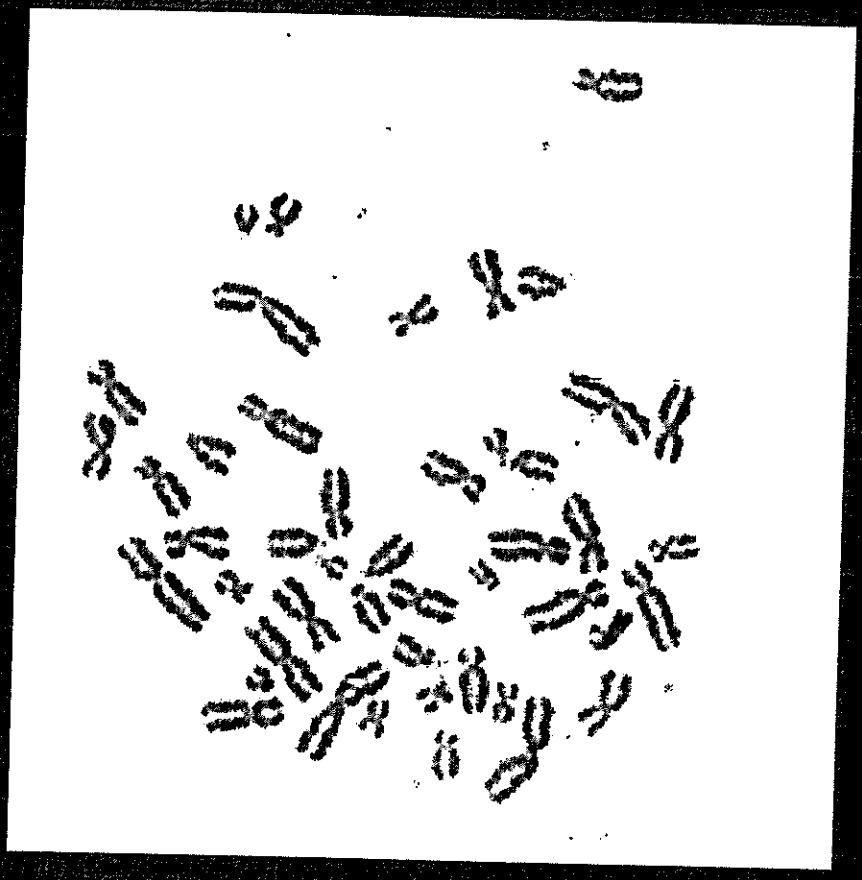
New Zealand Nuclear Test Veterans' Study – a pilot project (Sister Chromatid Exchange)



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New Zealand Nuclear Test Veterans' Study – a pilot project (Sister Chromatid Exchange)

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Thanks go to all the nuclear test veterans who participated in the study, together with all those men who volunteered as control subjects.

We also wish to thank the Returned Servicemens' Association for their willingness to assist with our selection of the control group. It is much appreciated.

Special thanks go to Dr Geoff Rickards for his astute critique of the study, and to the staff at Massey University Health Clinic who assisted with the coding of blood. Thanks also to Professor Neil Pearce, Cheng Soo and Dr Ted Drawneek for their statistical expertise. We are also grateful to Chris Kendrick, Judy Blakey, Liz Nickless, Chad Johnson, Louise Edwards for their participation and many others who gave generously of their time to assist us with this project.

Responsibility for all information presented in this report lies with the authors.

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❖ OVERVIEW

The results reported here demonstrate the presence of elevated chromosomal disturbances in peripheral blood lymphocytes of New Zealand nuclear test veterans nearly fifty years after the Operation Grapple series of nuclear tests. The effect size is weak but nevertheless observable and significant.

A statistically significant increased level of sister chromatid exchange (SCE) frequency was observed in the veterans compared to a matched control group, even after adjustment for confounding factors. This assay is accepted internationally as an indicator of genotoxicity, which leads us to conclude that the New Zealand nuclear test veterans have experienced some genetic damage as a consequence of their involvement in Operation Grapple. These veterans should thus be considered an "at risk" group that deserves special medical monitoring.

Because chromosomal disturbances involve the hereditary material, we would suggest that the children of these veterans also deserve investigation.

❖ INTRODUCTION

In 1957/58 the British Government conducted a series of nuclear tests at Christmas Island and Malden Island in the mid-Pacific Ocean. This series of detonations was given the codename "Operation Grapple". These islands were previously part of the Line Islands group but are now part of the country known as Kiribati. Operation Grapple consisted of 9 nuclear detonations between May 1957 and September 1958. A series of 3 atomic (fission) detonations occurred over the ocean near Malden Island. A further 4 detonations of atomic (fission) devices occurred over the ocean at Christmas Island in addition to 2 smaller thermonuclear (fusion) devices over land.

The Grapple series involved several naval vessels from Britain, Australia, New Zealand and Fiji. Two New Zealand frigates attended the series of detonations: the HMNZS Pukaki and the HMNZS Rotoiti. Over the course of these tests a total of 550 (as close as can be ascertained) New Zealand naval personnel manned these ships. Their duties consisted of witnessing the detonation of the nuclear devices and collecting weather data.

During the Operation Grapple tests, the New Zealand vessels were stationed at various distances of between 20 and 150 nautical miles upwind from ground zero, the point on the ocean surface above which the devices were detonated (Crawford, 1989). The Pukaki was present in all of the 9 tests, while the Rotoiti was present only at the first 4 tests. Table 1 (page 2) shows the detonation and distance information for each of these ships.

The unavailability of data from film badges worn by the participants during these tests makes it difficult to establish with certainty whether or not these individuals received any radiation dosage, or if they did, to what degree. Nevertheless, since the tests, veterans have claimed, rightly or wrongly, that their quality of life has been affected as a direct result of their participation in Operation Grapple.

Table 1. The location and yields of each Operation Grapple test, and the position of each ship at the time of each detonation (Crawford, 1989).

					Distance From Ground Zero (Nautical Miles)	
Round	**Date**	**Island**	**Height (m)**	**Yield**	**Pukaki**	**Rotoiti**
Grapple 1	15/05/1957	Malden	2400 m	Megaton	50	150
2	31/05/1957	Malden	2300 m	Megaton	50	150
3	19/06/1957	Malden	2300 m	Megaton	150	50
X	08/11/1957	Christmas	2250 m	Megaton	132	60
Y	28/04/1958	Christmas	2350 m	Megaton	80	-
Z1	22/08/1958	Christmas	450 m	Kiloton	28	-
Z2	02/09/1958	Christmas	2850 m	Megaton	35	-
Z3	11/09/1958	Christmas	2650 m	Megaton	35	-
Z4	23/09/1958	Christmas	450 m	Kiloton	20	-

The veterans have also claimed that there is an increased prevalence of genetic disorders among them and their offspring. There have been reports of an increased frequency of multiple myelomas present in British veterans of such tests, based on the analysis of medical records for several thousand of the participants (Rabbitt Roff, 1999a,b). Many veterans have had a history of afflictions such as cataracts (Phelps-Brown et al., 1997) and arthritis, or have died due to diseases that could be attributed to radiation exposure, such as gastrointestinal or respiratory disorders and some types of cancers (Rabbitt Roff, 1997). Although several epidemiological studies have been conducted regarding the health of nuclear veterans from Britain, USA, Australia and New Zealand, all have yielded results that are inconclusive or non-significant (Pearce et al., 1990a,b; Rabbitt Roff, 1999b; Dalager et al., 2000; Muirhead et al., 2003), as have studies involving the health of their offspring (Reeves et al., 1999; McLeod et al., 2001a,b).

The small number of participants in the New Zealand group (550) was always going to make epidemiological studies difficult, as any radiation-induced cancers that might result would not easily be detectable against background and expected range of different cancers that may arise spontaneously (McEwan, 1988). Nevertheless, some studies have found moderately significant increases in the incidences of haematological cancers in the New Zealand veterans, such as leukemia, which may have arisen due to radiation exposure from the Operation Grapple tests (Pearce, 1990a). However, a comparison of the morbidity of the control group to the national cancer statistics showed that the group had abnormally low incidences of cancer, which may have skewed the results (McEwan, 1988). All of the claims made by the New Zealand nuclear test veterans thus far have been based on epidemiological evidence or anecdotal evidence and have yet to be supported experimentally.

For this reason a controlled genetic study was conducted to determine whether or not the New Zealand naval personnel who witnessed the Operation Grapple series of tests have suffered any genetic damage. The report written here records the data gathered from a sister chromatid exchange (SCE) assay on 50 veterans and 50 controls. SCE has long been recognized as a sensitive and reliable test for clastogenicity, a clastogen being defined as any environmental agent which is harmful to DNA and chromosomes. The term genotoxicity (harmful to genes) is also often used in parallel. The detection of SCE in dividing blood lymphocytes is used to evaluate genetic damage from exposure to environmental genotoxic agents (Sarto et al., 1985; Tucker et al., 1993). Exchanges occur when DNA is replicating after an initial change in the form of DNA base damage (Uggla and Natarajan, 1983). In 2000, the IPCS (International Programme on Chemical Safety) published guidelines for the monitoring of genotoxic effects in humans (Albertini et al., 2000). In defining the significance of the endpoint and application of the sister chromatid exchange assay, the report states "The ready quantifiable nature of SCEs with high sensitivity for revealing toxicant-DNA interaction and the demonstrated ability of

genotoxic chemicals to induce a significant increase in SCEs in cultured cells... has resulted in this endpoint being used as an indicator of DNA damage in blood lymphocytes of individuals exposed to genotoxic (agents)."

This assay is thus accepted as an indicator of *in vivo* damage. Furthermore, it is an accepted tenet in the current study that any damage to DNA may lead to ill health and possibly result in intergenerational effects. Follow-up studies on individuals exposed to genotoxic agents have clearly demonstrated the predictive value of high chromosomal damage for subsequent health risk (Hagmar et al., 1994, 1998, 2001).

For a non-scientist, a logical question to ask is "what is sister chromatid exchange?" Briefly, when a cell is going to divide, the chromosomes (DNA) replicate longitudinally into two identical halves; each half is called a chromatid. This can be seen in Fig.1 (page 16). The term 'sister chromatid' refers to the two genetically identical chromatids that comprise each chromosome. In a normal healthy person it is not unusual for the sister chromatids of one chromosome to swap pieces with each other – they can break directly opposite each other and exchange their DNA (Fig.2, page 16). This is called a sister chromatid exchange and providing the frequency of SCEs is not high, this is not considered to be harmful; the exchange is between genetically identical components and should therefore theoretically not be of any consequence. Studies vary internationally as to how often this background exchange occurs in human chromosomes, because the living environment of human populations varies enormously, not to mention the possibility of ethnic differences. Laboratories also differ in how they conduct the technique which can lead to further variations in SCE frequency. Because there is no internationally accepted norm for background SCE frequency, valid comparisons between studies cannot be made and this can lead to debate as to what is harmful and what is not. But Carrano and Natarajan (1988) in a major report on population monitoring using cytogenetic techniques, note that the baseline SCE frequency in human peripheral lymphocytes averages

about 7-10 per cell in non-exposed individuals. Evidence of genetic damage is accepted if the number of SCEs in an experimental group is more significant statistically than a selected control group (Albertini et al., 2000). A significant increase in SCE frequency is accepted as an indication that the DNA of a target group has been damaged in some way. The technique cannot, however, be used as a diagnostic tool. It does not automatically indicate that a person is sick or even likely to become sick. But it certainly can be used as an alert signal for the possible future occurrence of ill health, and may offer in the veterans' case a possible explanation for the underlying cause of reported ill health. Any damage to DNA is universally accepted as being detrimental to a person's well-being. Many agents, for example, UV light, cigarette smoke and alcohol can increase the number of SCEs, which is why in the present study we obtained as much personal data as possible on possible confounding factors relating to a veteran's medical history, occupational history and lifestyle history.

Another important issue concerns the reason for performing the SCE assay in this study. Given the broad arsenal of assays available to scientists to detect genetic damage, it is necessary to justify why this particular test was applied here. The rationale is based on three premises: (1) internalized radionuclides are known to be inducers of SCEs as corroborated by several authors (Aghamohammadi et al., 1988; Nagasawa et al., 1990a,b, 1991; Nagasawa and Little, 1992; Geard, 1993; Prabhavathi et al., 1995; Schmid and Roos, 1996; Deshpande et al.,1996; Sonmez et al., 1997; Lehnert and Goodwin, 1997 and Miller et al.,1998, the latter in their study on depleted uranium), (2) radionuclides are known to remain in the body for many years (Hande et al. 2003) coupled with the known longevity of some lymphocytes for several decades, and (3) studies of Chernobyl clean-up workers have shown evidence of genetic damage via the SCE assay several years after the event (Lazutka and Dedonyte, 1995; Lazutka et al., 1999).

In summary of the above, everyone shows a certain number of SCEs on their chromosomes, but any increase in the number of SCEs compared to a matched control group is interpreted as being indicative of some agent in the bloodstream causing damage to the chromosomes, even though the cause itself may be unknown. It is universally accepted that any elevation in the frequency of SCE compared to a 'normal' population is correlated with genetic damage.

One of the reservations the researchers had in embarking upon this study was whether one could detect any evidence of genetic damage that could be attributed to an event which took place so long ago. Fifty years or more is a long time and few like studies have ever been attempted. Nevertheless, research conducted by several authors supports our view that the study was a worthy endeavour. As quoted previously, Hande et al. (2003) working in David Brenner's laboratory at Columbia University, New York, showed convincingly that past exposure to densely ionizing radiation can leave a unique permanent signature in the genome. Their research confirmed that radiation products can remain in the body for many decades and result in long term genetic effects. They conducted a study of healthy former nuclear-weapons workers who were occupationally exposed from 1949 onwards in the former Soviet Union. The radiation workers were employed either in plutonium manufacturing/processing facilities or in a nuclear reactor facility. High yields of chromosome aberrations were seen in both the highly exposed workers and in the reactors. Significantly, they demonstrated long term retention of a fraction of the plutonium intake. Autopsy data were used to calculate lung clearance of plutonium. For the plutonium workers studied by Brenner's group, an average of 50% of the bone marrow plutonium dose was deposited in this tissue after 1983, 25% was deposited after 1993 and 8% was deposited after 1998. This means that for some workers who were exposed in 1949, it has taken nearly 50 years for the plutonium to be deposited in a different extrapulmonary organ.

Furthermore, it has been known for some time that some lymphocytes are very long-lived, in excess of 20 years, which means that radiation-induced aberrations can still be observed in cells that were present as peripheral lymphocytes at the time of exposure (Awa et al., 1978; Buckton et al.,1978). A search of the literature relevant to the current study showed that people who had been exposed to radiation several years previously still showed evidence of genetic damage. These studies include single cases, with accidentally incorporated tritiated water 11 years previously (Lloyd et al., 1998) and an Estonian accident in 1994 (Lindholm and Edwards, 2004), as well as group studies of radiation workers with 11 – 22 years of employment (Bauchinger et al., 1997), Chernobyl workers examined up to 8 years after their exposure (Lazutka and Dedonyte, 1995; Salissadis et al., 1994,1995; Snigiryova et al., 1997) and from A-bomb survivors measured about 50 years after exposure (Lucas et al. 1992, 1996a; Nakamura et al., 1998).

Notwithstanding the above research, our views were tempered by other studies such as that of highly exposed victims of the Goiania accident in Brazil in September 1987 (Straume et al., 1991; Natarajan et al., 1998). A decline of damage over time is noted when observing some parameters (dicentric frequencies in lymphocytes decrease with time) whereas other parameters of damage remain high (translocation, deletion, aneuploidy and frequency of hypoxanthine guanine phosphoribosyltransferase-deficient ($HPRT^-$ mutants)).

