. On this model, early infections are protective, at least relative to the same infections occurring later. However, some evidence cited in this chapter implies a leukaemogenic risk of infections occurring very early, in pregnancy. Here, the plausible hypothesis is that a specific agent, probably a virus, is responsible, rather than non-specific infections stimulating B-cells.

6.47 The studies by Kinlen have found an association between population mixing and the risk of leukaemia. While no particular biological mechanisms have been identified to account for this increased risk, a plausible explanation is that it could result from a specific, possibly viral agent, which is transmitted to 'carriers' or 'susceptibles' within the population. Susceptibles may include those who have been relatively protected from infections until brought into contact with carriers by population mixing. A feature of this concept is that the risk of leukaemia is dependent on the proportion of susceptibles and carriers in the community, in addition to the level of population mixing occurring at any time.

For example, the simplest scenario of the population mixing hypothesis would be a raised leukaemia incidence that occurs as a single 'surge' in an indigenous rural population immediately after a population influx, followed by a decline. This does not seem compatible with the sustained pattern of raised incidence in Seascale, which affects both indigenous and incoming children. It is possible, however, that the pattern seen in Seascale may reflect the influence of secondary factors such as the continued influx of susceptibles, relative isolation due to socio-economic status etc, as considered above (paragraphs 6.39 to 6.41). This makes it difficult to derive unambiguous predictions which would allow the hypothesis to be refuted by any single set of observations.

6.48 A further difficulty concerns the issue of dose response. If leukaemia incidence is raised in relation to population mixing, is this likely to be a simple proportionality? In order to examine this possibility it would be necessary to define a measure of population flux. Table 6.1 shows that it is possible to identify situations in which the relative risk associated with population mixing is two or more. We might, in principle, be able to measure the level of population flux for a situation in which the relative risk is two (ie. an excess relative risk of one). The level of population flux at Seascale would have to be about ten times as large to account for the excess, using this assumption. However, a linear proportionality may not be plausible, a non-linear relation with 'saturation' of the effect at some unknown level seems more likely. As Kinlen has noted, "Epidemics...do not show a linear dose-response relationship with the level of contact between susceptible and infected individuals" (Kinlen 1995). In the absence of such a relationship, it seems impossible to say whether the increased population flux in Seascale is sufficient to explain the increased leukaemia incidence or not. These ambiguities contrast with the relatively precise predictions which can be made in relation to radiation based hypotheses. As seen in other chapters of this report, it is the large numerical discrepancies which serve to refute the radiation based hypotheses considered earlier.

6.49 These difficulties do not mean that infection based hypotheses are untenable. On the contrary, many scientists working in the field now believe that an infective aetiology is likely for at least some leukaemias and that population mixing plays some role. However, these ideas are relatively new and have not yet been developed to the point at which quantitative predictions can be made. Until this is possible, it is premature to conclude that infection-based hypotheses alone can provide a satisfactory explanation for the unusual pattern of leukaemia in Seascale.

CHAPTER 7

THE HISTORY OF THE ROYAL ORDNANCE FACTORIES SITED AT SELLAFIELD AND DRIGG IN THE 1940s AND A HISTORICAL REVIEW OF CHILDHOOD CANCER IN SEASCALE

Introduction

7.1 In this report, we have focused our investigations on the evidence surrounding the incidence of childhood cancers in Seascale in the period 1963 to 1992 whilst Sellafield (as Windscale) has been a nuclear site. However, it came to our attention when considering the various potential causes discussed in the previous chapters, that we needed information on the activities in the area prior to the commissioning of the Sellafield Nuclear Site, and also on the local rate of childhood cancers prior to the increased incidence observed after 1963.

7.2 We were also aware of several anecdotal reports that an excess of childhood cancer had occurred in Seascale prior to the building of the nuclear installation at Sellafield. Certain reports have suggested that this excess was identifiable as early as the First World War. Other reports have implied a link with the building and operation of the Royal Ordnance Factories at Drigg and Sellafield in the 1940s.

7.3 We therefore requested an analysis of death certificates of the relevant populations, back to 1900. This analysis was carried out by Professor Cartwright and his team at the Leukaemia Research Fund Centre for Clinical Epidemiology in Leeds. The results of this study are described later in this chapter. We also asked the COMARE Secretariat to conduct a document search of files held in the Public Records Office (PRO) relating to the operation, during the 1940s, of two Royal Ordnance Factories (ROF) situated at the sites currently occupied by Drigg and Sellafield. The Ministry of Defence (MoD) also provided important details from PRO documents and MoD Army Historical Branch. A summary of the relevant historical information is given in paragraphs 7.4-7.28 below. Because of the nature of the documents found in the PRO it was not possible to reference them in the usual format. The form in which these documents are to be found is described in the Annex to this chapter. However, four main sources provided the bulk of the information given below. These are marked as references a-d in the Annex. The various headings are marked as to which of these references are applicable to the information quoted. Actual quotes from the documents are contained within quotation marks.

Summary of Royal Ordnance Factories' operations.

[reference: (a)]

7.4 In 1939 it was decided that a third TNT (trinitrotoluene) production plant (the others were in Wales and Scotland) was required to meet war-time requirements. This factory was sited at Drigg situated to the south of Seascale. Construction began in 1940 with local unskilled labour being recruited from the Whitehaven and Cleator Moor areas. Skilled labour was generally not available within the local area and was recruited from all parts of the British Isles. Most unskilled workers had to be transported up to 25 miles by road and rail to the site. Between June and December 1940 up to 4000 construction workers were employed on site and hostel accommodation was provided at Millom, Silecroft and Eskdale. It is worth noting that Drigg village had a pre-war population of 420.

7.5 Because of increasing demand, the manufacture of TNT commenced on 6 March 1941, although the factory was far from complete. An appreciable amount of civil engineering work was carried out concurrently with production. Much of the production workforce was recruited from the construction workforce. The great majority of these people had no experience of chemical plant although it is recorded that they adapted themselves to the new working conditions in a relatively short time. Four years later it was recorded that the factory personnel were composed of trained and experienced chemical workers.

7.6 TNT output rose to 200 tons weekly by 5 July 1941 and to 400 tons weekly by 13 December 1941. ROF Drigg was the first TNT factory to produce over 500 tons per week and its maximum output was over 600 tons per week.

Factory effluent.
[reference:(a),(c)]

7.7 The Drigg factory effluent was described as “essentially acidic” and discharged without any preliminary treatment into the sea. In the case of Sellafield, discharge was into the mouth of the river Ehen. An effluent report by the ‘Water Pollution Research Laboratory’ dated January 1945 and entitled “Report on the Effect on the Estuaries of the Rivers Calder and Ehen of Waste Waters from ROF 39” (ROF 39 being ROF Sellafield), was commissioned following complaints by Egremont and District Anglers’ Association and the Cumberland County Council that effluent from ROF Sellafield was affecting fish stocks in the two rivers. This report noted that the Sellafield discharge was sufficiently acidic to kill fish in a very short time.

7.8 The estuary survey concluded that “under the conditions prevailing in 1944 it might have been possible for fish to swim from the rivers Calder and Ehen to the sea provided they swam close to the banks of the estuary; the water in the middle of the estuary would rapidly have proved fatal to them”.

Workforce
[reference:(b), (a)]

7.9 ROF Sellafield was the last TNT factory of the war to be built. Construction appears to have been carried out from late 1941 and TNT production started in March 1943. Although of a similar capacity to Drigg, Sellafield was not required to have the same output as Drigg but still achieved an output of over 400 tons per week. When complete the two sites employed approximately 3000 workers. Although not stated, it may be assumed that a similar number of construction workers were employed at Sellafield as at Drigg. Sellafield was essentially administered from Drigg. It is noted in the files that both factories were ordered to stop production of TNT on “VJ+1 day”, (ie the day following victory in Japan day).

Working conditions.
[reference:(a)]

7.10 Considerable problems were encountered at Drigg when TNT production first started. Many of these problems were encountered in the sulphuric acid production section. In the denitration plant nitric acid recovery was originally poor (less than 50%) with unrecovered acid “splashed all over the plant”. In addition “films of nitrobody on floors and walkways rendered working conditions hazardous. The plant deserved its unenviable reputation”.

7.11 Originally, the fume exhaust from the nitric acid concentrators was vented direct to atmosphere which resulted in considerable damage to the roof and girder work of the building. Also, in the sulphuric acid concentration plant, liquid flowed in open channels inside the building. Sulphur dioxide and other gases were vented from these open channels which “permeated the whole building and caused unnecessary discomfort to the operators. The atmospheric conditions were deplorable”.

7.12 Women workers were first engaged at Drigg in September 1941 but not as plant operators until February 1942.

7.13 In the course of the operation of the Drigg plant there were three fatalities, two as a result of ammonia off-loading activities, one as a result of a fall in the boiler house. No further details are listed.

Medical department.

[reference:(a)]

7.14 Originally, the Drigg facilities were poor with “one State Registered Nurse (SRN) and a few first aid workers” housed in an inappropriate building with “quite inadequate equipment”. However, by 1943, the medical department consisted of a Medical Officer (MO), five SRN’s, a cleaner and an ambulance driver, housed in a properly equipped surgery. Some of these facilities were shared with Sellafield.

7.15 The medical department was responsible for worker inspections. All TNT and MNT (mononitrotoluene) workers, lead workers, laundry and laboratory workers were inspected at least once a month. If problems were found, workers were given “out of contact” work within the factory. Home visits were also carried out.

7.16 By 1942, the incidence of mild cases of TNT poisoning had created “a problem in rehabilitation”. In the great majority of cases the MO advocated precautionary measures to take operatives out of contact with TNT for one month. This problem was solved by starting a market garden. However, after two successful seasons the project was abandoned “because circumstances prevented the canteen Manageress from utilizing the produce”.

7.17 Limited detail is available on the housing built for workers at the two sites in the local area. Apart from hostel accommodation noted above, the files examined list a further hostel situated at Yottenfews for Sellafield workers and the following housing for married workers (at both sites) built between 1941 and 1946.

Housing.

[reference:(c)]

- 24 houses in Drigg
- 24 houses in Seascale
- 17 houses in Yottenfews
- 64 houses in Egremont
- 196 houses in Windscale/Sellafield (Anon, 1946)

However, this information may be incomplete.

7.18 All of the following data related to the Sellafield site when it was in the process of being handed over to Courtaulds Ltd. The information available is not complete but the following is a summary of what was found.

Decontamination and demolition of site buildings.

[reference:(c)]

7.19 An expert “decontamination squad” was on site during all demolition work. All site equipment and machinery appears to have been either removed to other ROF sites or decontaminated and sent for scrap and an inventory is on file, but it is not clear whether this is exhaustive.

7.20 As to site buildings, the information is terse but some examples are listed below:

“One of the construction worker huts (brick and wood construction with concrete floor) sold to British legion”.

One worker hut sold to ROF Drigg Social club.

All equipment removed from Laboratory, Nitration buildings, Acid Storage, Sulphiting and Magazines and buildings abandoned.

Laboratory building A9; Roof, windows sold to Millom Iron Works: Rest abandoned.

7.21 There is a note that all areas to be handed over to Courtaulds would be decontaminated and secured as “Not Potentially Dangerous”, with the one exception of the deep drains and foundations which could not be decontaminated and also that “any work carried out on these structures must not proceed without the advice of appropriate Ministry experts”.

7.22 Site clearance by Courtaulds had been under way for over a year, when it was decided that Sellafield would become the site for the Windscale works and the site reverted to its former tenants, the Ministry of Supply.

Site clearance.
[reference:(d)]

7.23 In September 1947 the Ministry of Works took over the site from the Courtaulds' contractors. In the design of Windscale, only a few buildings were earmarked for permanent retention; these were a canteen, a stores building, a boiler house, an administration building and some small ancillary buildings. All process buildings were demolished. The biggest task was to remove the nitrate mixing plants and the storage magazines.

7.24 The mixing plants were protected by earth traverses which surrounded the buildings and isolated them from each other. These traverses were 20 ft high, 70 ft wide at the base and 3 ft wide at the top. This amounted to approximately 13,000 cubic feet of earth for each of the twelve plants. Disposal of this earth was effected by using it to raise the level of the eastern half of the site, where it sloped towards the river, sometimes to a depth of 5 ft.

