

**Expert Witness Statement for Tribunal Case
Don Battersby and Anna Smith
vs.
Secretary of State for Defence**

Professor C. V. Howard. MB. ChB. PhD. FRCPath.

*10 Bratwell Road
Coleraine BT51 4LB
County Londonderry*

I have been asked by appellants in the First Tier Tribunal to provide my expert opinion on three issues of relevance to their case. These are:

1. The issue of whether Chronic Lymphocytic Leukemia (CLL) is caused by radiation exposure
2. The question of the adequacy of current radiation protection models as applied to the genotoxicity of the element Uranium. Specifically, the binding of Uranium to DNA and the enhancement of natural background radiation exposure by Uranium bound to DNA, and also enhanced internal exposures from Uranium nanoparticles in the human body through photoelectric effects.
3. The evidence of genotoxic exposures of the veterans as shown by excess levels of congenital illness in their offspring.

1. Background

I qualified in medicine in 1970. I am a toxico-pathologist specialising in the problems associated with the action of toxic substances on health. I was until recently Professor of Bioimaging at the University of Ulster and am presently Emeritus Professor in the same University. I have published over 130 peer reviewed papers and a number of book chapters concerning the effects of environmental pollutants on health, particularly during the developmental period. My CV is attached.

I am a Fellow of the Royal College of Pathologists, Past President of the Royal Microscopical Society, Member of the British Society of Toxico-Pathologists, Past President of the International Society of Doctors for the Environment and Member of the European Teratology Society. I served for 6 years as a toxicologist on the UK Government DEFRA Advisory Committee on Pesticides

Recently I was engaged as an expert by WHO Europe as the lead author on a published Background Document, of 50 pages, addressing Nanotechnology and Health (<http://www.euro.who.int/en/health-topics/environment-and-health/health-impact-assessment/publications/2013/nanotechnology-and-human-health-scientific-evidence-and-risk-governance.-report-of-the-who-expert-meeting-1011-december-2012,-bonn,-germany>).

I am familiar with the pathology of leukaemias and have published in the field [1, 2, 3]. Additionally I have published a number of papers and chapters on cancer and

environmental influences and have edited a book on the topic [4, 5, 6]. I have also addressed the epidemiological topic of the average of onset of a variety of cancers in the UK population [7]. I have contributed to the development of techniques for the sensitive detection of DNA damage [8,9]. Most recently I was invited to contribute a chapter on 'Cancer and Environmental Influences' which is published in the Springer Encyclopedia of Bioinformatics [10].

As part of my research at the University of Ulster into the effects of nanoparticles I have been interested in the issue of photoelectron amplification of external photon radiation (gamma radiation, X-rays) by particles of elements high atomic number and supervised a PhD student who investigated this effect through experimental work with gold nanoparticles and by computer modelling [11, 12]. This issue is of relevance to the health effects of Uranium nanoparticles such as those created by the explosion of Atomic and Hydrogen Bombs.

References to background

[1] Ball L.M., Hinchliffe S.A., Howard C.V., Jiang Y. & van Velzen D. (1993). 'Automated image analysis of silver stainable nucleolar organising regions in childhood acute lymphoblastic leukaemia.'. *Cancer Therapy and Control* **4** Suppl.4: 331-337.

[2] Ball L.M., Pope J., Eccles P., Howard C.V., & van Velzen D. (1994). 'PCNA/Ki-7 dissociation in childhood lymphoblastic leukaemia.' *Cell Biology International*, **18**: 869-874.

[3] Ball L.M., Hinchliffe S.A., Bataringaya J., Howard C.V., England K.E. & van Velzen D. (1994). 'Relationship between MDR- gene expression and Ag-NOR pattern in childhood lymphoblastic leukaemia.'. *Cancer Therapy and Control*, **4**: 3-9.

[4] Nicolopolou-Stamati P, Hens L, Howard C V and Van Larebeke N (Author/Editors). *Cancer as an Environmental Disease*. (Kluwer Academic Publishers, Dordrecht, The Netherlands, 2004, ISBN 1-4020-2019-8) 236

[5] Howard C.V. and Newby J.A. 'Could the increase in cancer incidence be related to recent environmental changes?'. In *Cancer as an Environmental Disease*, auth/eds Nicolopolou-Stamati P, Hens L, Howard C V and Van Larebeke N (Kluwer Academic Publishers, Dordrecht, The Netherlands, 2004, ISBN 1-4020-2019-8) 39-56.

[6] Newby J & Howard C.V. (2005). Environmental influences in cancer aetiology. *J. Nutr. And Envir. Med.* **15**: 56-114.