The researchers were also conscious of the fact that an investigation such as the one conducted here has the potential to be highly contentious. Thus it was crucial that considerable attention be devoted to the design of the study. For this reason, psychology researchers who are experienced in conducting human studies were pivotal in this investigation. Their expertise was valuable in constructing the selection process for both the veterans and the control group. The procedure by which these two groups were selected is detailed in the Materials and Methods section. Strict criteria were applied for inclusion of

participants in the study, together with the gathering of extensive personal information on lifestyle history, occupational history and medical history in an attempt to account for as many confounding factors as possible which may have a bearing on the results. Selection was stratified across the North Island of New Zealand to ensure similar geographic location of veterans and controls, in case for some unknown reason locality was a factor influencing the results.

❖ MATERIALS AND METHODS

(1) Population and sampling procedure

Fifty male New Zealand naval nuclear test veterans (exposed group) and 50 male age-matched controls participated in the study. Participant age (at the date of their interview) ranged from 58 to 76, with the mean age for the exposed and control groups being 65.9 years (SD = 3.1) and 66.5 years (SD = 3.8), respectively. All were North Island residents, selected by the the following procedure.

Names of volunteer veterans were communicated to the researchers through the Office of Veterans' Affairs. A letter of invitation from the War Pensions Medical Trust Board was mailed out to all nuclear test veterans in the North Island listed on the Board's database. Also included with the letter was a Preliminary Inclusion Criteria Questionnaire (see Appendix I) along with an addressed FREEPOST envelope which was returned to the research team at Massey University with the completed questionnaire. Information furnished enabled the researchers to decide whether a veteran was included/excluded from the potential participant pool.

A respondent database was compiled from all those who posted their completed Preliminary Inclusion Criteria Questionnaire to Massey University. A *potential participant pool* was formed by excluding any respondents who failed to meet specific inclusion criteria. A *final participant pool* was formed by randomly selecting the specified number of participants from the potential participant pool database.

Matched control subjects were selected from a pool of volunteers according to criteria identical to the veterans, but with the essential difference that they did not participate in Operation Grapple. Ex-servicemen were selected as controls where possible, most from the army. Some ex-policemen were also chosen. Ex-

naval servicemen were excluded as control subjects on the grounds of controversy as to whether the frigates involved were completely "clean" upon returning to New Zealand and subsequently manned by other crew who may have been theoretically exposed to contamination. Ex-airforce personnel, except for ground crew, were also excluded for reasons of possible increased past exposure to cosmic radiation. Vietnam veterans were also not included in either the control or experimental group because there is a risk that these people have been adversely affected by possible exposure to Agent Orange. Neither was any man selected, control or veteran, who had previously worked in the timber industry, received prolonged exposure to solvents, or was currently receiving chemotherapy or radiotherapy. Selection of both veterans and controls was stratified across the North Island to achieve a random geographical distribution of participants.

Selected final participants were sent an Information Sheet (E = experimental; C = control), Consent Form and Detailed Questionnaire (Appendix II) that gathered information relating to their life events and general health. This was necessary in order for the researchers to take into account any other factors that may be causing chromosomal damage, if it appeared, other than possible effects of nuclear radiation. The participants were asked to sign the consent form, fill in the detailed questionnaire and return these to the researchers at Massey University.

On receipt of a detailed questionnaire, a face-to-face interview was arranged and conducted by a psychologist skilled in eliciting memory recall. This was in order to clarify if necessary any incomplete details in their responses, and secure more information related to any substances that might potentially affect the blood sample that would be used for analysis. It was important in this study that we obtained the best recall data possible to validate our results, which is why a face-to face interview with a trained interviewer was essential. A blood sample was collected at the same time as the interview, or else arrangements were made to collect a sample from the participant at a later convenient date. The whole study

was conducted following strict ethical guidelines as specified by the World Medical Association Declaration of Helsinki. Ethics approval to conduct the study was given by the Massey University Human Ethics Committee and the following regional hospital ethics committees: the Manawatu/Whanganui Ethics Committee, the Taranaki Ethics Committee, the Hawke's Bay Ethics Committee, the Bay of Plenty Ethics Committee, the Wellington Ethics Committee and the Auckland Ethics Committee.

Each blood sample collected was coded with a number so that the researchers could eventually link a name with that code. This code, no name, was written on the side of each blood tube and delivered to the Massey University Student Health Clinic in Palmerston North. Medical assistants at the Clinic recoded each tube with a new number and kept a record linking the codes which were eventually revealed at the conclusion of the study. This ensured that no member of the research team could identify a veteran from a control. The blood samples were then collected from the Clinic for genetic analysis. The study was conducted blind in order to remove bias from the analysis. The codes were broken and veterans/controls identified only after all genetic analyses were completed. The blood collected was used only for chromosome analysis and for no other purpose. All genetic information obtained about an individual remained strictly confidential.

(2) Lymphocyte cultures

Two culture tubes were established for each participant. Each tube contained 5 ml of Medium-199 (GibcoBRL, Cat. No. 31100-035), 1 ml of fetal bovine serum, (GibcoBRL, Cat. No. 10093-136), and 0.1 ml of phytohaemagglutinin (PHA) M form (GibcoBRL, Cat. No.10576-015). Using the WBC count, calculations were made to obtain 3.25-million cells/per culture tube by adding approximately 0.3-0.6 ml of blood from the second samples. When conducting the SCE technique it is imperative that the WBC is constant (Bender et al., 1992a). 10^{-2} M 5-Bromodeoxyuridine (BrdU) (Sigma, B-9285) was added to each culture tube

(Falcon, 8 ml polystyrene, round-bottom tube, 13 x 100 mm style), adjusted to give a final concentration of 20μM. The culture tubes were incubated at 37 C for 72 h, which included a treatment with colchicine (0.05%, BDH, Prod. 27805FM) for 1 h.

(3) Harvesting

Harvesting of cells and slide preparation were accomplished using the modified Fluorescence-Plus-Giemsa (FPG) method (Perry and Wolff, 1974). Culture tubes were removed from the incubator after 72 h, mixed gently then centrifuged for 10 min at 1000 rpm. Supernatant was gently removed from the top leaving approximately 1 cm above the pellet. Deposits were mixed thoroughly with a vortex stirrer for 5 sec, to avoid clotting, then resuspended in 5 ml of warm KCl (0.075 M) hypotonic solution at 37 C. The tubes were then mixed gently by inversion 6-8 times and incubated at 37 C for 10 min. The tubes were centrifuged again for 10 min and the supernatant removed from the top leaving approximately 1 cm above the pellet. Deposits were mixed well again with the vortex stirrer for 3 sec. They were then resuspended in 5 ml of acetic acid (6%) under constant agitation and kept for 5 min at room temperature. Cultures were once again centrifuged and the supernatant removed. Cultures were resuspended in 8 ml of ice cold fixative (Methanol : Acetic Acid = 3 : 1), centrifuged immediately and the supernatant removed. This last step was then repeated. Finally, after removing the supernatant to 5 mm without disturbing the pellet, 2-3 drops of fixative was added to give a cell suspension of light turbidity. Slides were removed from an acid alcohol solution (1 ml of 1 M HCl and 50 ml of 95% ethanol) and dried at room temperature. Two to three drops of cell suspension were dropped along the acid-washed, air-dried slide. Ten slides were prepared per donor.

(4) Fluorescence-plus-Giemsa (FPG) staining

Fluorescence-plus-Giemsa staining protocol was a modification of methods devised by Wolff and Perry (1975). This procedure is based on UV sensitivity of

heavily BrdU-labeled DNA. The one-week-old prepared slides were soaked in Sorensen's buffer solution (pH 6.8) for 5 min and rinsed in distilled water. The air-dried slides were mounted using fluorochrome Hoechst 33258 (bisbenzimide) solution (5 μg ml^{-1}) and covered with coverslips for 30 min (in dark). Hoechst 33258 staining photosensitizes degradation of BrdU-stimulated DNA, creating single-strand nicks. After 30 min coverslips were removed by rinsing with Sorensen's buffer and washed with distilled water (in dark). To avoid chromosome damage, slides were mounted in McIlvaine's buffer (pH 7.0), covered with coverslips, and illuminated with 356 nm UV light for 2.5 h (at a distance of approximately 10 cm). Coverslips were removed by rinsing with Sorensen's buffer and washed with distilled water (in dark). The slides were immediately incubated for 20 min in sodium citrate buffer (2 x SSC, pH 8.0) at 65 C to elute small DNA fragments. Slides were stained in Giemsa (10%) (Gurr; BDH, Prod. 350864X) in Sorensen's buffer (pH 6.8) for 7-10 minutes then rinsed in Sorensen's buffer for 2-3 minutes. Air-dried slides were mounted in DPX.

(5) Scoring criteria

The 10 microscope slides of every participant were randomly coded (a - j) and examined serially. Fifty consecutive second mitotic metaphase cells per participant, which showed good chromosome morphology, differential staining for SCE and no chromosome overlapping, were selected. The images were captured by a JVC 3-CCD Colour Video Camera using Silicon Graphics and Image Capture software and scored for SCE from the computer screen at 1000X magnification. SCEs were expressed per cell, so it was necessary for a full complement of 46 chromosomes to be present. SCEs were analysed according to guidelines of Swierenga et al. (1991). (See over the page for reproduction of Figure 3.8 from Swierenga et al.'s paper).

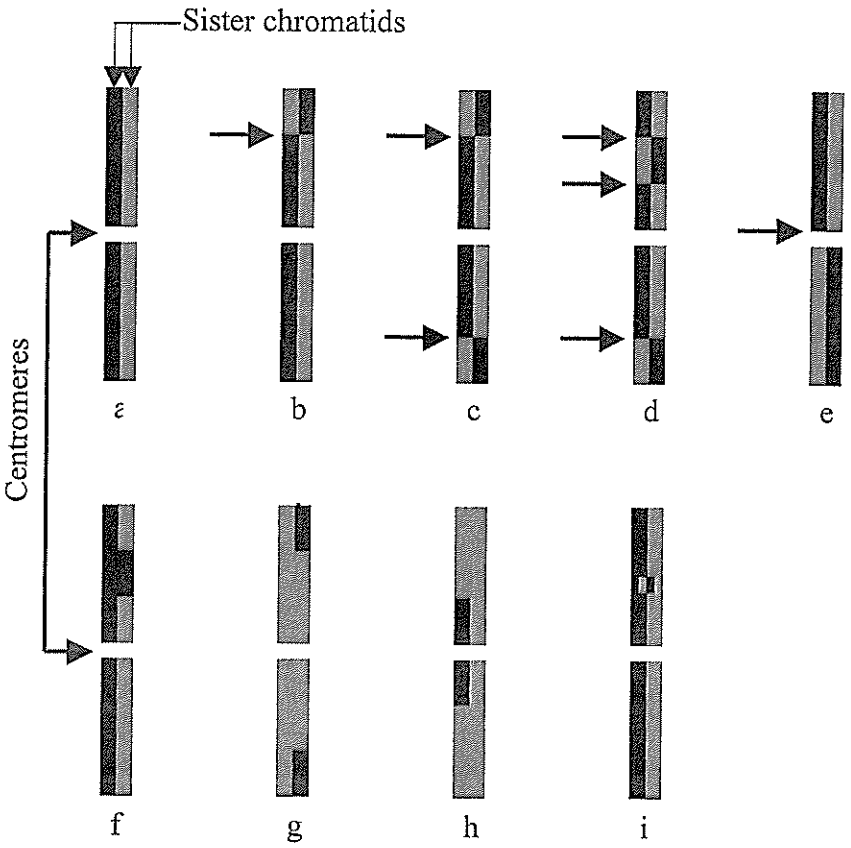

Figure 3.8: Diagrammatic representation of various differential staining patterns observed after incorporation of BrdU into replicating DNA: **(a)** No SCE, **(b)** a single SCE (arrow), **(c)** two SCEs, **(d)** three SCEs, **(e)** SCE at the centromere, **(f)** not counted as SCE, **(g & h)** incorporation of BrdU for more than two complete cycles of DNA synthesis, **(i)** reciprocal pattern of staining less than one chromatid in width and not counted as SCE (Swierenga et al.,1991).

❖ RESULTS

Fig.1 is a c-metaphase spread showing a standard karyotype of human chromosomes in a dividing peripheral blood lymphocyte. Cells cultured in BrdU for 2 cycles generated differential staining of sister chromatids as illustrated in Fig.2. Up to 50 cells from each of 50 experimental subjects and 50 control subjects were scored for the frequency of sister chromatid exchange in c-metaphase preparations. Difficulties with harvesting the cells of some participants, even after repeated culturing, resulted in 28 of the veterans and 16 controls with preparations where less than 50 cells were scored.

From a total of 2,057 cells, the control group scored a mean of 11.07 (SD = 4.08, 95% CI = 10.89-11.24) SCEs per cell compared to the nuclear test veterans, who from a total of 1,635 cells scored a mean of 11.88 (SD = 4.42, 95% CI = 11.67-12.10). The range of SCEs was 2 to 28 for the controls and from 1 to 34 for the veterans.

A *t*-test showed that the mean SCE is significantly higher for the experimentals than the controls ($t = 5.741$, df = 3365, $p<0.001$). The variance in the SCE for the experimentals is significantly higher than for the controls (Levene's test: $F = 8.732$, $p = 0.003$). If a single median SCE is calculated for each subject, then a non-parametric Kruskal-Wallis test shows a significantly higher median for the experimentals (sum of medians = 2731) than for the controls (sum of medians = 2219), $p = 0.0479$.

Fig.3 (page 17) shows that as the SCE value increases, the proportion of experimentals to controls with that SCE also increases. In other words, there are proportionately more experimentals and less controls at higher levels of damage. Fig.4 (page 18) is an identical plot but with the outliers (SCE values for which there were <30 data points in the calculation of the proportion) included. This

plot shows that those outliers with the highest SCE frequencies (above an average of 24) are experimental participants (a proportion of 1). Interestingly, that participant with the lowest average SCE frequency of 1 was also an experimental.

The data were also analyzed by eliminating those participants, in both the controls and the experimentals, where <10 cells were scored, on the basis that inclusion of these individuals may be distorting the information gathered. Even with this correction the difference was still significant ($p = 0.033$).

A *t*-test also showed no significant difference in the means between the controls and the experimentals for age, alcohol consumption, tea/coffee intake and medical X-ray dosage, but a significant difference was observed between the two groups for cigarette smoking over the last 50 years, based on self-reported information. The experimentals had smoked on average for 27.44 years and the controls on average for 16.82 years. Amount of tobacco intake was estimated from personal data gathered. Obviously this information can only be approximate, but a UNIANOVA test with the SCE transformed to give equal variances still showed a significant difference ($p = 0.03$) in mean SCE between the experimentals and the controls even when an adjustment is made for smoking.

The proportion of High Frequency Cells (HFCs) at the 95th percentile in both the experimentals and controls was also calculated. The 95th percentile was at SCE = 19; thus HFCs were defined as those cells with an SCE frequency >19. Table 2 (page 18) shows a cross-tabulation of HFCs against the experimentals and controls. The experimentals have fewer than expected ordinary cells and more than expected high-frequency cells. A Pearson chi-square test ($\chi^2 = 11.836$, df = 1) shows that the difference is significant ($p = 0.001$) The proportion of HFCs is significantly higher in the experimentals (5.82%) than in the controls (3.59%).