7.25 However, when the site had been raised to the desired level, considerable quantities of soil and building spoil remained to be disposed of. This was achieved by filling the southern half of Sellafield Tarn which was situated to the west of the site. It is recorded that in 1960 this filled area was the site of a football and cricket field used by the labour force employed to build the Calder Hall power station.

7.26 Frequently during demolition, floors made of acid-resisting brickwork would catch fire. The explanation for this phenomenon was that the process buildings had become impregnated with chemicals (possibly ammonium nitrate and TNT) which were ignited by the friction or sparks caused by the jackhammers used to break up the brickwork.

7.27 Drainage from the old site was only retained in part, ie storm and soil drainage. All other drains were removed. This was to ensure that if any future spillage of radioactive materials occurred the active liquid could not seep into old or unused drains and be transported to other areas of the site.

7.28 Demolition and site clearance lasted until the summer of 1948, but building activities were being carried out concurrently.

7.29 Mortality and its cause was reviewed for the Whitehaven district, for the years 1900-1945. This work was carried out because we were aware that in the past there had been several reports that an excess number of deaths from childhood cancer occurred in Seascale, during this time period.

Childhood Cancer-Mortality

7.30 The area was subdivided into the two southernmost parishes of Seascale and Gosforth and the 'rest' of Whitehaven District. Two age groups (0-24, 25+) were used and three causes of death: leukaemia/lymphoma, other cancers and other causes. Deaths recorded from the Sellafield/Windscale areas, although part of Seascale parish, were recorded separately. In all 38,329 death registrations were examined.

Table 7.1 Number of Deaths between 1900-1945

	Ages 0-24			Ages 25+		
	Leukaemia Lymphoma	Other Cancers	Other Causes	Leukaemia Lymphoma	Other Cancers	Other Causes
Seascale civil parish	0	0	23	0	40	233
Sellafield/Windscale	0	0	17	0	5	37
Gosforth civil parish	0	0	80	0	39	380
Rest of Whitehaven	17	50	12,987	47	2,864	21,510

7.31 No leukaemia/lymphoma deaths occurred among residents in either of the two parishes in the south part of the district, although the diagnosis in others was made throughout the time period.

7.32 Estimates of the Seascale population were made in order to compute an expected number of leukaemia/lymphoma deaths. The calculated expected leukaemia/lymphoma case numbers were 0.27 for 0-24 year olds and 0.68 for 25+.

7.33 In the period 1941-45, Seascale had a large chemical factory either in construction or productive operation within a few miles both to the north and south of the village. This was the only location, as far as can be determined, where two such factories were situated in such close proximity. The conditions of work in the two factories were only tolerable because of the demands of wartime production and there is evidence of chemical toxicity in workers. Despite these poor environmental and working conditions, there is no evidence of a raised incidence of childhood cancer or leukaemia in the area up to and including 1945. Seascale could be said to have been close to a large chemical factory, either in construction or operation, almost continuously since 1940. The hypothesis, that the influx of workers into an isolated community may explain the excess of childhood leukaemia in Seascale, has been discussed in detail in Chapter 6 of this report. In view of this hypothesis, it is interesting to note that no cases of childhood leukaemia or cancer have been found in the Seascale or Sellafield parishes during the period 1900 to 1945. Large mobile workforces have been housed in the vicinity since that time, but were not housed in Seascale village in any number until 1949 when 180 houses were built for the nuclear workforce, with another 62 added in the early 1950s.

Conclusions

7.34 In our opinion, the evidence suggests that there was considerable potential for chemical contamination of the local environment during the war years. However, we do not believe that potential chemical pollution was likely to be a major factor influencing the incidence of childhood leukaemia in later years since the life time for such contamination in the soil is short and there would be a likelihood for effects on adults as well. No such effect has been observed.

ANNEX

DATA SOURCES-HISTORICAL REVIEW OF ROF SITES.

i. Most of the information in this chapter relating to the ROF sites was taken from two reports as detailed below:

(a). The History of the Royal Ordnance Factory Drigg” (Anon, 1946)

This report has no date, reference or author but was obtained from a file containing relevant correspondence which was all dated 1946.

(b). “Construction of Explosive ROF’s” (Smith, 1946)

This report was signed by D. Mack Smith. Again, it was undated, but accompanied by other documentation also dated 1946.

ii. Several other files were also examined. **(c).** These were mainly correspondence files relating to housing provision for workers and communications between the Ministry of Supply and the Ministry of Works and Courtaulds Ltd. The last set of documentation related to the decontamination and demolition of buildings on the Sellafield site, which was being cleared for sale to Courtaulds for development as an artificial silk (“Rayon”) manufacturing site. The sale was apparently never completed. This file, however, contained a report from the ‘Water Pollution Research Laboratory’ dated January 1945 and entitled “Report on the Effect on the Estuaries of the Rivers Calder and Ehen of Waste Waters from ROF 39” (ROF 39 being ROF Sellafield) (Anon 1945). This report was commissioned following complaints by Egremont and District Anglers’ Association and the Cumberland County Council that effluent from ROF Sellafield was affecting fish stocks in the two rivers.

iii. Details of the site clearance by the Ministry of Works, following the decision that Sellafield would become the site for plutonium production, were obtained from the book entitled:

(d). “WINDSCALE Problems of civil construction and maintenance” by Stuart Sinclair, George Newnes Ltd, London 1960 (Sinclair, 1960).

CHAPTER 8

GENERAL DISCUSSION

BACKGROUND

Previous reports

8.1 In the introduction we described briefly the findings of the Black Advisory Group report and our previous three reports. We concluded our previous reports with our views on the issues current at the time of writing those reports and we reiterate them here before discussing recent progress and the conclusions of this report.

8.2 When we were asked to review the scientific and epidemiological data relating to the Sellafield site and the village of Seascale for our present report, we had already concluded in our previous reports that there was a statistically significant increase in the incidence of childhood leukaemia and NHL in the vicinities of Sellafield, Dounreay, and Aldermaston and Burghfield.

8.3 In all three areas the authorised and accidental radioactive discharges could not, in our view, account for the observed increase in childhood leukaemia. However we noted a number of uncertainties in the dose and risk estimation procedure and we could not exclude completely the existence of some hitherto unknown and unexpected route by which some individuals could be exposed to increased levels of radiation. We had also considered the possible role of other factors, including chemical carcinogens, demographic phenomena and viruses, but at that time we were not aware of any specific evidence that these might have been responsible for the increased incidence of childhood leukaemia and NHL in the relevant areas.

8.4 At the time of writing our previous reports we could not exclude completely the possibility that these observations were a consequence of chance nor that they were due to the selection of the sites referred to us for our enquiries. However, the evidence considered, at that time, “tended to support the hypothesis that some feature of the nuclear plants examined leads to an increased risk of leukaemia and NHL in young people living in the vicinity of those plants”.

Current report

8.5 This report is the result of our recent review of the epidemiological, dosimetric and other scientific data relating to childhood cancer in the vicinity of the Sellafield site and new scientific evidence which has become available since the publication of the Black Advisory Group report in 1984 and COMARE’s first report in 1986. We have drawn conclusions and have clarified where progress has been made, for example in reducing the uncertainties in the dose and risk estimation procedure, and where uncertainties remain. Much of the recent work we have considered was done in response to recommendations by the Black Advisory Group and COMARE. Two broad questions are addressed by this report:

- i. has the higher than average rate of childhood cancers, first confirmed by the Black Advisory Group for 1955-1983, persisted in Seascale since 1984?
- ii. if so, what could be the cause and, specifically, what progress has been made concerning the possible hypotheses regarding causation since the time of the Black Advisory Group Report and our previous reports.

8.6 In previous chapters we have discussed in detail the epidemiological findings and the scientific evidence relating to the possible hypotheses regarding causation. In this chapter we provide a synthesis of those discussions and consider other possibilities not previously reviewed including possible combination of factors. Then we summarise our conclusions in the following chapter.

THE INCIDENCE OF CANCER IN THE VICINITY OF SELLAFIELD COMPARED WITH NATIONAL INCIDENCE.

8.7 The Black Advisory Group confirmed the excess of leukaemia and NHL in the vicinity of the Sellafield site in the period 1955 to 1983. The epidemiological data available at that time could not be analysed and interpreted in a totally unbiased way since they were inevitably based, in part, on the same information that had been used in suggesting that there was a cause for concern. The question of whether the apparent excess persisted could only be rigorously tested by analyses of additional data. Such analyses have been undertaken at our request (Draper *et al* 1993). The updated version of these analyses appears in Chapter 2 of the present report. This is primarily concerned with the period following publication of the Black report i.e. 1984 to 1992.

Lymphoid leukaemia plus NHL

8.8 The main conclusion (reported in Chapter 2) is that there was a significant excess of cases of lymphoid leukaemia plus NHL in Seascale at ages 0-24 during the period from 1984-92. This strengthens the earlier, similar, conclusion reached by the Black Advisory Group for the period up to 1983. There is some difference in the age-groups and disease categories of the cases observed in the two periods but we have been unable to draw any conclusions on the possible significance of this. The small number of cases precludes further statistical analyses.

Other Cancers

8.9 In the period 1963-1983 there was no suggestion of an excess of other cancers in the age-group 0-24. For 1984-92 there is a non-significant excess, based on two cases. This, together with the occurrence of an additional case in 1995 - after the period covered by the formal analyses - suggests that there may in fact be an increase in this group also, but neither the magnitude of the increase nor our degree of confidence in it is as high as for leukaemia/lymphoma (See Chapter 2).

Childhood cancer incidence in Cumbria and nationally.

8.10 There is no evidence that the prolonged increase in cancer incidence in Seascale extends to Cumbria generally, although a significant excess in North Egremont has been reported.

8.11 The wider geographical studies (Craft *et al* 1993, Draper, 1991), which were aimed at identifying possible variations in incidence rates, and the extent to which such variations could be explained by local demographic factors, do not suggest that the findings at Seascale can be accounted for by factors such as the socioeconomic status of the area or whether it is urban or rural. When Seascale is examined in the context of the national distribution of leukaemia/NHL, the incidence of these diseases in Seascale village is unusual and probably more extreme than elsewhere in this country.

THE POSSIBLE CAUSES OF THE CHILDHOOD CANCERS STUDIED

General

8.12 The cause of the majority of cases of childhood leukaemias and lymphomas that occur in the UK is unknown. Marked predisposition is associated with certain genetic disorders such as Down's Syndrome and ataxia-telangiectasia. Stewart and colleagues (1958) have shown a significant association, now widely accepted as causal, between obstetric x-rays and childhood leukaemia and other cancers. For children born in the late 1950s and early 1960s, before the risk was widely known and the practice reduced, this could have accounted for perhaps 5% of cases. Radiation is not, however, the only known cause of leukaemia. At present it is not possible to distinguish between cancers induced by radiation and those arising from other causes.

8.13 While epidemiological studies can find associations with putative causative factors, they cannot, in isolation, prove causation directly. There are many examples however, where epidemiological studies have suggested associations that have subsequently been shown to be causal.

8.14 We wished to assess so far as we could the possible causes of the particular pattern of disease seen in Seascale. Our primary remit was to consider whether some aspect of direct or indirect exposure to radiation was a factor. However, we needed to put such considerations in the context of the evidence for other possible causes. Furthermore, any explanation needs to consider why the excess is not seen generally in Copeland, the county district containing Seascale and Sellafield. The finding of the significant excess at Egremont has been the subject of a separate investigation (Wakeford and Parker, 1996) and was found to be much less extreme than the excess at Seascale.

8.15 When considering whether the cases in Seascale may have been caused by some environmental agent it was necessary to consider:

- i. what agents were in the environment
- ii. whether exposures in this village could have differed from those in villages elsewhere and
- iii. whether the Seascale population could be more susceptible or
- iv. whether a combination of some of, or all, of these factors could be relevant

It was also necessary for us to consider whether occupational factors associated with employment at the Sellafield site could be important, since many of the Seascale residents are, or may have been, employed at Sellafield and there is a large proportion of site-owned houses in Seascale, which may also be relevant to occupational factors.