[7] Newby JA, Busby CC, Howard CV and Platt MJ (2007). The cancer incidence temporality index: An index to show the temporal changes in the age of onset of overall and specific cancer (England and Wales, 1971-1999). *Biomedicine and Pharmacotherapy*. **61**: 623-630

[8] McArt DG; Wasson GR McKerr G; Saetzler K; Reed M; Howard CV (2009) Systematic random sampling of the comet assay. *Mutagenesis*; **24**: 373-378.

[9] McArt DG, McKerr G, Saetzler K, Howard CV, Downes CS, Wasson GR (2010). Comet assay sensitivity in assessing DNA damage and repair in different cell cycle stages. *Mutagenesis*; **25**: 299-303.

[10] Howard CV & Staats G (2013). Cancer and Environmental Influences. In: W. Dubitzky, O. Wolkenhauer, K. Cho & H. Yokota (eds.), *Encyclopedia of Systems Biology*, DOI 10.1007/978-1-4419-9863-7, Springer Science+Business Media, LLC

[11] Elsaessar A, Busby C, McKerr G and Howard CV. Nanoparticles and Radiation. Poster Presentation Madrid 2009. Supplied.

[12] Elsaessar Andreas. Biophysical interaction of nanoparticles and radiation. PhD thesis University of Ulster, 2011.

2. Is ionizing radiation a cause of Chronic Lymphocytic Leukemia?

One of the veterans, Mr Don Battersby developed CLL and made a Pensions claim which was turned down. The reason was that the Ministry of Defence argued that CLL is not a radiogenic disease. Following an appeal, this question has to be revisited. The current balance of evidence is that CLL is a radiogenic disease. This has now been accepted by the US Federal Government for employee compensation cases [1] and a very recent study of Chernobyl liquidators published in 2013 [2], by a team of eminent researchers, has concluded that CLL is a radiogenic disease. This follows earlier studies of Chernobyl liquidators [3], Czech Uranium miners [4] and a published review [5].

The previous First Tier hearing made its decision based on a report by Prof Catovsky which I have seen. The argument [6a, 6b] advanced by Prof. Catovsky is difficult to follow. On the one hand, he believes that CLL may be a response to agents which cause selective clonal expansion:

“CLL a response to a limited set of antigens that promote cell division and clonal evolution”

which is a process that may result from exposure to internal radionuclides and radioactive particles in the lymphatic system, yet he seems to deny that CLL could be radiogenic. His emphasis of a genetic component is clearly important. However the genetic component of many cancers, including leukemias, has been addressed in a very large twinning study and has been shown to account for, at most, 25% of cases [7] leaving at least 75% of cancers caused by environmental influences.

Determining the aetiology of any cancer is primarily an epidemiological and scientific research question and not a clinical one. Therefore the fact that Prof Catovsky is, like me, a medically qualified doctor does not, in my opinion, confer on us any special insights. An epidemiologist or scientist working in the field of cancer causation could have equally valid opinions, based on the current scientific evidence. Prof Catovsky's belief that there are two types of CLL, an early onset one which may be radiogenic and a late onset one which is not, does not appear to be shared by anyone writing in the peer review literature and was not made any part of the Federal US government's decision, nor was such a possibility mentioned in any of the peer-reviewed papers that

I understand Dr Busby referred to in his evidence before the lower Tier. It is strange, therefore, that Prof Catovsky did not refer to the key Zablotska paper [2] nor to the US government decision [1] in his final report [6b].

The onset lag of many cancers and leukaemias would appear to be a function of the exposure dose and thus the rate of expansion of the cancer cell clone. High dose tends to lead to a faster onset than a chronic low dose exposure. However the clinical disease and its pathology remains essentially the same.