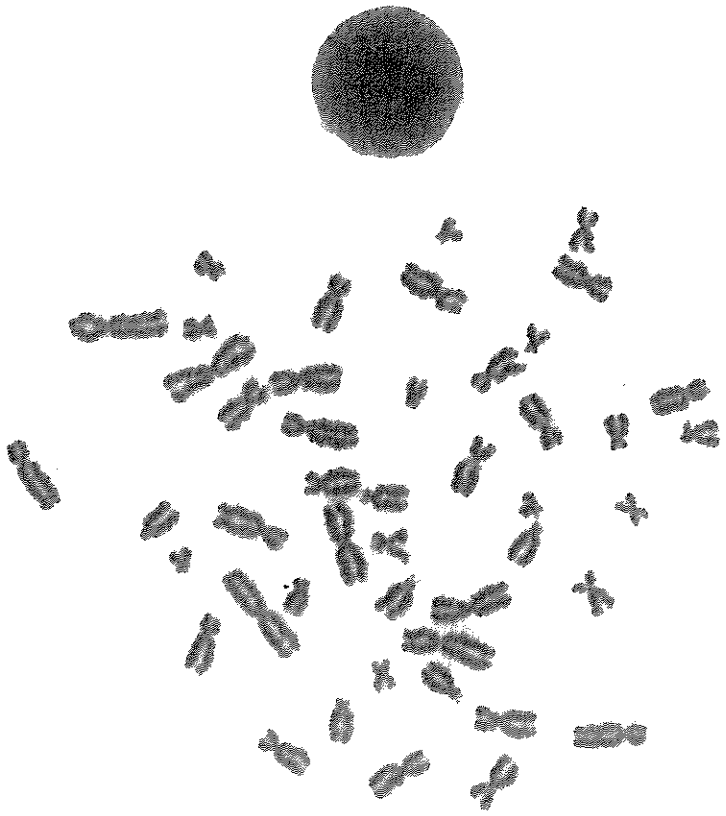

Fig.1 Standard human karyotype from a dividing peripheral blood lymphocyte.

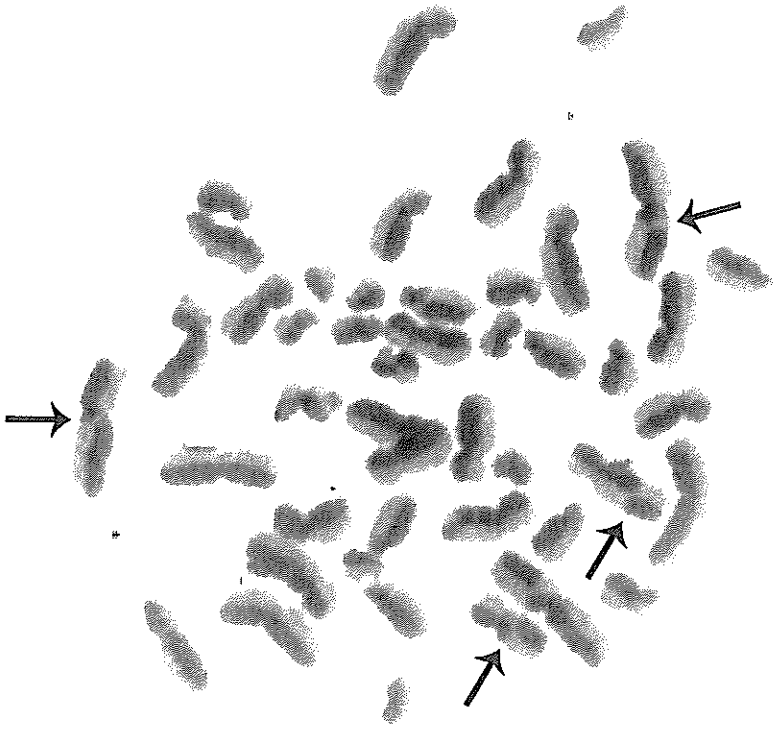

Fig.2 C-metaphase spread of a dividing peripheral blood lymphocyte cultured in BUdR. Note selected examples of sister chromatid exchanges (arrows).

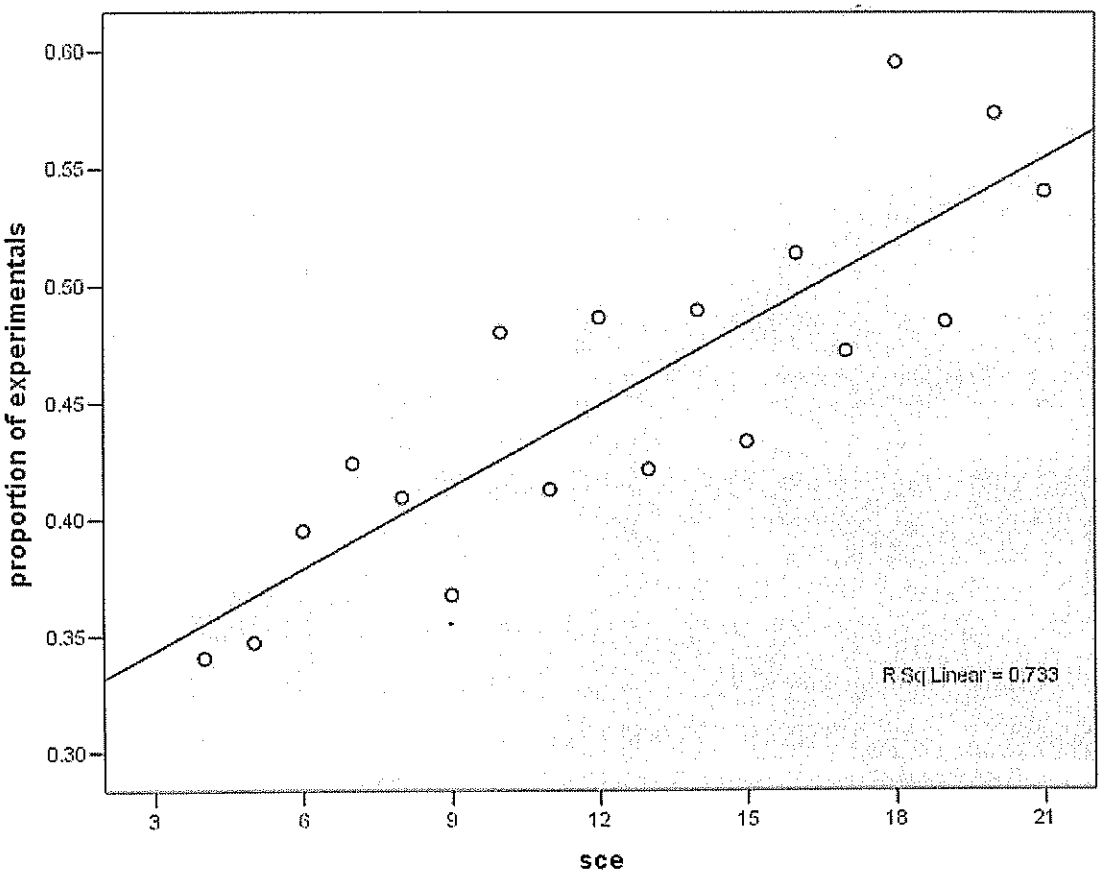

Fig.3 Graph showing the proportion of experimentals (veterans), from a total number of experimentals plus control group combined, at each level of SCE. Note the upward trend of a higher percentage of veterans compared to the controls with higher levels of SCE. Outliers with an SCE lower than 3 or higher than 24 are not included in this graph.

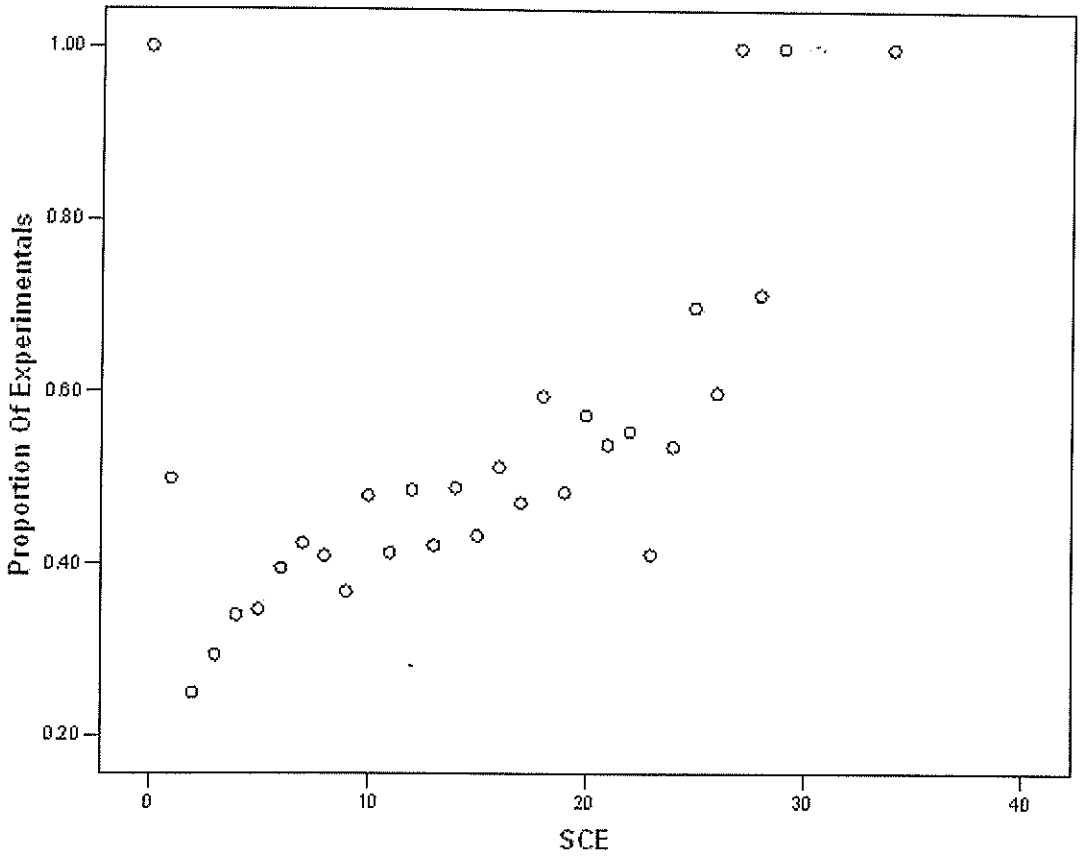

Fig.4 Graph showing the proportion of experimentals (veterans), from a total number of experimentals plus control group combined, at each level of SCE. Outliers with an SCE lower than 3 or higher than 24 are included in this graph.

GROUP		No. of HFCs with SCE >19 over total number of cells scored
Experimental:	Count	98/1683 (5.82%)
	Expected count	76.1/1633 (4.66%)
Control:	Count	74/2057 (3.59%)
	Expected count	95.9/2057 (4.66%)

Table 2. Numbers of high-frequency cells (HFCs) as a percentage of cells scored.

❖ DISCUSSION

Cytogenetic methods such as the analysis of SCE in peripheral blood lymphocytes have been widely used for biological monitoring of humans exposed to harmful environmental agents in order to establish whether or not they have sustained genetic damage (Nilsson et al., 2005; Bilban et al., 2005; DeMarini, 2004; Vijayalaxmi and Obe, 2004; Li et al., 2003; Li et al., 2004; Norppa, 2004a,b; Hatjian et al., 2000; Terzoudi et al., 2003; Akba et al., 2003; Albertini et al., 2003; Takeshita, 2003; Nagayama et al., 2003; Meltz, 2003; McCarroll et al., 2002; Carere et al., 2002; Pitarque et al., 2002; Shaham et al., 2001; Shaham et al., 2002; Zeljezic and Garaj-Vrhovac, 2002; McDiarmid et al., 2001; McDiarmid et al., 2004; Hagmar et al., 2001; Snyder and Green, 2001; Jakab et al., 2001; Lazutka and Dedonyte, 1995; Prabhavthi et al., 1995; Braselmann et al., 1994; Hai et al., 1996). The list above is by no means exhaustive and is but a few from hundreds of similar studies. Modern molecular and chromosomal techniques now allow geneticists to explore the possibility of whether certain individuals have undergone or are currently at risk of occurring genetic damage as a consequence of exposure to harmful agents. Sister chromatid exchanges (SCE) are classically considered a sensitive cytogenetic endpoint of testing the genotoxic risk associated with exposure to mutagenic and carcinogenic agents. In the current study, we conducted an investigation of New Zealand nuclear test veterans using the SCE assay to ascertain whether or not these men have received any genetic damage as a consequence of performing their duties in witnessing the Operation Grapple series of atomic bomb tests.

When embarking upon this study, the researchers were well aware of the contentiousness of the findings, irrespective of whether evidence of genetic damage was observed or not. For this reason, considerable time and thought was given to experimental design. Strict preliminary inclusion/exclusion criteria were applied to reduce the possible influence of factors that could severely impact on our findings. For instance, Vietnam veterans were not included in

either the control or experimental group because there is a risk that these people have been adversely affected by possible exposure to Agent Orange. Neither was any man selected, control or veteran, who had previously worked in the timber industry, received prolonged exposure to solvents, or was currently receiving chemotherapy or radiotherapy. This was followed by a meticulous process of questioning every participant to match the controls as well as was practicable and to ensure that all possible confounding factors were taken into consideration. It was also imperative that the study was conducted blind in order to remove any bias in our analysis.

In discussing our findings, several points need to be addressed. First, concern must be expressed at the high SCE frequencies observed in both the veterans and controls. This was unexpected from our past experience and upon comparison with most of the international literature, although Dewdney et al. (1986), using a slightly higher concentration of BrdU of 25μM (we used 20μM), reported an SCE frequency of 15.7 in females and 13.8 in males in a normal population. Baseline levels similar to this have also been reported by other workers (Galloway and Evans, 1975; Lambert and Lindblad ,1980).

Various possibilities could account for our observed high frequencies. Theoretically the explanation could be methodological or biological. If it were methodological, the cause could be attributed to one of a number of possibilities. For instance, it could be laboratory error; maybe the concentration of bromodeoxyuridine was incorrect (high concentration of BudR can itself increase SCE frequency); maybe dilutions were wrong or the white blood cell count scored incorrectly. All these factors could influence the SCE frequency. We subsequently rechecked all our procedures and no mistakes were found. In the past, sera was known to affect the baseline frequency (Carrano and Natarajan, 1988) but this is an unlikely factor today with the use of modern culture media.

Das and Sharma (1984) found that the frequency of SCEs in human lymphocytes increased as a function of culture temperature and was a maximum at 40 C. Temperature measurements of our incubator over a 3-day period (set at 37 C) found a fluctuation of only $\pm$0.1 C.

Another methodological possibility is statistics. We rechecked our figures closely and similarly found no error. Three different statistics groups analysed the data and all arrived at the same conclusion. The authors are also acutely aware that scoring of SCEs is fraught with difficulties. Despite following established published guidelines that are accepted internationally, there is always a margin of error. No two laboratories can legitimately claim that their method of scoring is exactly the same. Determining what is a sister chromatid exchange is normally straightforward, but there are circumstances where interpretation requires experience. Unconscious bias in scoring must always be considered a possibility. Although unlikely, a potential bias could exist for a researcher to examine more closely (and thus favour) those slides where SCEs are more frequent and thus record an SCE in circumstances where interpretation is equivocal. This could distort the data. We attempted to cover these potential error traps by employing only one researcher to score all the slides, with over 20 years experience of examining chromosomes and considerable experience in using the SCE assay. Furthermore, by having the blood samples recoded by an independent organization (Massey University Student Health), neither the person collecting the blood, nor any member of the research team, could distinguish a veteran's slide from a control slide.

Faced with not knowing a possible methodological explanation for our results, we turn our attention to possible biological explanations. One possible explanation for the high SCE frequency in both the veterans and the controls is age. It is well known from many studies that SCE frequency increases with age. Lazutka et al. (1994) in their study of sister chromatid exchanges and their distribution in human lymphocytes in relation to age, sex and smoking, found a range of SCE

scores from 7.2 to 16.06. Age was a statistically significant factor in their study, which is consistent with the results of other investigations (Sōper et al., 1984; Sarto et al., 1985; Husum et al., 1986). In offering an explanation for this trend, Singh et al. (1990) note that an age-related decline occurs in DNA repair competence among a small subpopulation of lymphocytes and that such repair-deficient cells may accumulate more damage and may have more SCEs.