THE HYPOTHESES WHICH HAVE BEEN CONSIDERED

i. Radiation hypotheses

8.16 The Black Advisory Group considered the hypothesis that an association existed between the incidence of childhood leukaemia and other cancers and the doses received from environmental exposure of the local population to radioactive discharges, in addition to other radiation sources. The Black Advisory Group concluded that the estimated radiation dose received by the local population from the Sellafield discharges and other sources could not account for the observed leukaemia incidence on the basis of current scientific knowledge, although the group noted that there were considerable uncertainties in the available data. In addition, the Group outlined the following remote possibilities (para 4.85 Black Advisory Group report):

- i. there may be an unusual concentration of highly susceptible children in the Seascale area,
- ii. there may have been undetected discharges that have given rise to doses to the public greatly different to those believed to have occurred,
- iii. the effects of ingestion, inhalation and/or absorption of high LET emitters may have been grossly underestimated,
- iv. the model used to calculate red bone marrow dose may have been inaccurate.

8.17 In our Second and Third reports, emphasis was placed on the uncertainties in the dose and risk calculation, especially with respect to the fetus and small child, high LET effects, and prolonged low level exposure to radiation. We speculated particularly on whether there were any other ways in which exposure to radiation (either via discharges or occupational mechanisms) could be implicated, namely:

Discharges

- i. that unknown pathways in the environment could have led to a section of the population being exposed to higher than expected levels of environmental radioactivity,

Occupational

- ii. that exposure of the gonads could lead to effects in subsequent offspring,
- iii. that there were unrecognised pathways of exposure whereby radioactive material was inadvertently removed from the site by workers and transferred to the home environment,

Sensitivity

- iv. that the biological effect of particular types of radioactive materials (principally alpha emitters) may be much greater than has been supposed,
- v. that different tissues and cell types may have greater differences in sensitivity to radiation than previously thought, principally fetal haemopoietic tissue and lymphoid tissue in the bronchial and intestinal regions of young people.

ii. Non-radiation hypotheses

8.18 This Committee, as well as the Black Advisory Group, also speculated in previous reports on whether factors, other than radiation, could be relevant to the incidence of leukaemia around the sites examined by COMARE. These factors were:

- i. the social class distribution of the local population, (childhood leukaemia is known to have been more common in the highest two social classes),
- ii. the influx of an outside workforce into a previously isolated community,
- iii. possible infectious agents, e.g. there are known viral associations with particular types of leukaemia,
- iv. exposure to chemicals used in or discharged from particular nuclear installations,
- v. an effect from a combination of the factors described above.

8.19 In the preceding chapters we have examined the evidence for each of these hypotheses individually. In the period since publication of our last report, no major new hypotheses have been proposed. In this chapter we consider the relative weight of the evidence for these hypotheses. Our objective in this report is to assess advances in scientific knowledge, especially from work undertaken as a result of recommendations in the Black and COMARE reports, to analyse where uncertainties have been resolved and where they remain, and to advise on whether further research work is needed to resolve the remaining uncertainties. We discuss the various hypotheses considered in this report in the appropriate sections below.

RADIATION HYPOTHESES

Environmental radiation

Direct effect of authorised and accidental discharges

8.20 The initial observation of an excess of childhood leukaemia and NHL in Seascale led the Black Advisory Group to consider whether environmental exposure to radioactive discharges from the Sellafield site nearby had been a factor since radiation was known to be, and remains, a recognised cause of leukaemia. The first question to be addressed, therefore, is whether the doses from the radioactive discharges were high enough to account for the leukaemia cases on the basis of current scientific knowledge.

8.2 This was the original hypothesis considered by Black and this Committee in our first report, but it was thought to be unlikely to be correct because the radiological doses estimated by NRPB in their reports R171 and R171 addendum were too small to explain the excess on the basis of current scientific knowledge, by a factor of 250. However, both Black and COMARE stressed the uncertainties involved in the dose and risk estimation procedure. In particular, there are many assumptions and estimates in the chain of calculations leading to the assessed population dose and risk particularly with regard to the distribution, retention and excretion of radionuclides in the body. Similarly, in our first report (para 4.9) we emphasised that there were uncertainties in:

- i. estimation of radionuclide levels through environmental pathways,
- ii. estimation of doses to the local population,
- iii. estimation of risks.

8.22 Both Black and this Committee stressed that these uncertainties were general to radiological assessments and had led to the recommendations in the Black report for more direct measurements of radiation in humans (Black 1984, Recommendation 6) and more work on habit data, metabolic factors and high LET radiation (Black 1984, Recommendation 7).

NRPB Dosimetry Analysis

8.23 Since publication of the Black and COMARE reports, a large body of new scientific data has been produced relating to the methods used to estimate radiation doses and risks from environmental exposure to radionuclides with a view to reducing these uncertainties. NRPB have, therefore, recalculated dose and risk estimates, contained in NRPB R-276, in the light of these advances in scientific knowledge. We have addressed the main advances in knowledge and the important differences between NRPB-R171 and its addendum and NRPB's new assessment in NRPB R-276, and the major remaining uncertainties in the dose assessment from environmental radiation exposure in Chapter 3.

Conclusions relating to environmental radiation

8.24 In the discussion section of Chapter 3, we review the specific questions raised in our first three reports and the results of further research and we have concluded that although there are residual uncertainties:

- i. it is unlikely that there are major unrecognised pathways in the environment,
- ii. it is possible there are unknown biological pathways affecting the handling of individual radionuclides in different physicochemical forms within the body but there is no evidence to highlight particularly those radionuclides characteristic of the Seascale environment,
- iii. it is unlikely that the biological effect of particular types of radioactive materials (principally alpha emitters) is much greater than has been supposed,
- iv. it is estimated that the doses attributable to discharges (less than 10% of the total dose) experienced by Seascale residents are about 200 times too small to account for the leukaemia/NHL excess.

8.25 Having sought to minimise these remaining uncertainties environmental radiation alone seems highly unlikely to have been the sole cause of the Seascale cases.

Occupational Factors

8.26 As we stated in our second report, we are aware of the fact that many of the people who live near Sellafield, and in Seascale in particular, work at the nearby nuclear installation and there is a high proportion of AEA houses which could be relevant to “time of residency factors” in Seascale. This raises the possibility that the excess of childhood leukaemia could be partly related to parental occupation associated with Sellafield operations. There are two possible mechanisms by which such an effect could be mediated:

- i. paternal preconception irradiation
- ii. unrecognised pathways of exposure via workers

Both of these are considered further below.

Paternal preconception irradiation. (PPI)

8.27 The possibility that paternal exposure to ionising radiation may lead to leukaemia in offspring was first raised in a study of the outcome of diagnostic X-rays (Graham *et al*, 1966). This has become known as the Paternal Preconception Irradiation (PPI) hypothesis and implies that radiation-induced mutations occur in the male germ line and cause a predisposition to leukaemia or NHL in the next generation. Gardner (1990) suggested that paternal germ cell mutations from occupational exposure of the gonads to ionising radiation could increase the leukaemia rate in subsequent offspring sufficiently to explain the excess in Seascale. The Gardner hypothesis is considered in depth in Chapter 4 of this report and our main conclusions are summarised here.

8.28 Gardner *et al* (1990), concluded that the observed geographical excess of leukaemia and NHL among children near Sellafield could be explained by the statistical association with paternal employment and external recorded radiation dose. We have found no other epidemiological study which appears to have supported Gardner’s findings in Seascale in relation to preconception radiation effects. In fact, more detailed analyses have failed to support the Gardner hypothesis.

8.29 The principle that susceptibility to human leukaemia can be inherited is not in doubt. Furthermore, there is experimental evidence in animals indicating that activation of genes which are associated with cancer in later life are not so disabling as to be incompatible with live birth and we conclude, therefore, that there is no *a priori* reason why a human leukaemia-associated mutation should not be transmitted in this way. The issue is therefore the dose of radiation which might be required to mutate such genes at the frequency required to account for the Seascale leukaemia excess.

8.30 In chapter 4 we discussed the evidence that the level of risk implied by known radiation-induced mutation rates is inconsistent with the current best estimates of occupational dose to parents of Seascale cases. The quantitative considerations lead us to believe that the size of any such effect so far demonstrated is too small by several orders of magnitude to explain the Seascale phenomenon.

8.31 It has been suggested that the measured dose of external radiation may be a surrogate measure for internal exposure to radionuclides or to chemicals. However, the HSE study found no association with internal dose. There are a number of studies which provide evidence regarding possible mechanisms affecting localisation of some radionuclides and which suggest that testicular doses could be higher than conventional dosimetry would predict. Such alternative explanations are open to the objection that there are no generally accepted human data to support them and there is no evidence that any relevant internal radionuclide exposure would be unique to Seascale, in particular to the small percentage of the workforce living in Seascale.

8.32 In summary, we conclude that while there remain some important questions about the microdosimetric and biological aspects of germ cell response to radiation, these are highly unlikely to introduce sufficient error in the estimate of radiation dose to explain the Seascale phenomenon. Moreover, none of the postulated dosimetric theories offers a coherent biological explanation as to why excess leukaemia incidence should be confined to Seascale when the potentially exposed worker population is widely spread throughout West Cumbria.

Unrecognised pathways via workers

8.33 We have also considered whether there were unrecognised pathways of exposure via workers whereby radioactive material was inadvertently removed from the site and transported to homes or other 'on-site' activities which could lead to an increased risk of 'off-site' exposure. We have reviewed the evidence from three studies performed on housedust in workers' and non-workers' homes in Seascale and found that low levels of some radionuclides, not usually detected at these levels in the general environment, have been found in some houses. It is not clear whether these findings can be attributed entirely to transfer from the general environment, or whether some component was transferred by workers from the workplace to the home. However, the data we have seen indicate that radionuclides in housedust in Seascale are not likely to have been a significant source of dose.

NON-RADIATION HYPOTHESES

Role of chemicals in causing childhood Leukaemia.

8.34 Some adult leukaemias are associated with occupational exposure to certain chemicals. These levels of exposure are likely to be much higher than the environmental levels to which children are exposed and there are no data showing a link between such exposures and cases of childhood leukaemia, although much higher levels of exposure resulting from chemotherapy may cause leukaemia. Any hypothesis that the Seascale cluster is due to exposure to chemical discharges from the Sellafield site would need to take into account the fact that adult leukaemia rates in Seascale are not elevated.

8.35 Data relating to the possible exposures of past Seascale residents to toxic chemicals in the general environment are poor and it is not possible to obtain such data retrospectively but their exposure was not judged to be higher than that of people living near to other chemical plants which discharge similar amounts of the same types of chemicals. We have found no evidence to link the children in Seascale with direct exposure to unusual environmental levels of toxic chemicals.

8.36 While parents of Seascale children may have undergone unquantifiable levels of occupational chemical exposure, our conclusions regarding transgenerational mutagenesis given elsewhere apply equally to damage caused either by radiation or by chemicals.

8.37 We found no evidence that chemical exposures to Seascale residents differed from exposure to those resident in some other areas of the country. We conclude that exposures to chemicals alone is unlikely to explain the observed excess of childhood leukaemia in Seascale.

Role of infection in causing childhood leukaemia.

8.38 A number of studies have suggested that childhood leukaemia is more common among higher socio-economic groups (Draper 1991). It has also been estimated that the risk of childhood ALL may be doubled in isolated towns and villages (Alexander *et al*, 1990). Alexander *et al* (1990) have proposed that the lifestyle in isolated communities, especially those of higher socio-economic status, is conducive to an unusual exposure to some specific infectious agent or to general infections. Greaves (1989) has proposed that reduced exposure to antigenic challenge in infancy leads to greater proliferation of immune cells as a result of later infection.

8.39 Kinlen and colleagues have carried out a number of analyses relating to areas in which there have been high levels of population mixing, particularly between persons from urban and rural backgrounds such as occurs in the construction of remote industrial plants, and have found a small but significantly increased incidence of childhood leukaemia. This effect has been attributed to the bringing together of infectious and susceptible individuals in abnormal numbers. The infectious agent is thought to be either of a non-specific nature or perhaps a leukaemogenic virus or viruses.

8.40 An unusual feature of Seascale which we discussed in Chapter 6 of this Report is the situation in the past with regard to previous discharges to sea of raw, untreated sewage, from both Seascale village itself and from the sanitary systems provided for the many hundreds of migrant construction workers accommodated in hutments on the Sellafield site. We noted the evidence that children played on the beach close to the sewage outflow and the possibility of exposure to sewage-borne infectious agents mediated either through direct contact or via seaspray. Thus, a readily identifiable route existed via which, in the postwar years up to 1984, Seascale children could have been intimately exposed to above-average levels of infectious agents from migrant workers. Whilst we are unable, given current scientific knowledge, to comment on the question whether there might be an association between infectious agents from sewage and childhood leukaemia, we cannot rule out the possibility that such exposure may be relevant to the leukaemia excess in the area, given the known association between particular viruses and some types of adult leukaemia in other parts of the world.