References to Section 2

- [1] Federal Register /Vol. 77, No. 24 /Monday, February 6, 2012 /Rules and Regulations; DEPARTMENT OF HEALTH AND HUMAN SERVICES
42 CFR Part 81 [Docket Number NIOSH-209]RIN 0920-AA39
Guidelines for Determining Probability of Causation Under the Energy
Employees Occupational Illness Compensation Program Act of 2000;
Revision of Guidelines on Non-Radiogenic Cancers
- [2] Zablotska LB, Bazyka D, Lubin JH et al (2013) Radiation and the risk of Chronic Lymphocytic Leukemia among Chernobyl cleanup workers. *Environmental Health Perspectives* 121(1) 59-65
- [3] Abramenko I, Bilous N, Chumak A et al. (2012) DNA repair polymorphisms in B-cell Chronic Lymphatic leukemia in sufferers of the Chernobyl Nuclear Power Plant accident. *J.Radiol.Res.* 53 497-503
- [4] Rericha V, Kulich M, Rericha R et al (2006) Incidence of leukemia, lymphoma and multiple myeloma in Czech Uranium miners. *Environmental Health Perspectives.* 114 (6) 818-822
- [5] Richardson DB, Wing S, Schroeder J et al (2005) Ionizing radiation and chronic lymphocytic leukemia. A Review. *Environmental Health Perspectives.* 113 (1) 1-5
- [6a] Letter by Prof Catovsky 16 Feb 2011 on Mr Battersby (D25)
- [6b] Supplementary report by Prof Catovsky prepared on the instructions of the Treasury Solicitor's Department Jan 2013 (catovsky070113D3T25A.pdf)
- [7] Lichtenstein P, Holm NV, Versakalo PK et al (2000) Environmental and heritable factors in the causation of cancer. *New Engl J Med.* 343(2) 78-85

3. Anomalous radiation effects from Uranium particles and internal Uranium exposures.

3.1 Both Atomic (fission) bombs and Thermonuclear (fusion) bombs rely on Uranium as fissile material and also as various tampers and neutron reflectors. Thus the bombs all contain large amounts of U-238 by mass. The intense heat generated by the detonations will cause the vapourisation of the Uranium and lead to its condensation as nanoparticles and micron diameter particles. This is not my particular area of expertise and I will move to the question of the genotoxicity and other internal effects

of exposures to Uranium both as molecular species and as particles. First, there is significant evidence that Uranium genotoxicity is not safely modeled by the current risk model [1].

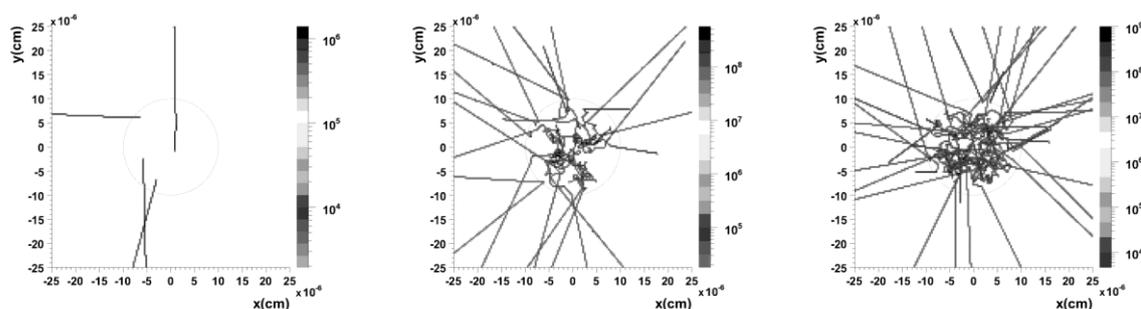
3.2 My own research has focused on photoelectron amplification of background and other photon radiation by elements of high atomic number. What follows is from a presentation of the mathematical modelling of photoelectron amplification by particles of Gold and Uranium carried out by my PhD student Andreas Elsaessar and presented at a conference on nanoparticles in Madrid and elsewhere [2]. What the results demonstrated is that there is a significant predicted photoelectron amplification effect. This would result in a high ionization density near the surface of the Uranium particle and therefore the “dose” to any material close to the particle would be high as a result of the high degree of absorption of external photon radiation. Since the current radiation risk model, that of the ICRP effectively models living tissue as water, this effect is not incorporated into current radiation protection calculations.

3.3 Electromagnetic radiation and matter interact predominantly by three different mechanisms: Compton scattering, the photoelectric effect and pair production. Compton scattering basically describes the loss of incident effect, electrons absorb the incident photon energy and are either emitted or lose energy in secondary processes. For energies below 1MeV, the photoelectric effect is the predominant one. The cross section for the photo-electric effect is proportional to the atomic number Z to the power 5 and roughly proportional to the incident photon energy to the power $-7/2$. between 0.5 and 5 nanometers.

Most of the photoelectrons produced in an absorbing material lose their energy through electron-electron scattering and Bremsstrahlung. Therefore, the escape depth of photoelectrons generated within solids is usually secondary electrons proportional to their mass. Hence, irradiated particles with diameters in the range of a few nanometers will emit most of the generated photoelectrons without internal reabsorption. Therefore, nanoparticles are likely to emit the largest quantity of photoelectrons in proportion to their mass. Furthermore, secondary electron emission of high Z materials could provide a partial explanation of the toxicity of various heavy metals. This is particularly an issue for the element Uranium which has the highest atomic number ($Z=92$) of any naturally occurring element. Due to their size, nanoparticles can penetrate into the human body and some are able to reach the cell nucleus. This may be crucial in explaining the toxicity of incorporated nanoparticles of materials with a high atomic number Z [3].