An alternative explanation to methodology is environmental influence(s). For some unexplained reason we may have detected something in the New Zealand environment that has or is adversely affecting the chromosomes in all these older participants. This is only conjecture but it is a factor that warrants further investigation. Another possibility is that there is something in the past history of military personnel in particular that has affected them which is now being expressed as an increase in SCE frequency. There may be some covariate, so far undetected, that has affected both groups of men causing elevated SCE frequencies. This also warrants further exploration.

One covariate that warrants addressing is cigarette smoking. The information we gathered on lifestyle habits shows that the veterans were heavy smokers, much more than the controls. *Current* cigarette smoking is known to be a powerful SCE-inducer. Many papers testify to this fact. But it is important to note that approximately 6 months after cessation of cigarette smoking, SCE frequencies return to normal (Lazutka *pers. comm.*). In a major study of a large human population sample (353 healthy employees of the Brookhaven National Laboratory with data obtained from scoring 16,898 cells for sister chromatid exchanges), Bender et al. (1988) found no significant difference in SCE frequency between former smokers and non-smokers. Similarly, Shaham et al. (2001) reported a mean number of SCEs/chromosome that was negligibly higher in current smokers (0.25) than non-smokers or past smokers who scored identical frequencies of 0.24. Thus although the New Zealand nuclear test

veterans were heavy smokers in the past, any genetic damage resulting from this past exposure cannot be detected by the SCE technique.

Another issue is the small difference in SCE frequency observed between the veterans and the controls. A difference of less than one SCE between the veterans and the controls is not huge, although many studies report evidence of genetic damage around this range (Lazutka, 1999; McDiarmid et al., 2001). Bender et al. (1988), in their study cited above, reported a mean SCE frequency of 9.02 in current smokers and 8.08 in non-smokers and concluded that this was a very significant difference ($p<0.001$ by a simple t test). Furthermore, as previous workers have mentioned, there has always been a significant background of genetic defect in human populations that could mask the genotoxic effect of the agent under investigation (Zeljezic and Garaj-Vrhovac, 2004).

Given the above reservations and strictures, we have in our study found evidence of a statistically higher frequency of SCE in the nuclear test veterans as compared to an unexposed control group, even when adjustments are made for age, smoking, alcohol, coffee/tea consumption and medical X-ray exposure. No detectable difference could be ascertained when all the covariates listed in the extensive questionnaire (Appendix II) governing lifestyle history, occupational history and medical history were examined, although we accept the theoretical possibility that some confounding factor has been overlooked. From the data gathered, however, we are led to the conclusion that there is some factor(s) involving this group of men which has resulted in them showing evidence of greater genetic damage, more than expected in a 'normal' New Zealand population of men of similar age. Having applied stringent inclusion/exclusion criteria for the study in order to accommodate all likely confounding factors, our results are supportive of the view, by any reasonable analysis, that a measurable amount of genetic damage in the nuclear test veterans can be attributed to their past experience in taking part in Operation Grapple.

The effect size, however, is small, contributing only a low single percentage figure of the observable damage. This means, that of all the variables observed, the veterans' past experience in taking part in Operation Grapple as a contribution towards the observed SCE frequency is minor compared to other effects grouped together. Nevertheless, one cannot ignore the fact that a significant difference is still seen after all likely covariates are eliminated. Substantiating this argument is the high level of High Frequency Cells, an accepted indicator of genetic damage (Carrano and Moore, 1982), observed in the veterans. Table 2, which shows the proportion of veterans with high levels of genetic damage is illuminating, and together with the data shown in Figs.3 and 4 would support the view that irrespective of the major confounding factors, some explanation is warranted for this observation. Interestingly, Silva et al. (1996) report that increased levels of SCEs in chronic exposures to clastogenic agents often result from the presence of a small subpopulation of lymphocytes having very high SCE frequencies. Lazutka (1999) refers to the presence of rogue cells, defined as a cell which has 5 or more chromosome-type aberrations, including one exchange (polycentric, ring chromosome, translocation or inversion) with increased frequency of aberrations in lymphocytes of Chernobyl clean-up workers.

Having discovered elevated SCE frequencies in the New Zealand nuclear test veterans, the next question to be addressed is what is causing this. The chief investigator of the study, Dr Al Rowland, recently attended a key meeting in St Andrews (the 7th International Conference on DNA repair, Chromosomes and Cancer) followed by an identical address at the Congress of the International Cytogenetics and Genome Society in Granada, Spain, where the findings of this research was delivered to a highly respected community of scientists. The St Andrews meeting in particular was a select group of international scientists experienced in radiation research. Both these meetings may be considered as peer review, although we stress that the views expressed in this report may not

reflect the opinions of all scientists in attendance at these forums. That genetic damage was detected is evident from the statistical analysis, but views were polarized at both meetings as to whether the observed effect could be attributed to radiation. The main reason for doubt is predicated on the substantial amount of information which shows that ionizing radiation is known to be a poor inducer of SCEs. This is true if one considers only *ex vivo* irradiation (radiation exposure from an external source) with high energy waves such as gamma-rays and X-rays. *In vivo* (internal) exposure to ingested alpha particles, however, is quite the contrary. A considerable amount of research has shown that very low levels of alpha particles that are emitted from certain radioactive substances are powerful inducers of SCEs, which is not surprising considering the high relative biological effectiveness (RBE) of alpha particles (see Figs 1-16 and 1-17 of Zeman 2000 in Appendix III). At 100KeV/μm (high linear energy transfer [LET]), alpha particles possess an RBE 10 – 20x that of gamma rays. It is important to note here the studies of Little and others who have reported that mammalian cells exposed to very low fluences of alpha particles, whereby only 1 – 3% of the cell nuclei are traversed by a particle, show evidence of genetic effects, including specific gene mutations and sister chromatid exchanges even in neighbouring, non-irradiated ("bystander") cells (Nagasawa and Little, 1992, 1999, 2002). These results indicate that genetic damage may be induced by low doses of alpha-radiation in cell nuclei not actually traversed by an alpha-particle. This could have serious implications in interpreting data, as with the current study, where elevated SCE frequencies are observed, yet these may originate from perhaps almost undetectable traces of radiation still present in the veterans' system.

The concept of clastogenic factors was first described by Holliwell and Littlefield (1968) in attempting to explain chromosome damage induced by plasma from irradiated patients. They postulated an indirect effect of X-irradiation. This idea was subsequently supported by the work of Goh and Sumner (1968) who advanced the view that breaks in normal human chromosomes were induced by a transferable substance in the plasma of irradiated persons exposed to total-

body irradiation. These so-called clastogenic factors (CFs) were found also in plasma from A-bomb survivors (Pant and Kamada (1977) followed by a substantive investigation by Emerit et al. (1990, 1991, 1994a,b, 1995a,b,c, 1997). The significance of their findings, not accepted by all the scientific community, was the discovery of clastogenic factors supposedly induced as a consequence of radiation exposure, in some cases several decades previously. More recently, Nagasawa et al. (2002) conducted an experiment where cells were irradiated in the presence of Filipin, an agent that disrupts lipid rafts, effectively inhibiting membrane signaling. Sister chromatid exchanges and HPRT mutations that could be induced by very low fluences of alpha particles (mean doses 0.17-0.5cGy) were completely suppressed in bystander cells in the presence of Filipin. They conclude that membrane signaling may play an important role in the bystander effect of radiation. Interestingly, the effects in *directly* irradiated cells do not appear to be mediated via the cell membrane.

One of the accepted tenets of the SCE technique is that it records clastogenic activity only from agents present in the blood at the time of conducting the assay. It follows, then, that if the elevated SCE frequency observed in the New Zealand nuclear test veterans were to be attributed to radiation effects, then this would imply, *a priori*, that radionuclides were still present in their system, notwithstanding the possible presence of surrogate clastogenic factors. This raises the question of whether this is a plausible hypothesis. A survey of the literature would indicate that radionuclides may indeed remain in the body for several decades. Salient in this respect is recent elegant work conducted in David Brenner's laboratory, noted earlier in the Introduction (Hande et al., 2003). A study of ex-plutonium workers from the former Soviet Union who were exposed to radioactivity as far back as 1949, shows that 8% of the cancers occurring in 1998 can be attributed to the redepositing of radionuclides to new tumour sites. Their *in situ* hybridization studies further show that past exposure going back several decades can leave a permanent signature in the genome.

If the New Zealand nuclear test veterans were exposed to radioactive substances, then alpha-emitters such as uranium, plutonium and americium could have been deposited in the bone marrow as well as bone, and perhaps released slowly over a long period of time. Theoretically these particles, if present in the veteran's bloodstream, could be the source responsible for elevation in SCE frequency.

In addition to alpha-particles remaining in the body for several decades, the point should also be noted that some lymphocytes are known to be long-lived. For example, samples taken many years after exposure from patients with radiation-treated ankylosing spondylitis (Buckton et al., 1978) and from human beings exposed to atomic bombs in Hiroshima and Nagasaki (Awa et al., 1978) have confirmed that some lymphocytes are very long-lived, in excess of 20 years. This means that radiation-induced aberrations can still be observed in cells that were present as peripheral lymphocytes many years previously at the time of exposure.

Summarizing so far, the main points to note are that very low fluences of alpha particles can induce SCEs, perhaps directly or via some clastogenic factor, and that alpha particles and some lymphocytes are known to remain in the bloodstream for decades.

Our results support the findings of other researchers who have investigated possible genetic damage in individuals exposed to radiation. Both Japanese and Russian laboratories have been active in this field. Lazutka et al. (1999) report that "an analysis of variance showed that exposure to Chernobyl radiation (in the clean up workers) was the most significant factor influencing SCE frequency". They also state that "the main conclusion of this study is that even 3 – 8 years after the Chernobyl accident, radiation-induced chromosomal damage is still present in the lymphocytes of Chernobyl clean-up workers." The other two significant factors were smoking and alcohol abuse which is why these

confounding factors were analysed in the current New Zealand nuclear test veterans study. They also note that increased frequencies of SCE in Chernobyl clean-up workers were also unexpected, since it has been reported (as formerly noted) that SCE is not thought to be a very sensitive indicator of exposure to ionizing radiation (Carrano and Natarajan, 1988). It should be noted, however, that most of these studies were conducted upon radiation exposure *ex vivo*, not *in vivo* which requires the ingestion of radioactive substances. Contrary to the above, increased SCE frequencies have been reported in the case of occupational exposure to radionuclides (Gundy, 1989; Martin et al., 1991) and in laboratory experiments (Aghamohammadi et al., 1988). It should be noted that Martin et al. in their paper on men occupationally exposed to uranium, attributed the increase in SCE frequency to the chemical nature of uranium rather than its radioactive properties.

In his studies of Chernobyl clean-up workers, Lazutka (*pers.comm.*) advances the opinion that incorporated radionuclides might be the cause of an increase in SCE frequency. The authors of the current study of New Zealand nuclear test veterans are led towards the same conclusion that residues of radiation particles may still be present in the soma of the veterans, and if so, presumably in tiny amounts that may be difficult to detect even if testing were conducted on these men today. It is plausible that the influence of genomic instability caused by ionizing radiation may play a role in the elevated SCE frequencies observed.

It is important to note that one cannot equate the percentage of genetic damage attributable to one variable with some perceived "equivalent percentage" of ill health. Statistical significance of genetic damage should be interpreted cautiously with regard to the biological significance. We have not been able to determine from our study the degree of influence that participation in Operation Grapple has possibly had on the veterans' health and it is not a debate we want to enter. We also wish to emphasize that the sister chromatid exchange assay cannot be applied as a diagnostic tool. Although it is a sensitive and powerful

technique for detecting genetic damage, which we report here in the New Zealand nuclear test veterans, it is not a predictor of specific health outcomes. We can make no judgement on specific health consequences. Nevertheless, the point must be made, based on extensive international studies, that genetic damage to any degree has the potential to result in an individual's health being adversely affected.

❖ SUMMARY

In this study, a significantly higher frequency of sister chromatid exchange (SCE) was observed in a sample group of New Zealand nuclear test veterans compared to a matched control group of New Zealand ex-servicemen.

Elevated frequency of SCE in a target group is an accepted indicator of clastogenicity/genotoxicity. From the data gathered we conclude that those men who participated in Operation Grapple have experienced a small but significant measure of genetic damage as shown by the SCE assay.

We do not exclude the possibility that some unknown confounding factor influenced the results, but we have not been able to detect it.

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❖ Appendix I

PRELIMINARY INCLUSION QUESTIONNAIRE

FULL NAME.....
(Please print)

ADDRESS.....

..... **Telephone**.....

AGE..... **(years)** **DATE OF BIRTH**.....

Please answer **YES** or **NO** or comment where appropriate to the questions below.

1. Have you served (including in other armed services, or in a civilian capacity), in any nuclear related area **other than** Operation Grapple?

   .....

2. Have you served aboard any vessel in the French testing at Muroroa?

   .....

3. Have you served in the Occupation Force of Japan (J-Force)? .....

4. Have you served on any ship stationed in Japan in relation to the Occupation force? (If so, state which ship)

   .....

please turn over for more questions on page 2

5. Have you served in Vietnam or Korea?

.....

6. Have you worked in any industry involving radiation or chemicals, i.e. radiation, X-ray departments, timber treatment, top dressing/crop spraying, toxin processing, toxin/chemical retrieval or dumping? (State)

.....

.....

7. Have you worked in any other area where you consider that it may have adversely affected your health? (State)

.....

.....

8. Have you received radiation treatment or chemotherapy for cancer?

.....

9. Is there any other information regarding your health that you consider may be relevant to the forthcoming research? State briefly.

.....

.....

.....

.....

.....

Please understand by responding to the questions above, signing and returning this form in the FREEPOST envelope:

a) that this is a **preliminary questionnaire expressing your interest** to take part in the study.
b) that you are **not** formally bound to take part in the study, and
c) that it does **not necessarily** mean that you will be selected to be a participant in the study.

Signature..... **Date**.....

Thank you for completing this form!

❖ Appendix II

NEW ZEALAND NUCLEAR TEST VETERANS: A PILOT STUDY

INFORMATION SHEET(E)

Thank you for expressing an interest in helping us with this Nuclear Test Veterans' Pilot Study, a study we now invite you to take part in. Before you agree, you should read the following information back- grounding the purpose of the study and your involvement in it, should you consent to take part.

Recently, we agreed to undertake two parallel studies, one funded by the New Zealand Nuclear Test Veterans Association and the other by the War Pensions Medical Research Trust Board. One aim of these studies is to find out if the genetic material of men exposed to a nuclear bomb blast during the 1950s might have been adversely affected. We also agreed to collect information that will help determine your current health status. Our names are Dr Al Rowland (Institute of Molecular Biosciences) and Dr John Podd (School of Psychology). Al is an expert in human cell analysis while John has expertise in research design and the collection and analysis of questionnaire data. We have worked together on several projects over the past few years. We can be contacted by telephone, Al at (06) 3569099 Ext 7977, and John at (06) 3569099 Ext 2067.

We are very keen to do the proposed study, having the full support of the War Pensions Medical Research Trust Board and the New Zealand Nuclear Test Veterans' Association. The purpose of this letter is to tell you more about the study and what you would be asked to do should you wish to be involved.

The study has two main purposes. The first is to examine human blood cells to see if some of the genetic material in those cells could have suffered damage due to exposure to the nuclear bomb blasts you witnessed in the Pacific in the 1950s. A relationship is known to exist between chromosome damage and ill health, such as some blood disorders and various cancers. In other words, as chromosomal damage increases so does the **risk** for some disorders increase. If we find evidence of suspected abnormal levels of damage to your chromosomes, it definitely does not mean you are sick, or

even likely to get sick. Rather, it is an alert signal that there is an increased risk for ill health. **Any results of chromosome damage that we might find should not be used by anyone, including your doctor, as a diagnostic result.** What we wish to find out, by comparing veterans who witnessed the nuclear bomb tests with other men who did not, is whether these tests have increased the level of chromosomal damage observed in one group as compared to another. However, if such evidence is found, no conclusions or claims can be drawn other than those made by similar chromosome analysis studies. That is, while there is a correlation between chromosome damage and ill health, any damage observed does **not mean you are sick.** This would require further investigation by your doctor.