8.41 Relevant factors which are present in Seascale and support the hypothesis that infection may play a role in the causation of the Seascale cases include:

- i. a previous social class structure biased towards the upper end of the spectrum,
- ii. geographic isolation and the potential for the receipt by the indigenous Seascale population of infectious agents from people migrating from distant urban areas,
- iii. the discharge of untreated sewage.

8.42 In attempting to relate a population mixing hypothesis to Seascale, none of the studies so far undertaken can give a quantitative estimate of risk. Analysis of a number of datasets gives risk estimates which are too small to account for the number of cases found in Seascale. We acknowledge that subgroups within these datasets can be identified which give higher estimates but such statistical analysis must be interpreted with great caution, especially when based on very small numbers of cases.

8.43 We conclude that there is insufficient evidence that infection related to population mixing is the sole cause of the Seascale cases, but it may have been one of a number of contributory factors and we will consider the point further below.

Combination of factors

8.44 None of the factors that we have discussed appears, on its own, to be able to account for the increased incidence of cancer in young people in Seascale. The estimated contribution of radiation exposure is very small and there is no evidence of unusual chemical exposure. The possible contribution of whatever phenomenon underlies the association of childhood leukaemia and areas with high social class and substantial population mixing does not, on present evidence, suggest a risk as large as that observed. It is possible to conjecture that if radiation exposure were at the upper limit from all sources, if there were some unknown chemical exposure, and if the infectious component (which is the most difficult to quantify) were much larger, then they might conceivably account for the excess, particularly if there are, in addition, a few “chance” events unconnected with any causative process.

8.45 It is, however, necessary also to consider the possibility that these factors might interact – that is if the effect of two factors operating together is greater than the two separate effects added together. Carcinogenesis is generally believed to be a multistage process involving a series of changes to cells and different factors may act on different parts of the pathway. Cigarette smoking and exposure to radon, for example, are known to act more than additively in causing lung cancer. In the present context we must consider whether the small radiation exposures that we have documented, whether environmental or occupational, could interact with another factor in Seascale, to produce an effect sufficiently “frequent” to account for the increased incidence.

8.46 We have concluded that the rate of conventional mutation to predisposition to leukaemia in the germ cells of occupationally-exposed fathers is insufficient to explain the excess of childhood leukaemia (see Chapter 4). If there were interacting factors operating during gestation or early life to increase the probability of predisposition actually leading to leukaemia, there would still not be enough predisposing mutations with which they could interact.

8.47 In Chapter 4, we discussed the current data available on “unconventional” changes that have been observed to occur at a higher frequency than conventional mutations. However we concluded that currently, there is no evidence that such

high frequency unconventional changes occurring in the germline could be responsible for childhood leukaemia.

8.48 Nevertheless these changes are poorly understood and may occur at high frequency; thus we cannot formally exclude the possibility of such an interaction between ionising radiation and, say, viruses (whether latent or exogenous). However, if one considers exposure to Seascale children early in life, the radiation dose is only marginally raised in comparison with that experienced by children in the surrounding area and is in any case lower than that due to natural radiation in some other parts of the country. Any radiation dose that is involved in such an interaction in Seascale must come largely from sources other than Sellafield and, therefore would be similar in nature to elsewhere. It would, therefore, be difficult to explain the uniqueness of the leukaemia incidence in Seascale.

8.49 In discussing the possible role of paternal exposure, we have considered the possibility that there is some mechanism by which radionuclides were concentrated in the germ cells of Sellafield workers in the sixties and seventies. While there is some evidence that such concentration is possible in principle, we have found no evidence to suggest that it might have occurred to a significant extent. If in practice it did occur, we might reasonably expect to have found some adverse consequences in Sellafield workers and their children who lived outside Seascale.

CONCLUSION

8.50 We therefore conclude that while the factor(s) operating which might explain the excess incidence of childhood leukaemia in Seascale could in principle have had an effect which was greater than the sum of the individual components, one of which might be the radiation exposure of Seascale residents. The greater part of the radiation exposure (NRPB estimate greater than 90%) came from sources other than Sellafield discharges. Such sources and levels of exposure are not unique to that locality.

8.51 In this chapter we have discussed the relevant evidence pertaining to the various hypotheses which have been invoked to explain the increased incidence of childhood leukaemia and NHL in Seascale. From our considerations we have reached various conclusions which are described in the next chapter.

CHAPTER 9

SUMMARY AND CONCLUSIONS

9.1 We have reviewed the epidemiological, dosimetric and other scientific data relating to Seascale and the Sellafield Nuclear Site which have become available since the publication of the report of the Black Advisory Group and our first report. A major aim of this report was to draw conclusions about the main advances in scientific knowledge since the time of the Black report and to clarify where progress has been made and where uncertainties remain. Our conclusions are reported below and the remaining uncertainties identified will form the basis of our advice and recommendations to Government.

EPIDEMIOLOGY

9.2 We have examined the incidence of cancer, according to five diagnostic groups defined in para 2.8, among young people age 0-24 living in the vicinity of Sellafield for the time period 1963 to 1992, the latter being the last year for which we have national data for comparison.

9.3 The whole period 1963-1992 was subdivided into the period examined by the Black Advisory Group (1963 to 1983) and the period following publication of the Black report (1984 to 1992) in order to see whether the raised incidence of malignant disease in young people identified by Black had persisted.

9.4 For the period 1963-1983, the conclusions of the Black report regarding an increased incidence of leukaemia in 0- 24 year olds, are confirmed. Our results show a significant increase in “all malignancies” (Observed (O) = 6, Expected (E) = 2.18, Observed/Expected (O/E) = 2.75, one sided probability (p) = 0.024) in 0-24 year olds in Seascale Ward, which is primarily due to a significant excess of cases of lymphoid leukaemia and NHL (O = 5, E = 0.49, O/E = 10.16, p = 0.00016). There was one case of cancer other than leukaemia or NHL.

9.5 The analysis for the “Post-Black” period 1984-1992 was designed to test the null hypothesis that no excess of leukaemia or other cancers in 0-24 year olds has occurred in the vicinity of Sellafield during that time period. We agreed the diagnostic groups, areas and calendar periods to be analysed in advance and these were based on the original Black findings.

9.6 Our main finding rejects the null hypothesis described in the paragraph above and strengthens the original Black observations because for the post Black period 1984-1992, for the age group 0-24 there is a significant excess of “all malignancies” in Seascale Ward (O = 5, E = 0.78, O/E = 6.4, p = 0.0012). This excess is composed of a significant excess number of cases of lymphoid leukaemia and NHL (O = 3, E = 0.16, O/E = 19.1, p = 0.0006). In addition there were two cases of other cancers which showed a non-significant excess (O = 2, E = 0.62, O/E= 3.2, p = 0.129).

9.7 Our overall conclusion is that there is good evidence for a continuing, significantly elevated level of all malignancies in young people (0-24) throughout the period considered in the Black report (1963-83) and our subsequent analysis

(1984-92), covering a total period of three decades. This is primarily due to a significant excess of lymphoid leukaemia and NHL throughout the period (1963-92). Although the relative increase in 1984-1992 was greater than that in 1963-1983, this was based on only three cases and the difference between the relative risks is not statistically significant. If we consider also the cases diagnosed outside the analysis period (1963-1992), there is the suggestion that “other cancers” might also be elevated.

9.8 The excess found among young people did not extend to the older age group 25-74, nor did it extend to the two county districts nearest to Sellafield or to Cumbria generally, although there was a less marked excess of leukaemia in Egremont.

9.9 When Seascale is examined in the context of the national distribution of childhood leukaemia plus NHL it is highly unusual and the most extreme relative increase in time and scale that has been observed. However, it should also be remarked that since leukaemia in children and young people is, in fact, a very rare disease, even the increase in risk reflected here, which appears to be confined to a small area, represents a small absolute risk and a small number of cases.

9.10 We have addressed possible reasons for these epidemiological findings and have considered a number of possible hypotheses which might explain the Seascale findings. We also note that any hypothesis has to explain why the excess is confined to Seascale.

RADIATION RISKS

9.11 First we considered the initial hypothesis, previously investigated by the Black Advisory group and in our first report, namely that an association existed between the doses received by the local population from environmental radiation and the incidence of childhood leukaemia and other cancers.

9.12 Since the time of the Black Report, we have obtained further data on routine and accidental discharges of radioactivity which are as comprehensive, complete and reliable as reasonably achievable. These data include a detailed reassessment of the aerial discharges during the early years of plant operation. This reassessment of aerial discharges, carried out by BNFL principally for litigation purposes, was made available to NRPB and ourselves.

9.13 At our request, and with our collaboration, NRPB carried out a complete reassessment of the doses and risks to the Seascale population in the light of this further information from BNFL and advances in scientific knowledge. The assessment is based on the recognised principles and methods of the International Commission on Radiological Protection, which have been recently revised. To cushion the assessment against some potential uncertainties in the dose estimates, NRPB also carried out a sensitivity analysis on selected major components or unusual pathways.

9.14 Changes from the previous assessment for the Black investigation and our first report include:-

- i. inclusion of the doses from the radioactive fallout from the Chernobyl accident and the radioactive discharges from the Albright and Wilson chemical plant,
- ii. a comprehensive review of BNFL discharges which has revealed to some important increases in atmospheric discharges in the early years of the operation of the Sellafield site,

- iii. the use of the most recent biokinetic and dosimetric models, which include a new respiratory tract model, changes in gastrointestinal uptake factors, use of physiological models with recycling for some elements and the use of comprehensive age-dependent models,
- iv. the use of new models to calculate the risk of radiation-induced cancer as described in a recent report on estimates of late radiation risks to the UK population and computing a best estimate rather than making 'worst case' assumptions.

9.15 Our principal conclusions regarding the original hypothesis (para 9.11) are listed below.

- i. For the study population in Seascale, natural radiation contributes the largest equivalent dose to the red bone marrow (80%) whereas the discharges from Sellafield, both routine and accidental contribute less than 9%. Medical exposures are estimated to contribute an equivalent dose of about 5% and weapons fallout about 6%.
- ii. In their report R276 the NRPB have concluded that in the study population in Seascale, that is 1348 children born between 1945 and 1992 and followed to their 25th birthday or 1992 whichever is sooner, the number of radiation-induced cases of leukaemia and NHL would be expected to be less than 1 (0.46). The number of other cancers expected from radiation exposure from all sources is also less than 1 (0.22). These estimates have to be compared with the 12 cases of leukaemia and NHL and 4 cases of other cancers observed in the Seascale population between 1955 and 1992.
- iii. The expected number of cases of leukaemia and NHL between 1945 and 1992 calculated to be attributable to radioactive discharges from Sellafield is less than 0.05. Considering Sellafield discharges alone, both routine and accidental, the associated doses would have had to be about 200 times greater to account for the excess number of leukaemia and NHL cases on the basis of current scientific knowledge. We consider the probability of such a discrepancy to be highly unlikely.
- iv. Having reviewed discharges and environmental monitoring data, and having noted previous underestimations of some airborne discharges, we consider that it is very improbable that the epidemiological findings could be attributed to undetected discharges, particularly of long-lived radionuclides, because the dose assessment relies primarily on the environmental monitoring data and only to a much lesser extent on the discharge data.
- v. Our review of habit data suggests that intakes of radionuclides have been not been substantially underestimated nor have environmental pathways delivered substantially greater doses than previously estimated. The sensitivity analysis provides supporting evidence.
- vi. We have considered the possibility that the biological effectiveness of particular types of radioactive material (principally alpha emitters) in particular tissues may be greater than presently attributed by the International Commission on Radiological Protection, the conventional radiation weighting factor of 20 being used in this report

(ICRP 60). However, as discussed in Chapter 3, and the sensitivity analysis, unreasonably large weighting factors for alpha radiation would be required for them alone to account for the epidemiological findings. Alpha radiation from all discharges is estimated to contribute only about 3% to the total equivalent dose from all sources to red bone marrow, whereas that from natural background alpha radiation is more than 10 times greater. We also draw some confidence from the NRPB's review conclusion that for leukaemogenesis "it would appear that there is no scientific basis for choice of an RBE value for alpha-radiation in excess of 20. Indeed, the evidence would support a somewhat lower value" (NRPB R276).

vii. We recognise that uncertainties inevitably remain. For example, fetal haemopoietic tissue and lymphatic tissue in the bronchial and intestinal regions of young people could have particular leukaemogenic sensitivity. It is also possible that uncertainties in biokinetic modelling of individual radionuclides in the body could lead to higher doses to relevant tissues than currently estimated, or that microdosimetric features of localisation within a tissue could lead to higher doses to some critically important cell type. However, it seems highly improbable that such factors would apply uniquely to the Seascale population, or that their dosimetric consequences would be sufficiently large for particular discharge radionuclides but not for any natural background radionuclides. We have found only one situation in the past where the high LET dose attributable to Sellafield discharges might have exceeded the high LET dose due to natural background, namely the high LET dose to the tracheobronchial lymph nodes. However, we know of no human data that suggests that human leukaemia can originate in the tracheobronchial lymph nodes, although it is recognised that many human lymphomas arise from lymph node tissue and these could include thoracic nodes.

viii. The possible microdosimetric effect of tritium was specifically considered. However, both the sensitivity analysis and the absence of effects in the Canadian group of workers having particular exposure to tritium, demonstrate no significant contribution from this source. These considerations are kept under review by the International Commission on Radiological Protection, whose latest recommendations have been used.