Taking a small blood sample from your arm (about 2 teaspoons) will take only a few minutes and will either by done at your local medical laboratory or by Chris Kendrick from Massey University. Chris is fully trained and authorised to take human blood samples. We have to take into consideration that over the past 40 or so years, activities such as tobacco smoking, alcohol intake, excessive exposure to X-rays or the sun, and a range of other things could also have brought about the genetic changes we will be looking for. Therefore, we have to gather further information to determine if any fraction of the damage we might find is due to these other factors. So, we will ask you to complete a questionnaire that seeks information on your life-style, occupation, and other matters that will help us determine the things we need to take into account in assessing your blood sample.

The second purpose of our study is to build a picture of your current health status. To do this, we will ask you to complete a number of questionnaires including ones about your memory for everyday events, your mood, your general health and how it affects daily activities, and any chronic illnesses you might have – like diabetes, heart problems, or chronic skin conditions. Some questionnaires will be sent to you by post. Others will need to be completed with the assistance of our Research Officer, Judy Blakey, in a face-to-face interview. Judy has a Masters degree in Psychology and is a very experienced interviewer having just completed interviews with over 200 hundred men in a large study of hearing aid use among Veterans.

We will be collecting blood samples and giving the same questionnaires to a group of men of about your age and who served in the Armed Forces about the same time that you did. However, this "control" group will not have been exposed to a nuclear bomb blast as you were. When we look at the data from this group compared to those exposed to nuclear radiation, the only major difference should be the exposure to radiation.

To sum up, if you take part in our study, we would like you to provide a blood sample and to complete some questionnaires. Your total involvement should take no more than two and a half hours. Of course, you have the right to decline to take part, and even if you do agree to "sign on", you have

the complete freedom to withdraw at anytime. You are in control! The only risk you are exposed to is having blood taken from a vein in your arm. The risk to you is negligible and no higher than having your own medical laboratory do this for some other purpose. If we detect any chromosomal abnormalities in your blood, or if we find you are scoring at an unusually high level on any of the questionnaires, we would advise you to see your own doctor.

The blood samples will be destroyed once the blood cultures have been established and questionnaires will be destroyed at the completion of the study. We do need you to provide your name but we give you, your blood sample, and your questionnaire responses a code number. We remove the first two pages of the questionnaire booklet containing your name and signature. These will be locked away securely in the senior researchers' offices (Al and John). From that point on, we use only your code number. In this way, no one other than the researchers can associate your responses with your name.

We expect that the results we get will be of sufficient interest to the scientific community to warrant publication. Please be completely assured that it will be totally impossible to connect your name to any of the published data. **Your name will not be disclosed.** We are very much concerned about your welfare. Therefore, we will endeavour to obtain the best possible data that circumstances will permit. However, as scientists, we must remain objective and unbiased and not be seen to be taking sides. If we did, then this would taint our reputation in respect of future work we do. We will pass our findings on to The War Pensions Medical Research Trust Board and the New Zealand Nuclear Test Veterans' Association. It will be their sole responsibility to decide what to do next.

Finally and most importantly, you have clear and distinct rights if you should decide that you want to take part in this study. You have the right:

- to decline to participate;
- to refuse to answer any particular questions;
- to withdraw from the study at any time;
- to ask questions about the study at any time during participation;
- to provide information on the understanding that your name will not be used unless you give permission to the researcher;
- to be given access to a summary of the findings of the study when it is concluded.

Please ring either Al or John if you have any concerns whatsoever about this study. We will be freely available to you at any time.

John Podd Al Rowland

NEW ZEALAND NUCLEAR TEST VETERANS: A PILOT STUDY

INFORMATION SHEET(C)

Thank you for expressing an interest in helping us with this Nuclear Test Veterans' Pilot Study, a study we now invite you to take part in. Before you agree, you should read the following information back- grounding the purpose of the study and your involvement in it, should you consent to take part.

Recently, we agreed to undertake two parallel studies, one funded by the New Zealand Nuclear Test Veterans Association and the other by the War Pensions Medical Research Trust Board. One aim of these studies is to find out if the genetic material of men exposed to a nuclear bomb blast during the 1950s might have been adversely affected. We also agreed to profile the current state of health of this group. Our names are Dr Al Rowland (Institute of Molecular Biosciences) and Dr John Podd (School of Psychology). Al is an expert in human cell analysis while John has expertise in research design and the collection and analysis of questionnaire data. We have worked together on several projects over the past few years. We can be contacted by telephone, Al at (06) 3569099 Ext 7977, and John at (06) 3569099 Ext 2067.

We are very keen to do the proposed study, having the full support of the War Pensions Medical Research Trust Board and the New Zealand Nuclear Test Veterans' Association. We have already obtained a group of veterans who were exposed to a nuclear bomb blast. What we now need is a comparison group who are very similar to these men but who were not so exposed. In reality, the best we can do is to get a group of men who served in the armed forces around the same time as the exposed veterans. The comparison group will therefore be of about the same age and hopefully will have a similar background. And that's where you come in. You are a NZ Veteran, of similar age to the exposed men, who has expressed interest in taking part in this study.

Before you agree to take part, there are a few things about the study you need to be aware of. The study has two main purposes. The first is to examine human blood cells to see if some of the genetic

material in those cells could have suffered damage due to exposure to the nuclear bomb blasts witnesse in the Pacific in the 1950s. A relationship is known to exist between chromosome damage and ill healt such as some blood disorders and various cancers. In other words, as chromosomal damage increases s does the **risk** for some disorders increase. What we wish to find out, by comparing veterans who witnessed the nuclear bomb tests with men like yourself who did not, is whether these tests have increased the level of chromosomal damage observed in one group as compared to another.

To make these comparisons, we need to take a small blood sample from your arm (about 2 teaspoons). This will take only a few minutes and will either by done at your local medical laboratory or by Chris Kendrick from Massey University. Chris is fully trained and authorised to take human blood samples. We have to take into consideration that over the past 40 or so years, activities such as tobacco smoking alcohol intake, excessive exposure to X-rays or the sun, and a range of other things could also have brought about the genetic changes we will be looking for. Therefore, we have to gather further information to determine if any fraction of the damage we might find is due to these other factors. So, we will ask you to complete a questionnaire that seeks information on your life-style, occupation, and other matters that will help us determine the things we need to take into account in assessing your blood sample.

The second purpose of our study is to build a picture of your current health status so we can compare it with the health profile of the exposed men. To do this, we will ask you to complete a number of questionnaires including ones about your memory for everyday events, your mood, your general health and how it affects daily activities, and any chronic illnesses you might have – like diabetes, heart problems, or chronic skin conditions. Some questionnaires will be sent to you by post. Others will need to be completed with the assistance of our Research Officer, Judy Blakey, in a face-to-face interview. Judy has a Masters degree in Psychology and is a very experienced interviewer having just completed interviews with over 200 hundred men in a large study of hearing aid use among Veterans.

To sum up, if you take part in our study, we would like you to provide a blood sample and to complete some questionnaires. Your total involvement should take no more than two and a half hours. Of course, you have the right to decline to take part, and even if you do agree to "sign on", you have the complete freedom to withdraw at anytime. You are in control! The only risk you are exposed to is having blood taken from a vein in your arm. The risk to you is negligible and no higher than having your own medical laboratory do this for some other purpose. If we detect any chromosomal abnormalities in your blood, or if we find you are scoring at an unusually high level on any of the questionnaires, we would advise you to see your own doctor.

The blood samples will be destroyed once the blood cultures have been established and questionnaires

will be destroyed at the completion of the study. We do need you to provide your name but you will see we give you, your blood sample, and your questionnaire responses a code number. We remove the first two pages of the questionnaire booklet containing your name and signature. These will be locked away securely in the senior researchers' offices (Al and John). From that point on, we use only your code number. In this way, no one other than the researchers can associate your responses with your name.

We expect that the results we get will be of sufficient interest to the scientific community to warrant publication. Please be completely assured that it will be totally impossible to connect your name to any of the published data. **Your name will not be disclosed.** We are very much concerned about the welfare of the veterans exposed to nuclear radiation. Therefore, we will endeavour to obtain the best possible data that circumstances will permit. However, as scientists, we must remain objective and unbiased and not be seen to be taking sides. If we did, then this would taint our reputation in respect of future work we do. We will pass our findings on to The War Pensions Medical Research Trust Board and the New Zealand Nuclear Test Veterans' Association. It will be their sole responsibility to decide what to do next.

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- to refuse to answer any particular questions;
- to withdraw from the study at any time;
- to ask questions about the study at any time during participation;
- to provide information on the understanding that your name will not be used unless you give permission to the researcher;
- to be given access to a summary of the findings of the study when it is concluded.

Please ring either Al or John if you have any concerns whatsoever about this study. We will be freely available to you at anytime.

John Podd

Al Rowland

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NEW ZEALAND NUCLEAR TEST VETERANS: A PILOT STUDY

CONSENT FORM

I have read the Information Sheet and have had the details of the study explained to me in written form. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time.

I understand that I have the right to withdraw from the study at any time, and to decline to answer any particular questions.

I agree to provide a sample of blood for chromosomal analysis on the understanding that I have access to my results, and that I be advised if any abnormalities are found. I understand that my blood sample will not be used for any other research, and will be disposed of sensitively.

I agree to provide information to the researchers on the understanding that my name will not be used without my permission.

(*The information will be used for this research and publications arising from this research project.*)

I agree to participate in this study under the conditions set out in the Information Sheet.

Signed .....

Name: *(please print)* .....

Date: .....

If you would like to receive feedback from this project in the form of a brief written report please tick the appropriate box below:

YES ☐ **NO** ☐

W				

New Zealand Nuclear Test Veterans Postal Survey: A Pilot Study

A research project conducted on behalf of the New Zealand War Pensions Medical Research Trust Board by independent researchers from Massey University

Please read the following instructions carefully:

- All the information you give us is in confidence and will be used only for the purposes of this study.
- Please attempt every question and be careful not to skip any pages.
- There are no right or wrong answers; we want the response which is best for you.
- It is important that you give your own answers to the questions. Please do not discuss your answers with others.
- Do not linger too long over each question; usually your first response is best.
- The survey is comprehensive and appears long; however, we have used a large print size to make the text easier to read.
- We suggest that you plan to answer the questions over a few sittings. You will find a bookmark inside the front cover, to help you mark your place, as you progress through the survey. Each of the four parts of the survey is also printed in a different colour, to help you monitor your progress.

W					

(Shaded area for Office Use Only)

Mail out date: (from Massey)

Date received: (at Massey)

You will be telephoned by a member of the research team, to set up an interview time and venue for the face-to-face interview.

Please enter your telephone number below:

Telephone number: STD CODE | | NUMBER | | | | | | | |

Interviews will take place as soon as possible after receipt of your completed mail out survey. If you know you will be away at *any time* during the next two months, or have regular commitments on specific days during this period, please specify the dates you will be away/otherwise occupied below, so as to assist us organise the interview schedule:

_____

_____

_____

_____

_____

_____

_____

Thank you. PART 1 begins on the next page.

New Zealand Nuclear Test Veterans Postal Survey

PART 1

Firstly, we would like some general background information about you. Please tick the circle ✓ next to the answer which you believe gives an accurate indication of your CURRENT situation, or write details in the spaces provided.

1 What is your date of birth? *(Please state* **day / month / year)**

				1	9		

day month year

2 What is your gender?

○ Male ○ Female

3 Which ethnic group/s do you belong to?
(You may tick more than one circle.)

○ 1 New Zealander of European descent
○ 2 New Zealander of Maori descent
○ 3 Pacific Islander
○ 4 Asian
○ 5 Other (Please specify)

_____

4 Which of the following best describes the area where you live?
(Please tick one circle.)

○ 1 Main Urban Area:	A city with population of 30,000 or more e.g. Palmerston North
○ 2 Secondary Urban Area:	A town / city with a population of between 10,000 & 29,999
○ 3 Minor Urban Area:	A town with a population of between 1,000 & 10,000
○ 4 Rural Centre:	A town with a population of between 300 & 1,000
○ 5 Rural Area:	Outside a town / city boundaries

Office Use Only

Please tick the circle ✓ which you believe gives an accurate indication of your CURRENT situation, or write details in the spaces provided.

Office Use Only

5 **Do you live . . . .** *(You may tick more than one circle.)*

- ○ 1 with your spouse / partner and no one else? 32
- ○ 2 with your spouse / partner and family?
- ○ 3 with relatives?
- ○ 4 alone?
- ○ 5 with other adults?
- ○ 6 in a rest home / nursing home / veterans' home?
- ○ 7 Other *(Specify in the space provided below)* 38

_____

6 **Are you retired?**

○ Yes *(please continue)* ○ No *(please go to Q8 below)* 39

7 **IF you ARE RETIRED what was your main occupation?**

_____ 40

8 **IF you ARE NOT RETIRED what is your main occupation?**

_____ 41

9 **What is your highest educational qualification?**
(Please tick one circle.)

- ○ 1 **Less than 3 years** at secondary school
- ○ 2 **From 3 to 5 years** at secondary school
- ○ 3 School qualifications, University Entrance and above
- ○ 4 Trade certificate or Professional certificate or diploma
- ○ 5 University degree, diploma, or certificate
- ○ 6 Other (Specify in the space provided below)

_____ 42

Please tick the circle ✓ which you believe gives an accurate indication of your CURRENT situation, or write details in the spaces provided.

10 **In which branch of the service were you employed?**
(You may tick more than one circle.)

1 ○ NZArmy

2 ○ RNZNavy

3 ○ RNZAirForce

4 ○ Other *(Please specify, for example, Royal Navy)*

_____

_____

_____

11 **What is/are your service number/s?**
(Please enter details in the boxes provided, below.
*Start entering data from the **LEFT hand side** of the boxes.*
When you have entered your number leave any spare boxes blank.
***If you have MORE THAN ONE service number**, please ensure you specify **WHICH BRANCH** each number is associated with, in the space provided **BENEATH** the boxes.)*

Service Number: ↓ *Start here* | | | | | | | | |
associated with ...

(Specify branch) _____

Service Number: ↓ *Start here* | | | | | | | | |
associated with ...

(Specify branch) _____

Service Number: ↓ *Start here* | | | | | | | | |
associated with ...

(Specify branch) _____

Office Use Only

4

49

55

58

64

67

73

Please tick the circle ✓ which you believe gives an accurate indication of your CURRENT situation, or write details in the spaces provided.

12 **Have you ever been in a situation where you have been exposed to a nuclear blast?**

○ **Yes** *(please continue)*

○ **No** *(please go to PART 2 on page 9)*

13 **Did you serve in OPERATION GRAPPLE?**

○ **Yes** *(please continue)*

○ **No** *(please go to Q17 below)*

14 **When did you serve in OPERATION GRAPPLE?**

From: ☐☐☐☐ (month / year) **To:** ☐☐☐☐ (month / year)

15 **What ship(s) did you serve on, in OPERATION GRAPPLE?**

_____
Ship(s)

16 **In what branch did you serve during OPERATION GRAPPLE?**

_____
Branch

17 **How many blasts were you exposed to?**

_____
number of blasts

Office Use Only

If you are NOT an Operation Grapple veteran, but have been exposed to a nuclear blast, please turn to page 8 to record your responses to the questions.

The instructions that follow apply ONLY to OPERATION GRAPPLE VETERANS:

Pages 5, 6 & 7 list NINE Operation Grapple blasts in order (by operation name, place & date). Please record your responses to the questions (such as the type of protective clothing worn; where you were at the time of the blast; how long you remained in the exclusion zone etc.) for EACH OPERATION GRAPPLE blast that you were exposed to.

Once you have completed listing details related to ALL the blasts that you were exposed to, please go to PART 2 on page 9.

Record if you were present (or not) at <u>EACH</u> blast listed below.

Office Use Only

1 Did you serve on GRAPPLE 1? *(Malden Island on 15 May 1957)*

○ Yes *(continue)* ○ No *(go to Q2 below)*

[1a] WHERE were you at the time of the blast? *(Specify below)*

[1b] What protective clothing did you wear at that time? *(Specify below)*

[1c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ○ Yes ○ No

[1d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[1e] What were you doing during this time? *(Specify below)*

2 Did you serve on GRAPPLE 2? *(Malden Island on 31 May 1957)*

○ Yes *(continue)* ○ No *(go to Q3 below)*

[2a] WHERE were you at the time of the blast? *(Specify below)*

[2b] What protective clothing did you wear at that time? *(Specify below)*

[2c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ○ Yes ○ No

[2d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[2e] What were you doing during this time? *(Specify below)*

3 Did you serve on GRAPPLE 3? *(Malden Island on 19 June 1957)*

○ Yes *(continue)* ○ No *(go to Q4 on page 6)*

[3a] WHERE were you at the time of the blast? *(Specify below)*

[3b] What protective clothing did you wear at that time? *(Specify below)*

[3c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ○ Yes ○ No

[3d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[3e] What were you doing during this time? *(Specify below)*

Record if you were present (or not) at <u>EACH</u> blast listed below.

Office Use Only

4 Did you serve on GRAPPLE X? *(Christmas Is. on 8 Nov. 1957)*

◯ Yes *(continue)* ◯ No *(go to Q5 below)*

[4a] WHERE were you at the time of the blast? *(Specify below)*

[4b] What protective clothing did you wear at that time? *(Specify below)*

[4c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ◯ Yes ◯ No

[4d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[4e] What were you doing during this time? *(Specify below)*

5 Did you serve on GRAPPLE Y? *(Christmas Is. on 28 April 1958)*

◯ Yes *(continue)* ◯ No *(go to Q6 below)*

[5a] WHERE were you at the time of the blast? *(Specify below)*

[5b] What protective clothing did you wear at that time? *(Specify below)*

[5c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ◯ Yes ◯ No

[5d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[5e] What were you doing during this time? *(Specify below)*

6 Did you serve on GRAPPLE Z1? *(Christmas Is. on 22 August 1958)*

◯ Yes *(continue)* ◯ No *(go to Q7 on page 7)*

[6a] WHERE were you at the time of the blast? *(Specify below)*

[6b] What protective clothing did you wear at that time? *(Specify below)*

[6c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ◯ Yes ◯ No

[6d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[6e] What were you doing during this time? *(Specify below)*

You should record if you were present (or not) at EACH blast.

Office Use On

0 7

→ 7 Did you serve on GRAPPLE Z2? *(Christmas Is. on 2 Sept. 1958)*

○ Yes *(continue)* ○ No *(go to Q8 below)*

[7a] WHERE were you at the time of the blast? *(Specify below)*

[7b] What protective clothing did you wear at that time? *(Specify below)*

[7c] Did you leave the exclusion zone immediately after your exposure to *this* blast? ○ Yes ○ No

[7d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[7e] What were you doing during this time? *(Specify below)*

0 8

→ 8 Did you serve on GRAPPLE Z3? *(Christmas Is. on 11 Sept. 1958)*

○ Yes *(continue)* ○ No *(go to Q9 below)*

[8a] WHERE were you at the time of the blast? *(Specify below)*

[8b] What protective clothing did you wear at that time? *(Specify below)*

[8c] Did you leave the exclusion zone immediately after your exposure to *this* blast? ○ Yes ○ No

[8d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[8e] What were you doing during this time? *(Specify below)*

0 9

→ 9 Did you serve on GRAPPLE Z4? *(Christmas Is. on 23 Sept. 1958)*

○ Yes *(continue)* ○ No *(go to Q10 on page 8)*

[9a] WHERE were you at the time of the blast? *(Specify below)*

[9b] What protective clothing did you wear at that time? *(Specify below)*

[9c] Did you leave the exclusion zone immediately after your exposure to *this* blast? ○ Yes ○ No

[9d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[9e] What were you doing during this time? *(Specify below)*

The entries below provide for responses from any participants who have been exposed to nuclear blasts OTHER THAN THOSE ASSOCIATED WITH OPERATION GRAPPLE. If this does not apply to you please go to PART 2 on page 9.

For <u>EACH BLAST</u> please record below:

Office Use Only

10 Where the blast occurred? _____

When? _____ day & month | 1 | 9 | | | year

1 0

[10a] WHERE were you at the time of the blast? *(Specify below)*

_____

[10b] What protective clothing did you wear at that time? *(Specify below)*

_____

[10c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ◯ Yes ◯ No

[10d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[10e] What were you doing during this time? *(Specify below)*

_____

11 Where the blast occurred? _____

When? _____ day & month | 1 | 9 | | | year

1 1

[11a] WHERE were you at the time of the blast? *(Specify below)*

_____

[11b] What protective clothing did you wear at that time? *(Specify below)*

_____

[11c] Did you leave the exclusion zone <u>immediately</u> after your exposure to <u>*this*</u> blast? ◯ Yes ◯ No

[11d] If you did NOT leave the zone immediately afterwards, how long did you remain in the area (in days)? _____ days

[11e] What were you doing during this time? *(Specify below)*

_____

Do you need any extra formatted sheets to complete the list of nuclear blasts to which you have been exposed?

◯ Yes ◯ No

(Extra sheets will be brought for you to complete during your face-to-face interview.)

PART 2 questions, related to your occupational history, begin on the next page. ☞

New Zealand Nuclear Test Veterans Postal Survey

PART 2

The first section focuses on your past occupational history. Please write details in the spaces provided.

A **Please list below ALL the occupations that you have had from 1950 until the present. For each entry record the start and end dates (month & year), and a brief description of the type of work. If you need to record more than 24 entries you can request that extra formatted pages be provided at your face-to-face interview.**

When you have completed recording your list of occupations *turn to page 12.*

	Occupation & type of work:	From date: month year	To date: month year	Office Use Only
[1]				3 – 9
[2]				11 – 14 – 20
[3]				22 – 25 – 31
[4]				33 – 36 – 42
[5]				44 – 47 – 53
[6]				55 – 58 – 64
[7]				66 – 69 – 75 – 77

A [contd.] Please continue to list below ALL the occupations that you have had from 1950 until the present. For each entry record the start and end dates (month & year), and a brief description of the type of work.

Please turn to page 12 when you have completed recording your list of occupations.

	Occupation & type of work:	From date: month year	To date: month year	Office Use Only
[8]				3 9 11
[9]				14 20 22
[10]				25 31 33
[11]				36 42 44
[12]				47 53 55
[13]				58 64 66
[14]				69 75 77
[15]				3 9 11
[16]				14 20 22

A [contd.] Please continue to list below ALL the occupations that you have had from 1950 until the present. For each entry record the start and end dates (month & year), and a brief description of the type of work.

Please turn to page 12 when you have completed recording your list of occupations.

	Occupation & type of work:	From date: month year	To date: month year	Office Use Only
[17]				2; 3 3.
[18]				3 4; 4.
[19]				4 5; 5,
[20]				5 64 64
[21]				65 7; 77
[22]				3 9 11
[23]				14 2(2;
[24]				2 3 3;

B Do you need any extra formatted sheets to complete your list of occupations since 1950 to be provided during your face-to-face interview?

◯ Yes ◯ No

3

Now we would like some specific information about any substances that you have been exposed to since 1950, in your *WORK, HOME OR ANY OTHER ENVIRONMENT*. Please tick the circle ✓ next to the answer which you believe gives an accurate indication of your situation, and where appropriate, write further details in the spaces provided.

Since 1950 have you EVER been exposed, either by breathing or direct skin contact, to any of the substances listed below? Please answer 'Yes' or 'No' to each substance that is listed. If you answer 'Yes' to a substance, try and remember when you were first and last exposed to that particular substance, and the total length of time that you were exposed to it (which should be recorded in months wherever possible, but otherwise specified – e.g. 10 days).

Example: If you were exposed to Asbestos you would tick 'Yes'; then

- *record the date you were first exposed – May 1976;*
- *record the date you were last exposed – Oct 1987;*
- *record the total length of time exposed during that entire period – 3 & a half months (which could represent more than one occasion when you were exposed to the substance during the stated period).*

Office Use Only

A 3 9 15

R 18 24 30

C 33 39 45

1 **Asbestos?**

○ Yes ○ No

First exposed: ___ month ___ year

Last exposed: ___ month ___ year

Length of time exposed: ___ in months, if possible

2 **Radiation (*EXCLUDING OPERATION GRAPPLE*)?**

○ Yes ○ No

First exposed: ___ month ___ year

Last exposed: ___ month ___ year

Length of time exposed: ___ in months, if possible

3 **Coal products?**

○ Yes ○ No

First exposed: ___ month ___ year

Last exposed: ___ month ___ year

Length of time exposed: ___ in months, if possible

Since 1950 have you EVER been exposed, either by breathing or direct skin contact, to any of the substances listed below? Please answer 'Yes' or 'No' to each substance that is listed. If you answer 'Yes' to a substance, try and remember when you were first and last exposed to that particular substance, and the total length of time that you were exposed to it (which should be recorded in months wherever possible, but otherwise specified – e.g. 10 days).

4 **Dust (such as wood or leather)?**

○ Yes ○ No

First exposed: month / year **Last exposed:** month / year **Length of time exposed:** in months, if possible

5 **Pesticides or herbicides?**

○ Yes ○ No

First exposed: month / year **Last exposed:** month / year **Length of time exposed:** in months, if possible

6 **Petroleum products?**

○ Yes ○ No

First exposed: month / year **Last exposed:** month / year **Length of time exposed:** in months, if possible

7 **Dyes?**

○ Yes ○ No

First exposed: month / year **Last exposed:** month / year **Length of time exposed:** in months, if possible

8 **Solvents?**

○ Yes ○ No

First exposed: month / year **Last exposed:** month / year **Length of time exposed:** in months, if possible

Office Use Only

D 48 54 60

H 3 9 15

P 18 24 30

D 33 39 45

S 48 54 60

9 Since 1950 have you EVER been exposed, either by breathing or direct skin contact, to ANY OTHER chemicals/substances?

○ Yes *(please continue)*

○ No *(please go to PART 3 on page 16)*

Office Use Only

If you answered 'Yes' to Q9 above can you think of the names of ANY OTHER specific chemicals/substances (other than the eight already identified on pages 12 & 13) which you know, or suspect that you were exposed to, by breathing or direct skin contact, in your *WORK, HOME OR ANY OTHER ENVIRONMENT,* since 1950? Please first write down the substance, and then the dates of your exposure to that substance, including the total length of time of your exposure, in the spaces provided below.

When you have completed recording your list of substances please go to PART 3 on page 16.

10a Substance: _____

First exposed: month ____ year ____ Last exposed: month ____ year ____ Length of time exposed: ____ in months, if possible

10b Substance: _____

First exposed: month ____ year ____ Last exposed: month ____ year ____ Length of time exposed: ____ in months, if possible

10c Substance: _____

First exposed: month ____ year ____ Last exposed: month ____ year ____ Length of time exposed: ____ in months, if possible

10d Substance: _____

First exposed: month ____ year ____ Last exposed: month ____ year ____ Length of time exposed: ____ in months, if possible

Office Use Only

3
9
15
18
24
30
33
39
45
48
54
60

If you need to continue recording more names of OTHER specific chemicals/substances (other than the eight already identified on pages 12 & 13) which you know, or suspect that you were exposed to, by breathing or direct skin contact, in your *WORK, HOME OR ANY OTHER ENVIRONMENT*, since 1950, space is provided below. Please first write down the substance, and then the dates of your exposure to that substance, including the total length of time of your exposure.

When you have completed recording your list of substances please go to PART 3 on page 16.

Office Use Only

10e Substance: _____

First exposed:		Last exposed:		Length of time exposed:
month	year	month	year	in months, if possible

3 9 15

10f Substance: _____

First exposed:		Last exposed:		Length of time exposed:
month	year	month	year	in months, if possible

18 24 30

10g Substance: _____

First exposed:		Last exposed:		Length of time exposed:
month	year	month	year	in months, if possible

33 39 45

10h Substance: _____

First exposed:		Last exposed:		Length of time exposed:
month	year	month	year	in months, if possible

48 54 60

Thank you for completing PART 2 of the survey.

PART 3 questions, which are related to your health, begin on the next page.

☞

PART 3

These questions focus on your health during the PAST 12 MONTHS. For each question, please tick the circle ✓ for the answer that best applies to you.

When you respond 'Yes' to a question you will be asked to list further details. Each question provides for a specific number of listed responses. If there is insufficient space to accommodate your entire list of responses, you will be able to indicate this at the end of PART 3. This will ensure that extra response sheets for those specific questions will be given to you for completion during your face-to-face interview.

Please do not skip any questions, and do take your time, as this will ensure that your responses are as complete as possible. If you wish to attach any extra notes of your own, you are welcome to do so.

Please note that "the PAST 12 MONTHS" is the period:

From: _____ To: _____

OR (recorded in month and year format)

From: month year To: month year

Office Use Only

You should ONLY refer to this time period whilst completing questions 1 to 6. To assist you remember these dates, they will be repeated at the top of each page.

1 Have you had any surgery during the past 12 months?

○ Yes *(please complete the list below, then go to Q2 on page 18)*

○ No *(please go to Q2 on page 18)*

Office Use Only

If you have had any surgery during the past 12 months, please list below, for EACH time that you had an operation, the reason for the surgery, and the date when you had it (recorded in month and year format).

Surgery: Date:

1a Reason: _____ month year

_____

_____

_____

Please note that "the PAST 12 MONTHS" is the period:

From: month year To: month year

1 contd. *If you need to list any further operations you had during the past 12 months, please continue to record the reason for each operation, and the date when you had it (specify the month & year). When you have completed entering your responses please go to Q2 on page 18.*

Surgery: **Date:** Office Use Only

1b Reason: _____ month year

_____

_____

1c Reason: _____ month year

_____

_____

1d Reason: _____ month year

_____

_____

1e Reason: _____ month year

_____

_____

1f Reason: _____ month year

_____

_____

1g Reason: _____ month year

_____

_____

1h Reason: _____ month year

_____

_____

1i Reason: _____ month year

_____

_____

19 25 31 37 43 49 55 61

Please note that "the PAST 12 MONTHS" is the period:

From: ☐☐☐☐ (month year) To: ☐☐☐☐ (month year)

2 Have you had any fevers during the past 12 months?

○ Yes *(please complete the list below, then go to Q3 on page 20)*

○ No *(please go to Q3 on page 20)*

If you have had any fevers during the past 12 months, please list below, for EACH time that you had a fever:

- **the illness that was associated with that fever**
- **the date when you had the fever (recording the month & year each time)**
- **the medication you took for the fever**

2a Illness: _____

_____

Date: ☐☐☐☐ (month year)

Medication: _____

_____

2b Illness: _____

_____

Date: ☐☐☐☐ (month year)

Medication: _____

_____

2c Illness: _____

_____

Date: ☐☐☐☐ (month year)

Medication: _____

_____

Office Use Only

☐☐☐ 3

☐☐☐ 6

☐☐☐ 10

13

☐☐☐ 16

☐☐☐ 20

23

☐☐☐ 26

☐☐☐ 30

33

Please note that "the PAST 12 MONTHS" is the period:

From: [ ][ ][ ][ ] (month / year) To: [ ][ ][ ][ ] (month / year)

2 contd. *Please continue to list any fevers you have had during the past 12 months. When you have completed entering your responses please go to Q3 on page 20.*

Office Use Only

2d Illness: _____

_____ 36

Date: [ ][ ][ ][ ] (month / year)

Medication: _____ 40

_____ 43

2e Illness: _____ 46

_____

Date: [ ][ ][ ][ ] (month / year)

Medication: _____ 50

_____ 53

2f Illness: _____ 56

_____

Date: [ ][ ][ ][ ] (month / year)

Medication: _____ 60

_____ 63

2g Illness: _____ 3

_____

Date: [ ][ ][ ][ ] (month / year)

Medication: _____ 7

_____ 10

2h Illness: _____ 13

_____

Date: [ ][ ][ ][ ] (month / year)

Medication: _____ 17

_____ 20

These next questions are about MEDICATION you have taken over the PAST 12 MONTHS.