9.16 To sum up, despite these remaining uncertainties, we consider the current estimate of the radiation doses to the Seascale population, due to both routine and accidental discharges, to be far too small to account for the observed excess of cases of leukaemia and NHL on the basis of present knowledge. Consequently, it seems highly unlikely that radioactive discharges from Sellafield have been the sole cause of the excess Seascale cases. Clearly, it is not possible to state categorically that environmental radiation, including natural background, could not have been a contributory factor for some Seascale cases, particularly if a combination of factors were involved. However, such a combination of factors would have to be unique to this particular locality and play a role in leukaemogenesis.

9.17 We have found no evidence that other radiation exposures to Seascale residents differed from those to residents elsewhere by virtue of unusual levels of environmental radiation (including radon), unusual medical procedures or experimental investigations.

OCCUPATIONAL FACTORS

9.18 There are two possible mechanisms by which parental occupation could increase the risk of cancer in their offspring;

- i. preconception effect through irradiation of the gonads
- ii. unrecognised pathways of exposure via workers

Paternal Preconception Irradiation (PPI).

9.19 Gardner et al (1990a) suggested that paternal germ cell mutations from exposure of the gonads to ionising radiation could increase the cancer rate in subsequent offspring sufficiently to explain the excess in Seascale. Although there is a plausible genetic and mechanistic basis for a PPI effect, we conclude that the level of risk implied by this explanation is inconsistent with the radiation doses actually received via occupational exposure and current estimates of genetic risk. Alternative explanations for this inconsistency have been suggested, in particular that the measured dose of external radiation may be a surrogate measure for internal exposure to radio-nuclides or to chemicals. Such data as exist do not support this suggestion.

9.20 While the principle that preconception paternal irradiation could cause cancer in offspring is currently sustained by a small body of experimental data in animals and by current knowledge of data on human genetic determinants of cancer, quantitative considerations of mutation rates according to accepted models have led us to believe that the size of any such effect so far demonstrated is too small, by at least an order of magnitude, to explain the Seascale phenomenon. We conclude that there remain some important questions about the microdosimetric and biological aspects of germ cell response to radiation, particularly in relation to internal radionuclides and the mechanisms by which effects may be transmitted through the germ cells at high frequencies (see Chapter 4). However, these are in our view most unlikely to explain the Seascale phenomenon alone since they would have to be unique to those workers (a minority of the work force) who lived in Seascale.

Unrecognised pathways via workers

9.21 In addition to the data on radioactive discharges from Sellafield, we have considered whether there were unrecognised pathways of exposure via workers whereby radioactive material was inadvertently removed from the site or other activities had led to an increased risk of exposure to on site radioactive materials. We have reviewed the evidence from three studies performed on housedust in houses in Seascale. Although the data we have seen indicate that such pathways via workers may have existed, they also indicate that radionuclides in housedust in Seascale are not likely to be a significant source of dose.

NON-RADIATION HYPOTHESES

Role of chemicals in causing childhood leukaemia

9.22 Whilst there is evidence that some *adult* leukaemias may be associated with *occupational* exposure to certain chemicals such as benzene, of which there were very large quantities discharged in the early years of plant operation, there are currently no data showing a link with *environmental* exposure and subsequent cases of *childhood* leukaemia. Any hypothesis which purports to explain the Seascale cluster as being due to exposure to chemical discharges from the Sellafield site would need to take into account that adult (25 to 74 years old) leukaemia rates in Seascale are not elevated and that the leukaemia rate is not similarly raised in other nearby villages. We found no evidence of exceptional chemical exposures to Seascale residents. We have concluded, therefore, that exposure to chemicals is unlikely to explain the observed excess of childhood leukaemia in Seascale.

Role of infection in causing childhood leukaemia

9.23 On the evidence that we have reviewed, we have concluded that it is probable that population mixing is a factor in the increase in childhood leukaemias described in some population groups. Therefore, it follows that the excess childhood leukaemia incidence in Seascale is likely to be causally associated, at least in part, with related demographic factors such as geographic isolation and mixing between residents who have migrated from different areas, or additional exposure to infections such as from a sewage outflow. Such factors may reflect the involvement of transmissible infectious agents in the aetiology of childhood leukaemia. However, it is not possible to quantify this effect in a satisfactory way in order to relate it to the effect of population mixing on leukaemia incidence in Seascale since no areas in the published studies are directly comparable with Seascale. The evidence, available at present, does not convince us that such a large relative risk persisting over more than three decades could be wholly attributed to population mixing.

OTHER POSSIBLE FACTORS EXISTING IN THE LOCALITY BEFORE THE ESTABLISHMENT OF THE SELLAFIELD NUCLEAR SITE

9.24 We investigated other factors unique to Seascale and its neighbourhood which might be associated with the epidemiological findings. In particular we investigated the activities in the Sellafield area before the establishment of the nuclear site and whether there was any sign of an elevated childhood cancer or leukaemia rate in Seascale before the site was developed.

9.25 In the period 1941-45, Seascale had a large chemical factory either in construction or productive operation within a few miles both to the north and south of the village. This has led to the presence of large mobile work forces housed in the vicinity since that time.

9.26 We analysed the death certificates for the period 1900-1945. Our analysis has shown that there was no evidence of an excess of childhood cancer or leukaemia in this part of Cumbria during that period

9.27 We conclude that it is unlikely that there was any unusual genetic predisposition to childhood cancer in the population of Seascale around 1950. It is possible to speculate that some carcinogenic factor entered the environment of Seascale about that time. It is also possible to conjecture that it is associated with the existence of the Sellafield site, perhaps with its construction, its operation, or its effect on the make-up of the local population, or on their lifestyle, or with some combination of these factors. However, it is not possible to demonstrate such associations or why they should be confined to the village of Seascale.

COMBINATION OF FACTORS

9.28 None of the factors that we have discussed appears, on its own, to be able to account for the increased incidence of cancer in young people in Seascale. We considered the possibility that these factors might interact. However, we have been unable to identify any such interaction that could explain the excess of lymphoid malignancies at Seascale. If there were an interaction between some factor and radiation it has to be acknowledged that the greater part of the radiation exposure of Seascale inhabitants comes from sources other than Sellafield and is similar to that experienced by the inhabitants of other parts of West Cumbria, indeed of the UK, which would make the elevated incidence of childhood cancer in Seascale alone difficult to explain.

MAIN CONCLUSION

9.29 We conclude that there has been a continuing excess of leukaemia and other cancers in 0-24 year olds in Seascale Ward in the post - Black period 1984 - 1992, primarily due to an excess of acute lymphoblastic leukaemia and non Hodgkin's Lymphoma (NHL). Taken together with the results for the earlier period 1955-62 (for which comparable statistical analysis is not possible) and 1963-1983, the data show that there has been a continued excess of leukaemia

and NHL in Seascale for four decades. Such evidence as we have does not indicate any excess between 1900 and 1945. We have investigated possible causes of the excess in later decades and conclude that:-

- i. On current knowledge, environmental radiation exposure from authorised or unplanned releases could not account for the excess. Much work has been done to reduce the uncertainties present in the previous assessment although some uncertainties do still remain.
- ii. On current knowledge occupational exposure to radiation is very unlikely to account for the excess. Although there are uncertainties regarding internal radiation exposures it is not clear how these could affect the population of Seascale and not the other residents of small towns and villages nearby where workers from the Sellafield site also live.
- iii. Other possible hypotheses regarding chemicals and infectious aetiology have been considered. We conclude that environmental exposure to chemicals is unlikely to offer an explanation although admittedly the data are sparse. We do, however, believe that a mechanism involving infection may probably be a factor affecting the risk of leukaemia and NHL in young people in Seascale.

9.30 We conclude that the excess of leukaemia and NHL in young people in Seascale for the period 1963 to 1992 is highly unlikely to be due to chance alone. Various factors considered above could affect the incidence of leukaemia and NHL but no one factor alone could account for the increase. We cannot rule out interactions between different possible factors but, as yet, have no way of quantifying their effects nor of saying why the interaction would be unique to Seascale.

9.31 We have now produced four reports to Government on the incidence of childhood cancer and leukaemia around particular nuclear installations. The first and present reports have been concerned with the Sellafield site. Our work to investigate the cause has entailed one of the most intensive investigations of a local public health concern, due to a suspected environmental problem, ever undertaken in the UK. In addition to our efforts, the input from Government in sponsoring research, from NRPB and many other independent research bodies and individuals, including industry, has been very substantial. Given this effort there exists a natural expectation of a clear and unambiguous answer to the key issues being addressed. Certainly, we are in no doubt that the raised incidence of leukaemia and NHL which has occurred in the young people of Seascale, and its persistence over several decades, is probably unique in this country.

9.32 We have examined leading current hypotheses and pathways by which the observed excess could have come about and have been unable to find any convincing explanation. We have, of course, been constrained by the fact that mechanisms involved in human leukaemogenesis are still not clearly understood. It is our view that current research efforts being undertaken in the UK and worldwide should eventually supply answers to these questions. However, until this research provides the required information we advise against further work specifically addressing the Seascale cluster until new insights into possible carcinogenic mechanisms suggest possible causes to test. We do recognise that the position should be monitored by the relevant health agencies and we make recommendations to that end in the next chapter.

CHAPTER 10

RECOMMENDATIONS

10.1 In this report we have concluded that the increased incidence of leukaemia and NHL in young people in Seascale for the period 1963-92 is highly unlikely to be due to chance alone and we have considered various factors which could affect the incidence of leukaemia and NHL. Despite the extensive review that we have undertaken we have been unable to highlight any single factor that would account for all the excess.

10.2 However, as we noted in the previous chapter, our review has caused us to conclude that there will be no benefit from continuing to investigate Seascale in isolation, in the absence of new evidence of particular causative characteristics which could be relevant to the Seascale cases.

Recommendation 1
(Chapters 2,4,6,8)

10.3 We note that there are a number of epidemiological studies underway which will examine the various hypotheses which have been discussed in this report. The United Kingdom Childhood Cancer Study is testing both radiation and non-radiation hypotheses, including infectious aetiology and possible predisposing features to carcinogenesis. We *recommend* that these should be supported to completion.

Recommendation 2
(Chapter 2)

10.4 We share the concern about the continuing excess of childhood and adolescent leukaemia and lymphoma and possible excess of other cancers in Seascale and we *recommend* that the incidence of leukaemia and other cancers in the area be kept under surveillance and reviewed periodically by the appropriate authorities, and that any new cases of leukaemia or other cancer be fully characterised.

Recommendation 3
(Chapters 2 & 7)

10.5 We *recommend* that the mortality/incidence of both childhood and adult leukaemia and other cancers in Seascale for the years 1946-62 be examined as thoroughly as possible to connect the mortality study of 1900-45 with the incidence studies of 1963-92.