Please note that "the PAST 12 MONTHS" is the period:

From: ____ ____ (month year) To: ____ ____ (month year)

3 Have you taken any medication prescribed by a doctor in the past 12 months (for example: blood pressure pills, antibiotics, insulin, tranquillisers, muscle relaxants, etc.)?

Office Use Only

○ Yes *(please complete the list below, then go to Q4 on page 23)*

○ No *(please go to Q4 on page 23)*

Please record below ANY PRESCRIBED MEDICATION taken during the PAST 12 MONTHS, & the REASON for taking it.

	Type of prescription medication taken:	From date: (month year)	To date: (month year)	Office Use Only
3a				9
	Reason:			15
3b				21
	Reason:			27
3c				33
	Reason:			39
3d				45
	Reason:			51
3e				57
	Reason:			63

Please note that "the PAST 12 MONTHS" is the period:

From: month year To: month year

3 contd. *Please continue to record below ANY PRESCRIBED MEDICATION that you have taken during the PAST 12 MONTHS, & the REASON for taking it. When you have completed entering your responses please go to Q4 on page 23.*

Office Use Only

3f Type of prescription medication taken: _____ From date: month year To date: month year — 69

Reason: _____ — 75

3g Type of prescription medication taken: _____ From date: month year To date: month year — 3, 6

Reason: _____ — 12

3h Type of prescription medication taken: _____ From date: month year To date: month year — 18

Reason: _____ — 24

3i Type of prescription medication taken: _____ From date: month year To date: month year — 30

Reason: _____ — 36

3j Type of prescription medication taken: _____ From date: month year To date: month year — 42

Reason: _____ — 48

3k Type of prescription medication taken: _____ From date: month year To date: month year — 54

Reason: _____ — 60

3l Type of prescription medication taken: _____ From date: month year To date: month year — 66

Reason: _____ — 72

Please note that "the PAST 12 MONTHS" is the period:

From: | | | | | month | year | To: | | | | | month | year |

3 contd. *Please continue to record below ANY PRESCRIBED MEDICATION that you have taken during the PAST 12 MONTHS, & the REASON for taking it. When you have completed entering your responses please go to Q4 on page 23.*

Office Use Only

3m Type of prescription medication taken: _____ From date: month year To date: month year

Reason: _____

3n Type of prescription medication taken: _____ From date: month year To date: month year

Reason: _____

3o Type of prescription medication taken: _____ From date: month year To date: month year

Reason: _____

3p Type of prescription medication taken: _____ From date: month year To date: month year

Reason: _____

3q Type of prescription medication taken: _____ From date: month year To date: month year

Reason: _____

3r Type of prescription medication taken: _____ From date: month year To date: month year

Reason: _____

3s Type of prescription medication taken: _____ From date: month year To date: month year

Reason: _____

Please note that "the PAST 12 MONTHS" is the period:

From: month year To: month year

4 Have you taken <u>any non-prescription</u> medication in the past 12 months (for example: aspirin, antacid, anti-histamine, sedatives, or other drugs)?

◯ Yes *(please complete the list below, <u>then</u> go to Q5 on page 25)*

◯ No *(please go to Q5 on page 25)*

Office Use Only 3

Please record below <u>ANY NON-PRESCRIPTION MEDICATION</u> that you have taken during the <u>PAST 12 MONTHS</u> & the <u>REASON</u> for taking it.

4a **<u>Type of non-prescription medication taken</u>:** _____ **<u>From date</u>:** month year **<u>To date</u>:** month year 6 9

Reason: _____ 15

4b **<u>Type of non-prescription medication taken</u>:** _____ **<u>From date</u>:** month year **<u>To date</u>:** month year 18 21

Reason: _____ 27

4c **<u>Type of non-prescription medication taken</u>:** _____ **<u>From date</u>:** month year **<u>To date</u>:** month year 30 33

Reason: _____ 39

4d **<u>Type of non-prescription medication taken</u>:** _____ **<u>From date</u>:** month year **<u>To date</u>:** month year 42 45

Reason: _____ 51

4e **<u>Type of non-prescription medication taken</u>:** _____ **<u>From date</u>:** month year **<u>To date</u>:** month year 54 57

Reason: _____ 63

4f **<u>Type of non-prescription medication taken</u>:** _____ **<u>From date</u>:** month year **<u>To date</u>:** month year 66 69

Reason: _____ 75

Please note that "the PAST 12 MONTHS" is the period:

From: month year To: month year

4 contd. *Please continue to record below ANY NON-PRESCRIPTION MEDICATION that you have taken during the PAST 12 MONTHS & the REASON for taking it that you have not already listed on the previous page. When you have completed entering your responses please go to Q5 on page 25.*

Office Use Only

4g Type of non-prescription medication taken: _____ From date: month year To date: month year 6 12

Reason: _____

4h Type of non-prescription medication taken: _____ From date: month year To date: month year 18 24

Reason: _____

4i Type of non-prescription medication taken: _____ From date: month year To date: month year 30 36

Reason: _____

4j Type of non-prescription medication taken: _____ From date: month year To date: month year 42 48

Reason: _____

4k Type of non-prescription medication taken: _____ From date: month year To date: month year 54 60

Reason: _____

4l Type of non-prescription medication taken: _____ From date: month year To date: month year 66 72

Reason: _____

Please note that "the PAST 12 MONTHS" is the period:

From: month year To: month year

5 Do you currently take any vitamins or herbal remedies, or have you done so in the past 12 months?

○ Yes *(please complete the list below then go to Q6 on page 27)*

○ No *(please go to Q6 on page 27)*

Office Use Only 3

Please record below ANY VITAMINS / HERBAL REMEDIES that you have taken during the PAST 12 MONTHS & the REASON for taking it.

5a Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year 9

Reason: _____ 15

5b Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year 21

Reason: _____ 27

5c Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year 33

Reason: _____ 39

5d Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year 45

Reason: _____ 51

5e Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year 57

Reason: _____ 63

5f Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year 69

Reason: _____ 75

Please note that "the PAST 12 MONTHS" is the period:

From: month year To: month year

5 contd. *Please continue to record below ANY VITAMINS / HERBAL REMEDIES that you have taken during the PAST 12 MONTHS (including the REASON for taking them) that you have not already listed on the previous page. When you have completed entering your response please go to Q6 on page 27.*

Office Use Only

5g Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year

Reason: _____ 6 12

5h Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year

Reason: _____ 18 24

5i Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year

Reason: _____ 30 36

5j Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year

Reason: _____ 42 48

5k Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year

Reason: _____ 54 60

5l Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year

Reason: _____ 6 12

5m Type of vitamin/herbal remedy taken: _____ From date: month year To date: month year

Reason: _____ 18 24

Please note that "the PAST 12 MONTHS" is the period:

From: month year To: month year

6 Have you had a vaccination in the past 12 months?

○ **Yes** *(please complete the list below then go to Q7 on page 28)*

○ **No** *(please go to Q7 on page 28)*

Please record below ANY VACCINATION that you have received in the PAST 12 MONTHS, and the DATE you had it.

Type of vaccination: **Date:** day month year

6a _____

6b _____

6c _____

6d _____

6e _____

Office Use Only

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7 **Have you ever had any DENTAL X-RAYS?**

○ **Yes** *(please continue)*

○ **No** *(please go to Q8 below)*

Did you have a dental X-ray ... ***(please tick ONE only)***

○ **.. within the last month?**

○ **.. within the last 6 months?**

○ **.. within the last 6-12 months?**

○ **.. over one year ago?**

8 ***(Please note the change in the time period you are asked to refer to in this question: Questions 1-6 all focused on "the past 12 months", but this question covers the period "since 1950".)***

Have you had any diagnostic or therapeutic X-rays (OTHER THAN DENTAL X-RAYS) since 1950?

○ **Yes** *(please complete the list below then go to Q9 on page 31)*

○ **No** *(please go to Q9 on page 31)*

Please record below the REASON FOR EACH X-RAY that you have had since 1950, the X-RAY SITE (e.g. chest), and the YEAR (e.g. 1972) that you had that X-Ray.

(Try to remember events in your life that required you to have an X-ray, and then link each event to a date.)

The reason for X-ray: **Year:**

8a **Reason:** _____ year

X-Ray Site: _____

8b **Reason:** _____ year

X-Ray Site: _____

8c **Reason:** _____ year

X-Ray Site: _____

Office Use Only

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8 contd. *If you need to continue listing any diagnostic or therapeutic X-rays (OTHER THAN DENTAL X-RAYS) that you have had since 1950, please continue as before.*

(Try to remember events in your life that required you to have an X-ray, and then link each event to a date. For each X-ray please record the REASON for having the X-ray, the X-RAY SITE, and the YEAR when you had it. When you have completed your list please go to Q9 on page 31.)

The reason for X-ray:

Year:

8d Reason: _____ year

X-Ray Site: _____

8e Reason: _____ year

X-Ray Site: _____

8f Reason: _____ year

X-Ray Site: _____

8g Reason: _____ year

X-Ray Site: _____

8h Reason: _____ year

X-Ray Site: _____

8i Reason: _____ year

X-Ray Site: _____

8j Reason: _____ year

X-Ray Site: _____

Office Use Only

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49

8 contd. *If you need to continue listing any diagnostic or therapeutic X-rays (OTHER THAN DENTAL X-RAYS) that you have had since 1950, please continue as before.*

(Try to remember events in your life that required you to have an X-ray, and then link each event to a date. For each X-ray please record the REASON for having the X-ray, the X-RAY SITE, and the YEAR when you had it. When you have completed your list please go to Q9 on page 31.)

The reason for X-ray: **Year:**

Office Use Only

8k Reason: _____ year

X-Ray Site: _____

8l Reason: _____ year

X-Ray Site: _____

8m Reason: _____ year

X-Ray Site: _____

8n Reason: _____ year

X-Ray Site: _____

8o Reason: _____ year

X-Ray Site: _____

8p Reason: _____ year

X-Ray Site: _____

8q Reason: _____ year

X-Ray Site: _____

8 contd. *If you need to continue listing any <u>diagnostic or therapeutic X-rays</u> (OTHER THAN DENTAL X-RAYS) that you have had since 1950, please continue as before.*

(Try to remember events in your life that required you to have an X-ray, and then link each event to a date. For each X-ray please record the <u>REASON</u> for having the X-ray, the <u>X-RAY SITE</u>, and the <u>YEAR</u> when you had it. When you have completed your list please go to Q9 on page 31.)

<u>The reason for X-ray</u>: **<u>Year</u>:**

Office Use Only

8r **Reason:** _____ ☐☐☐☐ year

_____

X-Ray Site: _____

24 28

8s **Reason:** _____ ☐☐☐☐ year

_____

X-Ray Site: _____

31 35

8t **Reason:** _____ ☐☐☐☐ year

_____

X-Ray Site: _____

38 42

9 Are you aware of any birth defects, or other genetic disorders, or inherited diseases that do / did affect …

.. your parents? ◯ Yes ◯ No

.. your brothers &/or sisters? ◯ Yes ◯ No

.. children of your brothers &/or sisters? ◯ Yes ◯ No

43 44 45

If you responded 'No' to <u>ALL</u> of the above please go to Q10 on page 32. If you responded 'Yes' to <u>ANY</u> of the above please record brief details below.

_____

_____

_____

_____

_____

48 54

10 Are you aware of any birth defects, or other genetic disorders, or inherited diseases that do / did affect ...

a) .. your <u>own</u> children? ◯ Yes ◯ No

b) .. your <u>own</u> grandchildren? ◯ Yes ◯ No

If you responded 'Yes' to (a) or (b) above, please record brief details below about the genetic health problems affecting <u>each</u> off-spring, including: whether that off-spring is your child/grandchild; their date of birth; their gender and the nature of their genetic disorder.

Office Use Only

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If you were unable to complete any of the PART 3 question response lists due to lack of space, and <u>you require extra formatted sheets</u> to complete during your face-to-face interview, please tick the SQUARE next to the relevant question/s below.

Q 1 – ANY SURGERY in the past 12 months ☐

Q 2 – ANY FEVERS in the past 12 months ☐

Q 3 - PRESCRIPTION MEDICATIONS in the past 12 months ☐

Q 4 - NON-PRESCRIPTION MEDICATIONS in the past 12 months ☐

Q 5 - VITAMINS/HERBAL REMEDIES in the past 12 months ☐

Q 6 - VACCINATIONS in the past 12 months ☐

Q 8 X-RAYS since 1950 ☐

Thank you for completing PART 3. Please ensure you have completed the response lists for <u>every</u> question, before continuing. If you have requested extra formatted sheets (as indicated above) these will be given to you at your face-to-face interview.

PART 4 starts on the next page. ☞

PART 4

PART 4 focuses on your diet, starting off with questions about your current eating and drinking habits. For each question please tick the circle ✓ for the answer that best applies to you, or write the details in the spaces provided. If you are unsure about how to answer any question, please give the best answer you can.

Please avoid ticking more than one circle per question, unless asked to do so.

1 Do you eat vegetables?

○ Yes ○ No

2 Do you eat meat?

○ Yes ○ No

3 Do you use diet sweetners?

○ Yes ○ No *(please go to Q4 below)*

How many diet sweetners do you use per day OR per week?

(Please enter the number of diet sweetners in the space provided below, and ALSO indicate whether this is per day OR per week by circling the appropriate description.)

_____ diet sweetners **per day OR per week**

number *(Circle one of these terms)*

4 Do you drink diet drinks?

○ Yes ○ No *(please go to Q5 on page 34)*

How many units (measured as 250ml, which is equivalent to an average size glass) per day OR per week?

(Please enter the number of 250 ml unit diet drinks in the space provided below, and ALSO indicate whether this is per day OR per week by circling the appropriate description.)

_____ 250ml diet drinks **per day OR per week**

number *(Circle one of these terms)*

Office Use Only

1 2 3 4 7 10

Office Use Only

5 **Are there any other comments that you would like to make regarding your diet that may not have been covered already? (e.g. do you follow a special diet such as low fat, high protein, low carbohydrate, etc.)**

_____

_____

_____

_____

_____

_____

_____

_____

13 19

6 **Do you drink coffee?**

○ Yes ○ No *(please go to Q8 below)*

20

How many cups do you drink per day OR per week?

(Please enter the number of 250 ml cups of CAFFEINATED COFFEE in the space provided below, and ALSO indicate whether this is per day OR per week by circling the appropriate description.)

_____ 250ml caffeinated coffee **per day OR per week**

number *(Circle one of these terms)*

23

7 **How often do you drink decaffeinated coffee?**

○ 1	○ 2	○ 3	○ 4	○ 5
all of the time	most of the time	some of the time	a little of the time	none of the time

24

8 **Do you drink tea?**

○ Yes ○ No *(please go to page 35)*

25

How many cups do you drink per day OR per week?

(Please enter the number of 250 ml cups of TEA in the space provided below, and ALSO indicate whether this is per day OR per week by circling the appropriate description.)

_____ 250ml tea **per day OR per week**

28

number *(Circle one of these terms)*

The next group of questions are about alcohol consumption.

As a guide a drink is:

- **a can or small bottle of beer (a third of a pub jug)**
- **a small glass of wine**
- **a nip of spirits (a 'single' in a pub)**

For each question, please tick the circle ✓ for the answer that best applies to you. Please do not skip any questions.

Please tick ONLY ONE circle in response to each question.