Recommendation 4

10.6 With regard to radiation specifically, our investigations have made us aware of several areas where an urgent need exists for improved knowledge. We consider that their investigation is both important for the scientific basis of radiation protection generally and for the evaluation of potential future problems in the field of radiation and public health. We therefore *recommend* support, wherever possible, for innovative research in the areas of:

- i. Uncertainties in estimating radiation doses and effects for particular target cells (Chapters 3&4) from:
 - (a) internal exposure to radionuclides in the developing embryo and fetus (*paras.* 3.46-52);
 - (b) internal exposure to radionuclides in tracheobronchial lymph nodes (*paras.* 3.88-90, 3.120);

- (c) biological hazards of ultra-short-range radiations including Auger emissions (*paras. 3.111, 4.34, 4.45*).
- ii. uncertainties in the differences between biological effects of radiations of differing quality (*Chapter 3, paras. 3.113-119*).
- iii. information on the specific nature of early molecular radiation events in somatic or germ cells that contribute to cancer initiation or development (*Chapter 4*). Particular information is required on
 - (a) the genetic basis of differences in radiation sensitivity in somatic or germ cells (*paras. 4.46-4.49*);
 - (b) the nature of radiation-induced high frequency events in somatic or germ cells (*paras. 4.61-4.64*);
 and the relevance to disease of
 - (c) radiation-induced mini-satellite mutations in somatic and germ cells (*para. 4.63*);
 - (d) radiation-induced genetic instability in somatic or germ cells (*para. 4.61*).
- iv. information on mechanisms of interaction between radiation and other agents (*Chapters 6 & 8*).

Recommendation 5
(*Chapters 8 & 9*)

10.7 We are aware that our inability to identify causative mechanisms to explain all the Seascale leukaemia and NHL excess reflects the present inadequate state of knowledge regarding the causes of childhood leukaemia. It is possible that this excess, and any others if they occur in future, will continue to elude explanation until underlying mechanisms are better understood. We expect such understanding to come from current and future initiatives in leukaemia and cancer research, whether related to radiation or not. We *recommend* that high quality innovative research, especially where it permits hypothesis testing, should be supported wherever possible, that this should be considered a necessary part of the remit of radiation protection, and that there should be continued liaison between funding bodies to ensure that essential research receives adequate priority for available funds.

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THE APPENDICES

APPENDIX A

GLOSSARY

Notes: the descriptions below are intended to help the reader understand the text; they are not necessarily definitive scientific terms, for which the reader is advised to consult specialist sources. Principal sources of published reference material consulted for this Glossary include the Chambers Nuclear Energy and Radiation Dictionary Ed. Prof. P M B Walker (Chambers 1992) and A Dictionary of Epidemiology Ed. John M Last (2nd Edition, OUP 1988).

This Glossary does not form part of the Report.

Underlined words are defined separately.

ABSORBED DOSE (Radiation)

The quantity of energy imparted by ionising radiation to a unit mass of matter such as tissue. Absorbed dose has the units J kg^{-1} and the special name gray (Gy).
1 Gy = 1 joule per kg.

ACTINIDES

A series of fifteen radioactive elements with increasing atomic numbers beginning with actinium (89) and ending with lawrencium (103). Many of them decay by the emission of alpha particles. Some can also decay by spontaneous fission or can be made to undergo fission by bombardment with neutrons and are therefore used as nuclear fuels. Only four of the actinides - actinium, thorium, protactinium, and uranium - occur in nature in significant quantity; the remaining 11 are produced artificially by bombardment of other related elements with high energy particles.

AGE-STANDARDISED RATES (ASRs)

For the purposes of this report, for ages 0-14 and 15-24, age-standardised rates (ASRs) have been calculated as simple averages of the age-specific incidence rates for the five year age groups they contain.

ALL see LEUKAEMIA

ALPHA EMITTER

A radionuclide which decays through emission of alpha particles.

ALPHA PARTICLE

A charged particle emitted during the radioactive decay of many heavy radionuclides. It is identical to the nucleus of a helium atom, consisting of two protons and two neutrons. An alpha particle has low penetrating power but high Linear Energy Transfer (LET).

AMERICIUM-241

A radionuclide with a half-life of 460 years, which decays with the emission of alpha particles and gamma rays. It is formed as a daughter product of the decay of plutonium-241.

AML see **LEUKAEMIA**

ANTIBODY

Any of a variety of proteins produced by the body in response to the presence of an antigen. By becoming attached to antigens on infectious organisms, antibodies can render them harmless or cause them to be destroyed.

ARGON-41

A radioactive form of the noble gas argon. Argon-41 is a beta and gamma emitter with a half-life of about 2 hours.

ASRs see **AGE-STANDARDISED RATES**

AUGER EFFECT

An atom ionised by the ejection of an inner electron can lose energy, either by the emission of an X-ray photon as an outer electron makes a transition to the vacancy in the inner shell, or by the ejection of an outer electron, the *Auger Effect*.

AUGER EMITTER see **AUGER EFFECT**

BACKGROUND RADIATION

The radiation level to which the general population is exposed. It consists of natural radiation from outer space, rocks, air, soil and substances within the human body, and from food. Natural radiation accounts for about 85% of the annual average radiation dose to members of the public. (The remainder comes from man-made radiation from medical radiation (about 14%) and radiation from nuclear weapons fallout, occupational exposures and nuclear discharges (about 1%).)

B-CELL see **B-LYMPHOCYTE**

BECQUEREL (Bq)

The international (SI) unit for the number of nuclear disintegrations occurring per unit time, in a quantity of radioactive material. Replaced the Curie (Ci) - $1 \text{ Bq} = 2.7 \times 10^{-11} \text{ Ci}$.

$1 \text{ Bq} = 1$ radioactive disintegration per second.

Because this is an extremely small unit, levels of activity expressed in Bq are often prefixed with Mega ($10^6 \text{ Bq} - \text{MBq}$), Giga ($10^9 \text{ Bq} - \text{GBq}$) and Tera ($10^{12} \text{ Bq} - \text{TBq}$).

BETA EMITTER

A radionuclide which decays through emission of beta particles.

BETA PARTICLE

A particle emitted from a nucleus during the radioactive decay of certain types of radionuclides. It has a mass and charge similar to that of an electron. It has greater penetrative power than an alpha particle, but is low Linear Energy Transfer (LET) radiation.

B-LYMPHOCYTE (B-Cell)

A type of lymphocyte, thought in humans to originate in bone marrow, that evolves into a cell that produces antibodies.

CAESIUM-134

A radionuclide which has a half-life of about 2 years and which decays with the emission of beta particles and gamma rays.

CAESIUM-137

A radionuclide which has a half-life of about 30 years and which decays with the emission of beta particles and gamma rays.

CANCER REGISTRATION

In England and Wales, formally coordinated but non-statutory scheme whereby all cases of cancer should be notified to regional registries, in agreed detail, as soon as possible after diagnosis. Coordination is undertaken by the National Cancer Registration Scheme. The data are forwarded to the Office of Population, Censuses and Surveys (OPCS) for collation and publication.

CARBON-14

A beta emitting radionuclide with a half-life of nearly 6000 years. It is an important source of natural terrestrial radioactivity, used as a dating method for organic material.

CHROMOSOMES

Rod-shaped bodies found in the nucleus of cells at the time of cell division. They contain the genes. Normal human cells possess 22 identical pairs + two sex chromosomes in each cell.

CLL see LEUKAEMIA

COLLECTIVE DOSE

Total radiation dose over a population group exposed to a given source. It is represented by the product of the average dose to the individuals in the group by the number of persons comprising the group. It is measured in person-sieverts (person Sv) otherwise known as Man-Sieverts.

COMMITTED EFFECTIVE DOSE

The sum of the products of the committed organ or tissue-equivalent doses and the appropriate organ or tissue weighting factors integrated over 50 years for adults and 70 years for children.

CONFIDENCE INTERVAL

Indicates the (im)precision of the study result as a measure of the real size of any risk. In this way a confidence interval conveys the effects of sampling variation on the precision of, for example, Age-Standardised Rates calculated from a limited time period etc. Specifically, the true rate is likely to be inside the 95% confidence interval on 95% of occasions, although the study rate remains the best estimate of the true value.

CRITICAL GROUP

Members of the population who because of their habits or sources of foodstuff are likely to have the highest exposure to radiation.

CYTOTOXIC

Poisonous to living cells; drugs having this property are used therapeutically in the treatment of certain cancers and leukaemias.

DAUGHTER PRODUCT see **DECAY PRODUCT**

DECAY

The process of spontaneous transformation of a radionuclide. The decrease in the activity of a radioactive substance.

DECAY PRODUCT

A nuclide or radionuclide produced by decay. A decay product may be formed directly from a radionuclide or as a result of a series of successive decays through several radionuclides.

DISCHARGES see **RADIOACTIVE DISCHARGES**

DNA

Deoxyribonucleic acid. The compound that controls the structure and function of cells and is the material of inheritance. The DNA molecule consists of two polynucleotide chains in the form of a double helix. The chains are linked by pairs of DNA bases, the order of which is the genetic code.

EFFECTIVE DOSE

The effective dose is the sum of the weighted equivalent doses in all the tissues and organs of the body. It takes account of the relative biological effectiveness (RBE) of different types of radiation and variation in the susceptibility of organs and tissues to radiation damage. Unit sievert (Sv).

EPIDEMIOLOGY

The study of the distribution of determinants of health-related states or events in specified populations and the application of this study to control of health problems. In the past 50 years or so, the definition of epidemiology has broadened from concern about communicable disease epidemics to include all phenomena related to health in populations.

EPIGENETIC

A heritable change in the properties of a cell that is not due to a mutation in DNA. It usually reflects an alteration in the degree of expression of a gene. Epigenetic changes are not permanent and may be unstable.

EXCESS RELATIVE RISK

Is the relative risk minus 1.

EXPECTED NUMBERS

The average number of events or cases that will occur in a specified location and time period if overall mortality or incidence rates apply to that location and time period.

EXTERNAL AND INTERNAL EXPOSURES

External exposure arises from radioactive sources which remain outside the body. Internal exposure arises from radioactive materials which are taken inside the body, through inhalation or ingestion. An alpha particle has a very short range and hence very little penetrative power, so that if it were to come from an external source it would be unlikely to penetrate the surface of the skin, giving up most of its energy in the dead surface skin layers. If, however, an alpha particle were emitted from a source that had been inhaled into the lungs its closer proximity to living cells could result in damage to those cells. Internal exposures are generally received from sources that have been inhaled or ingested. Beta and gamma radiation sources can give rise to either internal or external exposures.

FISSION

The spontaneous or induced disintegration of a heavy atomic nucleus into two or more lighter fragments (nuclei). The energy released in the process is referred to as nuclear energy.

FREE RADICAL

A grouping of atoms that normally exists in combination with other atoms, but can sometimes exist independently. Generally very reactive in a chemical sense.

GAMETE

A germ cell, such as a spermatozoon (male) or ovum (female), that fuses with another germ cell of the opposite sex during fertilization.

GAMMA RAYS

High energy photons, without mass or charge, emitted from the nucleus of a radionuclide following radioactive decay, as an electromagnetic wave. They are very penetrating but have a low Linear Energy Transfer (LET).

GENE

Unit of hereditary material arranged into linear sequence to form chromosomes, each gene occurring at a specific point. Composed of DNA having unique base sequence. (See DNA).

GENOME

The entire genetic material (DNA) of a cell.

GERM CELL/GERM LINE

Cell responsible for genetic continuity from one generation to the next. Primary germ cells (gonia) divide ultimately to form sperm or ova (gametes) which fuse with one another at the moment of fertilisation (conception).

GONAD

Organ (testis or ovary) in which germ cells reside.

GRANULOCYTE

A major sub-type of white blood cell whose principal function is to phagocytose (engulf and destroy) foreign particles and debris.

GRAY (Gy)

The international (SI) unit of absorbed dose. 1 Gy is equivalent to 1 joule of energy absorbed per kilogram of matter such as body tissue.

HAEMOPOIETIC (also spelled “haematopoietic”)

Blood-forming.

HALF-LIFE ($t_{1/2}$)

The time taken for the activity of a radionuclide to lose half its value by decay. During each subsequent half-life its activity is halved again so its activity decays exponentially.

HODGKIN’S DISEASE

A malignant disease characterised by enlargement of the lymph nodes, spleen and liver.

HYPOTHESIS

A suggested explanation for a group of facts or phenomena. See also null hypothesis.

ICRP

International Commission on Radiological Protection. It consists of experts in radiology, genetics, physics, medicine and radiological protection from a number of countries. Established in 1928, it meets regularly to consider the results of research on the effects of radiation and publishes recommendations on all aspects of radiological protection, including dose limits for man.

INCIDENCE

The number of instances of illness commencing, or of persons falling ill, during a given period in a specified population. More generally, the number of new

events eg new cases of disease in a defined population, within a specified period of time. The term incidence is sometimes used to denote “incidence rate”.

INFECTIOUS AETIOLOGY

The process by which disease is brought about by a transmissible agent, eg a virus.

ION

Electrically charged atom or grouping of atoms.

IONISATION

The process by which a neutral atom or molecule acquires or loses an electron. The production of ions.

IONISING RADIATION

Radiation which is sufficiently energetic to remove electrons from atoms in its path. In human or animal exposures, ionising radiation can result in the formation of highly reactive particles in the body (known as free radicals) which can cause damage to individual components of living cells and tissues. The term includes radiation at least as energetic as X-rays; gamma rays and charged particles such as alpha and beta particles are also forms of ionising radiation.

ISOTOPE

Nuclides containing the same number of protons (ie same atomic number) but different numbers of neutrons.

KRYPTON-85

A radioactive form of the noble gas krypton. It has a half-life of about ten years and decays by the release of beta particles and gamma rays. It is discharged into the atmosphere by some nuclear plants, especially as a fission product released from irradiated fuel when reprocessed.

LEAD-210

A radionuclide with a half-life of 25 years. It emits beta particles and gamma rays, and is a member of the natural uranium radioactive decay series.

LEUKAEMIA

A group of malignant diseases of the blood-forming tissues characterised by abnormal white blood cells which divide in a manner outside the control of the body. Most leukaemias start in the red bone marrow but some start in the lymphatic system. In all instances the bone marrow ends up being the main site of the disease. The principal groups are the Chronic Leukaemias (very rare in the 0-24 age group) and the Acute Leukaemias, of which acute lymphoblastic leukaemia (ALL, also known as acute lymphatic leukaemia) currently accounts for 75-80% of all cases of childhood leukaemia in the UK. Both ALL and non-Hodgkin's lymphoma (NHL, which is closely related to ALL) are diseases of lymphoid cells. Since chronic lymphocytic leukaemia (CLL) is very rare in the age-group 0-24, in this report the term “lymphoid leukaemia” refers essentially

to ALL. Acute myeloblastic leukaemia (AML, also known as acute myeloid or acute non-lymphoblastic leukaemia (ANLL)) is a disease of the myeloid bone marrow cells.

LINEAR ENERGY TRANSFER (LET)

A measure of the density of ionisation along the track of an ionising particle in biological tissue or other medium. Particles or rays of radiation are generally described as having a high or low LET - ie their tracks leave high or low density deposits of energy in the tissue they pass through. High LET radiation is more damaging to body tissue than low LET radiation.

LUNG CLASS see **RESPIRATORY TRACT ABSORPTION TYPE**

LYMPH NODES

Bean-shaped masses of tissue situated along the course of the lymphatic vessels which help protect against infection. A source of lymphocytes.

LYMPHATIC CANCER see **LYMPHOMA**

LYMPHOCYTE

A type of white blood cell that is part of the body's immune system.

LYMPHOMA

A malignant tumour of the lymphatic system (lymph nodes, reticulo-endothelial system and lymphocytes).

MEIOSIS

Type of cell division during the production of sperm or ova in which a nucleus divides into four daughter nuclei, each containing half the chromosome number of the parent nucleus.

MENDELIAN

Of or relating to Mendel's laws of heredity.

MINI-SATELLITES

Regions of DNA dispersed throughout the genome consisting of repetitive sequences. In some ("hypervariable mini-satellites") the number of repeated DNA bases are unstable and different in almost every individual - a property utilised in "DNA fingerprinting".

MUTAGEN

An agent (eg radiation or chemical) that can induce mutations.

MUTATION

A change in the structure or position of one or more genes that may be transmitted to daughter cells or organisms and which alters their characteristics. Certain specific mutations are involved in the process leading to malignant disease. Mutations occur spontaneously and may be induced by various agents (mutagens).

NEOPLASM

Tumorous tissue, not necessarily malignant but may progress to malignancy. (see TUMOUR).

NEOPLASTIC GENES

Genes in which mutations or epigenetic changes can contribute to a tumorous phenotype.

NHL see NON-HODGKIN'S LYMPHOMA

NOBLE GASES

The elements helium, neon, argon, krypton, xenon and radon-222. Their outer (valence) electron shells are complete, thus rendering them inert to all the usual chemical reactions.

NON-HODGKIN'S LYMPHOMA

A heterogenous group of childhood cancers whose primary cell of origin is in lymphoid tissue and which tend to form solid tumours. It is closely related to acute lymphoblastic leukaemia (ALL), both being part of a spectrum of disease, rather than truly separate entities, in most cases.

NUCLEAR SITE, ESTABLISHMENT OR PLANT

A facility which includes a nuclear reactor and/or capability for handling radionuclides associated with the nuclear fuel cycle.

NUCLEAR REACTOR

A structure in which neutron-induced nuclear fission can be sustained and controlled in a self-supporting chain reaction. In power reactors, the heat produced by fission is absorbed by coolant, producing steam which in turn powers a turbine for generating electricity. Some reactors can be put to other uses, eg materials testing, plutonium production. In a thermal reactor the fission is brought about by slow or thermal neutrons which are produced by slowing fast neutrons by the use of a moderator such as carbon or water. In a fast reactor, most of the fission is produced by fast neutrons and therefore requires no moderator. Most thermal reactors use uranium as fuel, in which the uranium-235 content has been artificially raised (this fuel is known as enriched uranium). Fast reactors use a mixture of plutonium and uranium dioxide.

NUCLEAR REPROCESSING

The processing of spent fuel from a nuclear reactor, to remove fission products and to recover fissile and fertile material for further use. Chemical solvents play a major role in this process.

NULL HYPOTHESIS

The statistical hypothesis that one variable has no association with another variable or set of variables, or that two or more population distributions do not differ from one another. In simplest terms, the null hypothesis states that the

results observed in a study, experiment, or test are no different from what might have occurred as a result of the operation of chance alone.

ODDS RATIO

The ratio of the odds of disease occurrence in a group with exposure to a factor to that in an unexposed group; within each group, the odds are the ratio of the numbers of diseased and non-diseased individuals.

ONCOGENE

A gene that has mutated to a form that contributes in a dominant fashion to a cancerous change in a cell.

ONE-SIDED TEST see p-VALUE

p-VALUE

The probability that, if a specified “null” hypothesis is true, the value of some statistic will be at least as extreme as that actually observed. In calculating this probability it will sometimes be appropriate to consider deviations in only one direction (one-sided significance tests); in other cases, deviations in either direction may be appropriate (two sided tests). Conventionally, if p (probability) is less than 0.05 “significant at the 5% level”, we take it to be unlikely that the deviation has arisen simply by chance and are inclined to “reject null hypothesis”, ie to seek some alternative hypothesis to explain the observations. Similarly, if p is less than 0.01 (significant at the 1% level) we are more persuaded that such an alternative hypothesis is necessary.

PARENT

In radioactive decay of one radionuclide (A) to another (B), A is the parent of daughter B.

PATERNAL PRECONCEPTION IRRADIATION (PPI)

A hypothesis suggesting that radiation-induced mutations in the germ line cause a predisposition to leukaemia or NHL in the next generation.

PERSON SIEVERT (person Sv) see COLLECTIVE DOSE.

PHENOTYPE

The constitution of an organism or cell as determined by the interaction of its genetic constitution and the environment.

PICA

A medical condition, usually in children, characterised by abnormal craving to “eat” substances such as clay, dirt, hair etc.

PLUTONIUM (Pu)

An element which exists in several different isotopic forms. The five main isotopes are:

- Pu-238: alpha emitter. Half-life c.86 years
- Pu-239: alpha emitter. Half life c.24,000 years
- Pu-240: alpha emitter. Half-life c.6,600 years
- Pu-241: beta emitter. Half-life c.13 years which decays to americium-241, which is an alpha emitter with a half-life of c.460 years
- Pu-242: alpha emitter. Half-life c.379,000 years

POISSON DISTRIBUTION/VARIABLE

A mathematical formula which describes the probability of observing each number of events (0,1,...) in equal units of time and/or space, where the mean rate of occurrence is low and is known, and events are occurring at random. The Poisson distribution is useful when calculating the number of times a rare event may be expected to occur in a large group of people.

POLONIUM-210

A radioactive element with a half-life of 140 days. During its decay it emits alpha particles and gamma rays. Polonium is a member of the natural uranium radioactive decay series.

POTASSIUM-40

A naturally-occurring radionuclide with a half-life of 1.27×10^9 years, which decays with the emission of beta particles and gamma rays.

PPI see **PATERNAL PRECONCEPTION IRRADIATION**

PRECONCEPTIONAL EFFECT

An event such as a mutation occurring in a germ cell before the moment of conception (fertilisation), ie while still in the parental gonad.

PROTO-ONCOGENES

Genes that may mutate into oncogenes.

RADIOACTIVITY

The property of radionuclides of spontaneously emitting ionising radiation. Measured in becquerels (Bq).

RADIONUCLIDE

A type of atomic nucleus which is unstable and which may undergo spontaneous decay to another atom by emission of ionising radiation (usually alpha, beta or gamma).

RADIUM-226

A naturally-occurring radionuclide with a half-life of 1,620 years, which emits alpha particles and gamma rays. It decays through a series of daughter products which emit alpha, beta and gamma radiation. Radium is a member of the natural uranium radioactive decay series.

RADON (Rn)

Radioactive element, the heaviest of the naturally-occurring noble gases. Two radioactive isotopes of radon give rise to nearly half the total radiation dose received from background radiation in the UK. These isotopes are radon-222 and radon-220; radon-222 is the first daughter product of the decay of radium-226, and has a half-life of 3.8 days and emits alpha particles. It decays through a series of daughter products which emit alpha, beta and gamma radiation. Radon-220 also occurs in the natural environment and is a decay product of thorium and thus is often known as thoron. It has a half-life of 54.5 seconds and emits alpha particles.

RBE see **RELATIVE BIOLOGICAL EFFECTIVENESS**

RED BONE MARROW

The cellular material found in bones in the axial skeleton (ie bones excluding the arms and legs) and is the organ responsible for producing cells in the blood. (In infants, because the demand for blood is so great, all bones are used for blood production). On average, red bone marrow produces 5 million cells every second, or 400 billion every 24 hours.

REGISTRATION see **CANCER REGISTRATION**

RELATIVE BIOLOGICAL EFFECTIVENESS (RBE)

The RBE of one radiation compared with another is the inverse ratio of the absorbed doses producing the same degree of a defined biological effect.

RELATIVE RISK (RR)

The ratio of the risk of disease or death among the exposed to the risk among the unexposed.

REPROCESSING see **NUCLEAR REPROCESSING**

RESPIRATORY TRACT ABSORPTION TYPE

Type F (F=fast) Materials are deposited materials that are readily absorbed into blood from the respiratory tract (fast rate of absorption). Type M(edium) Materials are deposited materials that have intermediate rate of absorption into blood from the respiratory tract. Type S(low) Materials are deposited materials that are relatively insoluble in the respiratory tract (slow rate of absorption).

RISK

The probability that an event will occur, eg that an individual will become ill or die within a stated period of time or age. Also, a non-technical term

encompassing a variety of measures of the probability of a (generally) unfavourable outcome. (See RELATIVE RISK).

RR see RELATIVE RISK

RUTHENIUM-106

Metallic element; a beta emitting fission product with a half-life of 372 days.

SEMINIFEROUS

Containing, conveying or producing semen eg a ~ tubule.

SIEVERT (Sv)

The international (SI) unit of effective dose, obtained by weighting the equivalent dose in each tissue in the body with ICRP-recommended tissue weighting factors, and summing over all tissues. Because the sievert is a large unit, effective dose is commonly expressed in millisieverts (mSv) - ie one thousandth of one sievert, and microsieverts (μ Sv) - ie one thousandth of one millisievert. The average annual radiation dose received by members of the public in the UK is 2.6 mSv.

SIGNIFICANCE TEST

A result that lies outside the range of values expected to occur, if some specified hypothesis is true, is said to be statistically significant. A probability (p-value) of 0.05 for such an occurrence is commonly used to separate “significant” from “non-significant” results. This boundary is arbitrary.

SPECIFIC ACTIVITY MODEL

A straightforward method of calculating doses from atmospheric releases of tritium and carbon-14. The basic assumption is that the radionuclide is in equilibrium with the stable form of its element. For example, with tritium the concentration of the radionuclide in water taken into the body by ingestion and inhalation is assumed to be the same as that in atmospheric water vapour.