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1 **Has a relative, or friend, or a doctor, or other health worker been concerned about your drinking, or suggested that you cut down?** 29

○ No ○ Yes - but not in the last year ○ Yes - during the last year

2 **Do you currently avoid drinking ALL alcohol because you have had difficulties in the past limiting the amount of alcohol that you drank?** 30

○ No *(please continue)* ○ Yes *(please go to Q10 on page 37)*

3 **Have you had a drink containing alcohol in the last year?** 31

○ Yes *(please continue)* ○ No *(please go to Q10 on page 37)* ○ Don't know *(please continue)*

4 **How often do you have a drink containing alcohol?** 32

○ monthly or less ○ 2 - 4 times a month ○ 2 - 3 times a week ○ 4 or more times a week

5 **How many drinks containing alcohol do you have on a typical day, when drinking?** *(Please tick ONLY ONE circle.)* 33

○ 1 or 2 drinks ○ 3 or 4 drinks ○ 5 or 6 drinks ○ 7 to 9 drinks ○ 10 or more ○ don't know

As a guide a drink is:

- a can or small bottle of beer (a third of a pub jug)
- a small glass of wine
- a nip of spirits (a 'single' in a pub)

For each question, please tick the circle ✓ for the answer that best applies to you. Please do not skip any questions.

Please tick ONLY ONE circle in response to each question.

6 How often do you have six or more drinks on one occasion? *(Please tick ONLY ONE circle.)*

○ never ○ less than monthly ○ monthly ○ weekly ○ daily or almost daily

7 How often during the last year have you found that you were not able to stop drinking once you had started?

○ never ○ less than monthly ○ monthly ○ weekly ○ daily or almost daily

8 How often during the last year have you failed to do what was normally expected from you because of drinking?

○ never ○ less than monthly ○ monthly ○ weekly ○ daily or almost daily

9 How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?

○ never ○ less than monthly ○ monthly ○ weekly ○ daily or almost daily

Office Use Only

34

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36

37

The following questions are about your smoking history. For each question, please tick the circle ✓ for the answer that best applies to you, or enter details in the space provided. Please do not skip any questions.

10a Do you currently smoke any substance other than tobacco?

○ Yes ○ No

10b Have you EVER smoked any substance other than tobacco?

○ Yes ○ No

11 Does anyone (including yourself) currently smoke tobacco products inside your home every day, or most days?

○ Yes ○ No

12 Do you currently smoke ANY tobacco products?

○ Yes *(please go to Q16 on page 38)*

○ No *(please continue)*

13 Have you ever been a smoker of ANY tobacco products in the past?

○ Yes *(please continue)*

○ No *(please go to PART 5 on page 40)*

14 Were you ever a regular, daily smoker of tobacco products, before you stopped smoking?

○ Yes ○ No

15a What date did you last smoke? *(please specify month and year)*

Date: ☐☐ month ☐☐☐☐ year **OR** ○ Don't know

15b About how many years did you smoke tobacco products before you stopped? *(Please specify below)*

_____ *years*

(If you currently DO NOT SMOKE ANY TOBACCO PRODUCTS please go to PART 5 on page 40)

Office Use Only

38 ☐

39 ☐

40 ☐

41 ☐

42 ☐

43 ☐

45 ☐☐

49 ☐☐

51 ☐☐

53

For each question, please tick the circle ✓ for the answer that best applies to you, or enter details in the space provided. Please do not skip any questions.

16 Do you currently smoke one or more tobacco cigarettes a day?

○ Yes *(please continue)* ○ No *(please go to Q19 below)*

17a *Please specify below the MONTH & YEAR you FIRST started smoking one or more cigarettes a day.*

month year

17b About how many years have you been smoking one or more cigarettes per day? *(please specify)* _____ *years*

17c Have you ALWAYS smoked one or more cigarettes per day from the date you specified above, right up until today's date?

○ Yes ○ No

18 About how many cigarettes do you smoke in an average day?

○ 1 to 10 a day? ○ 11 to 20 a day? ○ 21 to 30 a day? ○ 31 or more a day?

19 Do you currently smoke cigars?

○ Yes *(please continue)* ○ No *(please go to Q22 on page 39)*

20a *Please specify below the MONTH & YEAR you FIRST started smoking cigars.*

month year

20b About how many years have you been smoking cigars?

(please specify) _____ *years*

20c Have you ALWAYS smoked cigars from the date you specified above, right up until today's date?

○ Yes ○ No

Office Use Only

54 56 62 63 64 65 67 73 74

For each question, please tick the circle ✓ for the answer that best applies to you, or write details in the space provided. Please do not skip any questions.

Office Use Only

21 How often do you smoke cigars?

○ only occasionally ○ 1 cigar in an average day? ○ 2 to 3 cigars in an average day? ○ 4 or more cigars in an average day?

22 Do you currently smoke a pipe?

○ Yes *(please continue)* ○ No *(please go to the final instructions below)*

23a *Please specify below the MONTH & YEAR you FIRST started smoking a pipe.*

month year

23b About how many years have you been smoking a pipe?

(please specify) _____ *years*

23c Have you ALWAYS smoked a pipe from the date you specified above, right up until today's date?

○ Yes ○ No

24 How often do you smoke a pipe?

○ only occasionally ○ 1 pipe full in an average day? ○ 2 to 3 pipes full in an average day? ○ 4 or more pipes full in an average day?

→ ***Please check that you have answered every question that applies to you in PART 4, before turning to PART 5.***

☞

PART 5

The following questions focus on any long-term health problems that you may CURENTLY have.

Long-term health problems are more severe health problems that you have had for six months or more, or something that is likely to last for at least six months. Please tick the circle ✓ corresponding to the word 'Yes' OR 'No' to indicate if a doctor, nurse, or other health care worker has told you that you have any of the following long-term health problems. Please do not skip any questions.

(Please tick ONE CIRCLE on each line.)		Yes	No	Office Use Only
1a	Cancer?	○	○	1
1b	If you **DO** suffer from cancer, what type/s of cancer? *(specify below)*			5
1c	Have you ever received radiation therapy **OR** chemotherapy to treat your cancer?	○	○	6
2	Diabetes?	○	○	
3	Epilepsy?	○	○	
4	High blood pressure or hypertension?	○	○	
5	Heart trouble e.g. angina or myocardial infarction?	○	○	10
7	Stroke?	○	○	
7	Asthma?	○	○	
8	Other respiratory conditions e.g. bronchitis?	○	○	13
9	Stomach ulcer or duodenal ulcer?	○	○	
10	Chronic liver trouble e.g. cirrhosis?	○	○	14
11	Bowel disorders e.g. colitis or polyps?	○	○	
12	Hernia or rupture?	○	○	
13	Chronic kidney or urinary tract conditions?	○	○	18

Long-term health problems are more severe health problems that you have had for six months or more, or something that is likely to last for at least six months. Please tick the circle ✓ corresponding to the word 'Yes' OR 'No' to indicate if a doctor, nurse or other health care worker has told you that you have any of the following long-term health problems. ***Please do not skip any questions.***

	(Please tick ONE CIRCLE on each line.)	Yes	No	Office Use Only
14	Chronic skin conditions e.g. dermatitis or psoriasis?	○	○	
15	Arthritis or rheumatism?	○	○	
16	Hepatitis?	○	○	
17	Sight impairment or loss?	○	○	
18	Hearing impairment or loss?	○	○	
19	Glandular fever (Infectious mononucleosis)?	○	○	
20	Herpes?	○	○	
21	AIDS?	○	○	
22	Meningitis?	○	○	
23	Bacterial or viral infection?	○	○	

24 Do you currently have, OR have you ever had any OTHER MAJOR illness?

○ **Yes** *(please continue)* ○ **No** *(please go to Q25 on page 43)*

Please record (in the space provided below) any OTHER MAJOR ILLNESS, stating WHEN you were ill (month & year to month & year), and the TREATMENT for that illness. Provision is made for you to make 7 entries in this booklet. ***If this is insufficient space, extra formatted sheets will be brought to your face-to-face interview. When you have finished recording your entries please go to Q25 on page 43.***

[24a] Illness: _____

_____

_____

Treatment: _____

_____

From: month year

To: month year

[24b] Illness: _____

_____

_____

Treatment: _____

_____

From: month year

To: month year

24 contd. *Please continue recording (in the space provided below) any OTHER MAJOR ILLNESS (not already listed in PART 5 Q1 to Q23), stating WHEN you were ill (month & year to month & year), and the TREATMENT for that illness.*

If there is insufficient space, extra formatted sheets will be brought to your face-to-face interview. When you have finished recording your entries please go to Q25 on page 43.

Office Use Only

[24c] **Illness:** _____ **From:** ☐☐☐☐ (month year)

_____ **To:** ☐☐☐☐ (month year)

_____

Treatment: _____

_____

[24d] **Illness:** _____ **From:** ☐☐☐☐ (month year)

_____ **To:** ☐☐☐☐ (month year)

_____

Treatment: _____

_____

[24e] **Illness:** _____ **From:** ☐☐☐☐ (month year)

_____ **To:** ☐☐☐☐ (month year)

_____

Treatment: _____

_____

[24f] **Illness:** _____ **From:** ☐☐☐☐ (month year)

_____ **To:** ☐☐☐☐ (month year)

_____

Treatment: _____

_____

[24g] **Illness:** _____ **From:** ☐☐☐☐ (month year)

_____ **To:** ☐☐☐☐ (month year)

_____

Treatment: _____

_____

24 contd. Do you need any extra sheets at your face-to-face interview to record more entries for Q24?

◯ Yes ◯ No

25 Please list <u>any other illness</u> (including cold and 'flu) that you have experienced in the <u>PAST 12 MONTHS</u>. Record the <u>ILLNESS</u>, <u>WHEN YOU WERE ILL</u> (month & year to month & year), and the <u>TREATMENT</u> for that illness. Provision is made for you to record 9 entries in this booklet.

If there is insufficient space, extra formatted sheets will be brought to your face-to-face interview. When you have completed recording your entries please go to PART 5 on page 45.

Please note that "the PAST 12 MONTHS" is the period

From: [ ][ ][ ][ ] (month year) To: [ ][ ][ ][ ] (month year)

[25a] Illness: _____ From: [ ][ ][ ][ ] (month year)

_____ To: [ ][ ][ ][ ]

Treatment: _____

[25b] Illness: _____ From: [ ][ ][ ][ ] (month year)

_____ To: [ ][ ][ ][ ]

Treatment: _____

[25c] Illness: _____ From: [ ][ ][ ][ ] (month year)

_____ To: [ ][ ][ ][ ]

Treatment: _____

[25d] Illness: _____ From: [ ][ ][ ][ ] (month year)

_____ To: [ ][ ][ ][ ]

Treatment: _____

[25e] Illness: _____ From: [ ][ ][ ][ ] (month year)

_____ To: [ ][ ][ ][ ]

Treatment: _____

Office Use Only

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25 contd. *Please continue to record any other illness (including cold and 'flu) that you have experienced in the PAST 12 MONTHS. Record the ILLNESS, WHEN YOU WERE ILL (month & year to month & year), and the TREATMENT for that illness. Provision is made for you to make 9 entries in this booklet. If there is insufficient space, extra formatted sheets will be brought to your face-to-face interview.*

Please note that "the PAST 12 MONTHS" is the period

From: month year **To:** month year

[25f] **Illness:** _____ **From:** month year

_____ **To:**

_____

Treatment:

_____

[25g] **Illness:** _____ **From:** month year

_____ **To:**

_____

Treatment:

_____

[25h] **Illness:** _____ **From:** month year

_____ **To:**

_____

Treatment:

_____

[25i] **Illness:** _____ **From:** month year

_____ **To:**

_____

Treatment:

_____

Office Use Only

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25 contd. **Do you need any extra sheets at your face-to-face interview to record more entries for Q25?**

◯ Yes ◯ No

Thank you for answering PART 5.

Postal Survey Final Page

Before you place your completed survey in the addressed, FREEPOST envelope, please complete the check list below:

Please ...

- .. double check to see that you have NOT skipped any pages, as this is very easy to do! ☐
- .. triple check that you have entered ALL the details that you intended to, including any extra notes. ☐
- .. place your completed postal survey booklet in the supplied, addressed FREEPOST envelope. ☐
- .. post your completed survey booklet as soon as you have finished filling it in, and attended to the check list above. ☐

If you have any queries related to any aspects of this research project, please do not hesitate to contact us.

Research team contact details:

Telephone at:
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J.V.Podd@massey.ac.nz
Email Dr Al Rowland at:
R.E.Rowland@massey.ac.nz

Thank you, once again, for your time completing this survey.

❖ Appendix III

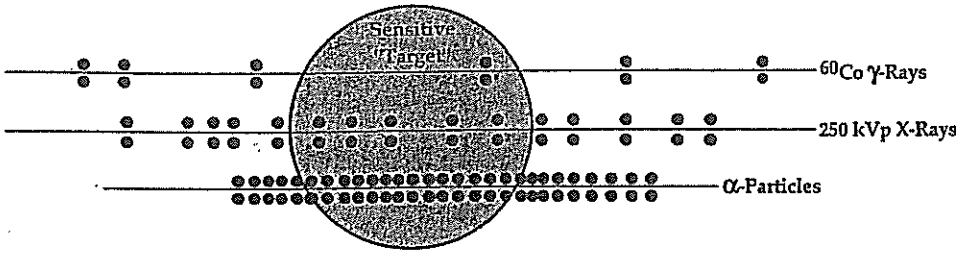

FIGURE 1–16.
Variation in the density of ionizing events along an incident particle's track for radiations of differing linear energy transfer (LET). The more closely spaced the ionizing events, the more energy will be deposited in the target volume, and, to a point, the more biologically effective per unit dose the type of radiation will be.

Zeman EM (2000)

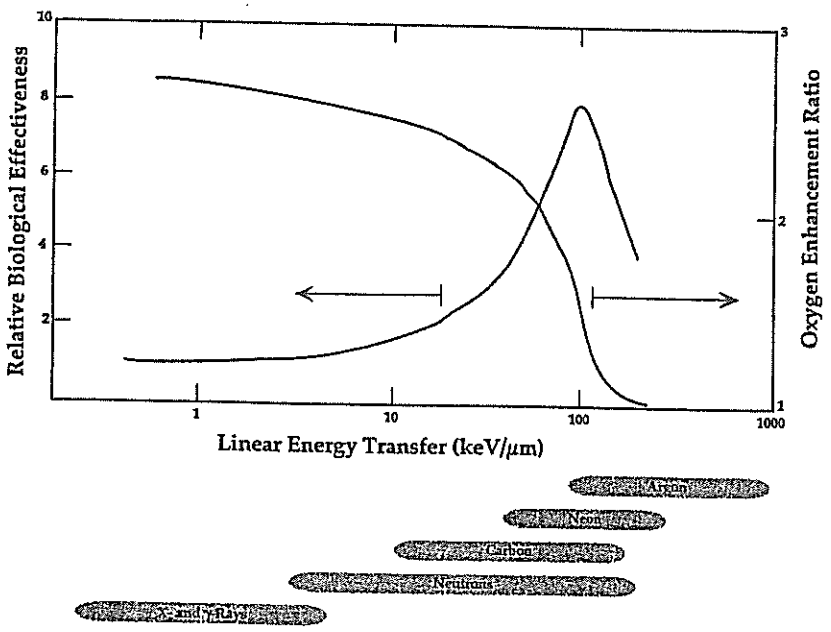

FIGURE 1–17.
Relative biologic effectiveness (RBE, left y-axis) as a function of linear energy transfer (LET) for a number of biologic endpoints, including production of chromosomal aberrations, cell killing, and tissue reactions. The RBE rises to a maximum corresponding to an LET of approximately 100 KeV/μm and then decreases as the LET continues to rise. Shown below the x-axis are the ranges of LET for photons, plus several different types of particulate radiations that have been used clinically. Also shown is the dependence of the oxygen enhancement ratio (right y-axis) on LET.

Zeman EM (2000)