SPERMATID

Any of the four immature male gametes that are formed from a spermatocyte, each of which develops into a spermatozoon.

SPERMATOCYTE

Immature male germ cell developed from a spermatogonium, that gives rise, by meiosis, to four spermatids.

SPERMATOGENESIS

The formation and maturation of spermatazoa in the testis.

SPERMATOGONIUM

Immature male germ cell that divides to form many spermatocytes. Plural = spermatogonia.

SPERMATOZOON

Male reproductive cell. Plural = spermatozoa.

STEM CELL

An undifferentiated cell that gives rise to specialised cells, such as blood cells.

STRONTIUM-90

A radionuclide with a half-life of 28.8 years which emits beta particles. It is a fission product from uranium and found in fallout from nuclear explosions and certain types of nuclear discharge. It possesses similar chemical qualities to calcium, and can therefore accumulate in bone.

T-CELL see T-LYMPHOCYTE

T-LYMPHOCYTE (T-Cell)

A type of lymphocyte that matures in the thymus, responsible for killing cells that are infected by a virus and inducing other cells (B-lymphocytes) to produce antibodies. (See ANTIBODY).

THORACIC LYMPH NODES see TRACHEOBRONCHIAL LYMPH NODES

THORIUM-232

A naturally-occurring radionuclide with a half-life of 1.3×10^{10} years, which decays with the emission of alpha particles and gamma rays.

TRACHEOBRONCHIAL LYMPH NODES (Thoracic lymph nodes)

Lymph nodes situated near the major air passages of the lungs.

TRANSGENERATIONAL EFFECT

In this report, an effect in the offspring resulting from exposure of a parent to some risk factor.

TRANSGENIC

An animal or plant into which genetic material from another organism has been introduced into the germ line.

TRITIUM

A radioactive isotope of hydrogen which emits beta particles, and has a half-life of 12.5 years.

TUMOUR

Mass of tissue formed by a new growth of cells, normally independent of the surrounding structures. Can be either benign or malignant.

TUMOUR SUPPRESSOR GENE

A gene whose normal function is to suppress the tumour-forming (“neoplastic”) potential of cells, often by countering the effects of oncogenes.

TWO-SIDED TEST see **p-VALUE**

UNDIFFERENTIATED CELL

An unspecialised cell that is capable of giving rise to specialised (“differentiated”) cells.

URANIUM (U)

A hard grey metal which exists in seven isotopic forms (U-233 - 239) of which the two most important are uranium-235 (the only naturally-occurring readily fissile isotope) and uranium-238. Both isotopes decay through a series of daughter products which emit alpha, beta and gamma radiation. Principal source of fuel for nuclear reactors.

LIST OF ABBREVIATIONS

Note: for a fuller definition of medical/scientific terms please refer to the Glossary

ALL	Acute Lymphoblastic (also known as Lymphatic) Leukaemia
AML	Acute Myeloid (also known as Myeloblastic) Leukaemia
ANLL	Acute Non-Lymphoblastic Leukaemia
ASR	Age-Standardised Rate
BNFL	British Nuclear Fuels Plc
cALL	Common ALL
CCRG	Childhood Cancer Research Group (Oxford)
CLL	Chronic Lymphocytic Leukaemia
COM	Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment
COMARE	Committee on Medical Aspects of Radiation in the Environment
DCS	Leukaemia Research Fund Data Collection Study
DH	Department of Health
DNA	Deoxyribonucleic acid
ENU	Ethyl nitroso-urea
HMIP	Her Majesty's Inspectorate of Pollution
HSE	Health and Safety Executive
ICD	International Classification of Diseases
ICRP	International Commission on Radiological Protection
LET	Linear Energy Transfer
MAFF	Ministry of Agriculture, Fisheries and Food
NHL	Non-Hodgkin's Lymphoma
NRCMDR	Northern Region Children's Malignant Disease Registry

NRCT	National Registry of Childhood Tumours
NRPB	National Radiological Protection Board
O/E	Observed over Expected
OPCS	Office of Population, Censuses and Surveys
PPI	Paternal Preconception Irradiation (Hypothesis)
RBE	Relative Biological Effectiveness
RR	Relative Risk
SEF	Sampling Efficiency Factor
THORP	Thermal Oxide Reprocessing Plant
UKAEA	United Kingdom Atomic Energy Authority

APPENDIX B

COMMITTEE ON MEDICAL ASPECTS OF RADIATION IN THE ENVIRONMENT

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Department of Health
Department of Health and Social Services (Northern Ireland)
Department of Trade and Industry
Health and Safety Executive
HM Industrial Pollution Inspectorate (Scottish Division)
HM Inspectorate of Pollution
Information and Statistics Division, Common Services Agency, NHS in Scotland
Medical Research Council
Ministry of Agriculture, Fisheries and Food
Ministry of Defence
National Radiological Protection Board
Office of Population Censuses and Surveys
Scottish Office Health Department
Welsh Office

APPENDIX C.

DECLARATION OF MEMBERS' INTERESTS CODE OF PRACTICE

INTRODUCTION

1. This code of practice guides members of COMARE as to the circumstances in which they should declare an interest in the course of the Committee's work.

2. To avoid any public concern that commercial interests of members might affect their advice to Government, Ministers have decided that information on significant and relevant interests of members of its advisory committees should be on the public record. The advice of the Committee frequently relates to matters which are connected with the nuclear industry generally and, less frequently, to commercial interests involving radioactivity and it is therefore desirable that members should comply with the Code of Practice which is set out below.

3. This code applies to members of COMARE and sub-groups or working groups of COMARE which may be formed.

4. For the purposes of this Code of Practice, the "radiation industry" means:

- a) companies, partnerships or individuals who are involved with the manufacture, sale or supply of products processes or services which are the subject of the Committee's business. This will include nuclear power generation, the nuclear fuel reprocessing industry and associated isotope producing industries, both military and civil;
- b) trade associations representing companies involved with such products;
- c) companies, partnerships or individuals who are directly concerned with research or development in related areas;
- d) interest groups or environmental organisations with a known interest in radiation matters.

It is recognised that an interest in a particular company or group may, because of the course of the Committee's work, become relevant when the member had no prior expectation this would be the case. In such cases, the member should declare that interest to the Chairman of the meeting and thereafter to the Secretariat.

5. In this code, "the Department" means the Department of Health, and "the Secretariat" means the secretariat of COMARE.

SCOPE AND DEFINITIONS

DIFFERENT TYPES OF INTEREST - DEFINITIONS

6. The following is intended as a guide to the kinds of interests which should be declared. Where a member is uncertain as to whether an interest should be declared he or she should seek guidance from the secretariat or, where it may concern a particular subject which is to be considered at a meeting, from the Chairman at that meeting. Neither members nor the Department are under an obligation to search out links between one company and another, for example where a company with which a member is connected has a relevant interest of which the member is not aware and could not reasonably be expected to be aware.

If members have interests not specified in these notes but which they believe could be regarded as influencing their advice they should declare them to the secretariat in writing and to the Chairman at the time the issue arises at a meeting.

Personal Interests

6.1. A personal interest involves payment to the member personally. The main examples are:-

- a) Consultancies or employment: any consultancy, directorship, position in or work for the radiation industries which attracts regular or occasional payments in cash or kind.
- b) Fee-Paid Work: any work commissioned by those industries for which the member is paid in cash or kind.
- c) Shareholdings: any shareholding in or other beneficial interest in shares of those industries. This does not include shareholdings through unit trusts or similar arrangements where the member has no influence on financial management.

Non-Personal interests

6.2. A non-personal interest involves payment which benefits a department for which a member is responsible, but is not received by the member personally. The main examples are:

- a) Fellowships: the holding of a fellowship endowed by the radiation industry.
- b) Support by Industry: any payment, other support or sponsorship by the radiation industry which does not convey any pecuniary or material benefit to a member personally but which does benefit their position or department eg:
 - i) a grant from a company for the running of a unit or department for which a member is responsible;
 - ii) a grant or fellowship or other payment to sponsor a post or a member of staff in the unit for which a member is responsible. This does not include financial assistance for students, but does include work carried out by postgraduate students and non-scientific staff, including administrative and general support staff.
 - iii) the commissioning of research or work by, or advice from, staff who work in a unit for which the member is responsible.

- c) Support by Charities and Charitable Consortia: any payment, other support or sponsorship from these sources towards which the radiation industry has made a **specific and readily identifiable** contribution. This does not include unqualified support from the radiation industry towards the generality of the charitable resource.

Trusteeships: where a member is trustee of a fund with investments in the radiation industry, the member may wish to consult the Secretariat about the form of declaration which would be appropriate.

Members are under no obligation to seek out knowledge of work done for or on behalf of the radiation industry within departments for which they are responsible if they would not reasonably expect to be informed.

DECLARATION OF INTERESTS

Declaration of Interests to the Department

7. Members should inform the Department in writing when they are appointed of their current personal and non-personal interests and annually in response to a secretariat request. Only the name of the company (or other body) and the nature of the interest is required; the amount of any salary, fees, shareholding, grant etc need not be disclosed to the Department. An interest is current if the member has a continuing financial involvement with the industry, eg if he or she holds shares in a radiation company, has a consultancy contract, or if the member or the department for which he or she is responsible is in the process of carrying out work for the radiation industry. Members are asked to inform the Department at the time of any change in their personal interests, and will be invited to complete a form of declaration once a year. It would be sufficient if changes in non-personal interests are reported at the next annual declaration following the change. (Non-personal interests involving less than £1000 from a particular company in the previous year need not be declared to the Department.)

Declaration of Interests at meetings and participation by members

8. Members are required to declare relevant interests at Committee meetings and to state whether they are personal or non personal interests. The declaration should include an indication of the nature of the interest.

- a) If a member has a current (personal or non-personal) interest in the business under discussion, he or she will not automatically be debarred from contributing to the discussion subject to the Chairman's discretion. The Chairman will consider the nature of the business under discussion and of the interest declared (including whether it is personal or non-personal) in deciding whether it would be appropriate for the relevant member to participate in the item.
- b) if a member has an interest which is not current in the business under discussion, this need not be declared unless not to do so might be seen as concealing a relevant interest. The intention should always be that the Chairman and other members of the Committee are fully aware of relevant circumstances.

9. A member who is in any doubt as to whether he or she has an interest which should be declared, or whether to take part in the proceedings, should ask the Chairman for guidance. The Chairman has the power to determine whether or not a member with an interest shall take part in the proceedings.

10. If a member is aware that a matter under consideration is or may become a competitor of a product process or service in which the member has a current personal interest, he or she should declare the interest in the company marketing

the rival product. The member should seek the Chairman's guidance on whether to take part in the proceedings.

11. If the Chairman should declare a current interest of any kind, he or she should stand down from the chair for that item and the meeting should be conducted by the Deputy Chairman or other nominee if he or she is not there.

12. Some members of the Committee may, at the time of adoption of this note, or (in the case of new members) of their joining the Committee, be bound by the terms of a contract which requires them to keep the fact of the contractual arrangement confidential. As a transitional measure, any member so affected should seek to agree an entry for the public record (see para 14) with the other party. If such agreement does not prove possible, the members shall seek a waiver permitting them to disclose their interest, in confidence, to the Chairman and the Secretariat. The Secretariat will maintain a confidential register of such disclosures which will not form part of the public record.

13. On adoption of this note members shall not enter into new contractual obligations which would inhibit their ability to declare a relevant interest.

RECORD OF INTERESTS

14. A record will be kept in the Department of the names of members who have declared interests to the Department on appointment, as the interest first arises or through an annual declaration, and the nature of the interest.

15. Information from the record will be made available by the secretariat to bona-fide enquirers and published by any other means as and where the Department deems appropriate.

Member	Company	Personal Interest	Company	Non-personal Interest
Prof B Bridges		None		None
Prof E Alberman		None		None
Prof K Boddy		None		None
Prof R Cartwright		None		None
Prof K Clayton	Nirex (UK) Ltd	Research contract		None
Dr S Darby		None		None
Prof T M Dexter		None		None
Dr G Draper		None		None
Prof O B Eden		None		None
Prof D Goodhead		None		None
Prof J Hendry		None		None
Prof P Smith		None	British Nuclear Fuels plc	Research grant
Dr M Spittle		None		None
Dr T Wheldon		None		None
Prof M Whitehouse	Managed Health Systems	Consultancy		None

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