3.4 In order to further investigate this, the interaction of incidence photon energy with 50nm particles of water, Gold ($Z=79$) and Uranium ($Z=92$) were examined using the FLUKA mathematical model, developed by CERN. The results shown in Fig 1 below indicate the effect. The tracks shown are photoelectron tracks emerging from the computer generated particle. Note that the water particle on the left represents 10 times the number of incident photons employed for the Gold and Uranium particles.

Fig 1 Photoelectron tracks emerging from (left to right) 10 nm particles of water ($Z=7.5$), Gold (Au; $Z=79$) and Uranium (U; $Z=92$) after irradiation with 100keV photons. Monte Carlo (FLUKA code) analysis. Track numbers are in proportion to the 4th power Z law (tracks are shown as projections on a flat plane). Note that the model uses 1000 incident photons for Au and U but 10,000 for water [9]



3.5 I conclude that this photoelectron amplification effect for high atomic number elements like Uranium is well accepted by physicists and is real. There is unequivocal evidence also that Uranium has strong chemical affinity for DNA [4]. The ICRP risk model does not incorporate either of these facts into its calculations of the effects of exposure to Uranium and that the existence of such effects could plausibly explain the many anomalous genotoxic effects found in those exposed to Uranium [5,6,7] These effects are also shown in studies of Test Veterans [8, 9] and those exposed to Depleted Uranium from weapons [10,11,12].

3.6 Finally it seems that the European radiation research organisation MELODI have recently realised that Uranium represents an anomalous hazard which is not safely modelled by the ICRPO approach and has committed a large amount of money to an investigation of the issue though a new project CURE: Concerted Uranium Research Europe [13].

In the report launching this development in March 2015 the authors write [13]:
... a large scale integrated collaborative project will be proposed to improve the characterization of the biological and health effects associated with uranium internal contamination in Europe. In the future, it might be envisaged to extend collaborations with other countries outside the European Union, to apply the proposed approach to other internal emitters and other exposure situations of internal contamination, and to open the reflections to other disciplines interested in the effects of internal contaminations by radionuclides.

This commitment might of itself raise doubt regarding the employment of the ICRP model to argue in the Tribunal that “doses” are too low to explain the quite clear genotoxic effects found in the veterans and their offspring.

References for Section 3

- [1] Busby C. Uranium Epidemiology. *JJ Epidemiology Prevent.* 2015 1(2): 009
- [2] Elsaessar A, Busby C, McKerr G and Howard CV. Nanoparticles and Radiation. Poster Presentation 2009. Supplied.
- [3] Busby Chris and Schnug Ewald (2008) Advanced biochemical and biophysical aspects of uranium contamination. In: (Eds) De Kok, L.J. and Schnug, E. *Loads and Fate of Fertilizer Derived Uranium*. Backhuys Publishers, Leiden, The Netherlands, ISBN/EAN 978-90-5782-193-6.
- [4] Huxley H E, Zubay G. Preferential staining of nucleic acid containing structures for electron microscopy. *Biophys. Biochem. Cytol*, 1961 11: 273-275
- [5] Zaire, R., Notter, M. & Thiel, E. Unexpected rates of chromosome instabilities and alteration of hormone levels in Namibian uranium miners. *Radiat. Res.* 1997, 147: 579-584
- [6] Guseva Canu I, Jacob S Cardis E, Wild P Cae'r –Lorho S, Auriol B, Garsi JP, Tirmarche M, Laurier D. Uranium carcinogenicity in humans might depend on the physical and chemical nature of uranium and its isotopic composition: results from pilot epidemiological study of French nuclear workers. *Cancer Causes Control* 2011, 22(11):1563-73.
- [7] Mc Geoghegan D, Binks K. The mortality and cancer morbidity experience of workers at the Springfields uranium production facility 1946-95 *J. Rad. Prot.* 2000, 322: 123-134
- [8] Rabbitt Roff S. Mortality and Morbidity of members of the British Nuclear Test Veterans' Association and the New Zealand Test Veterans Association and their Families. *Medicine, Conflict and Survival* 1999, 15 Suppl. No 1
- [9] Busby C and de Messieres M. Miscarriages and congenital conditions in offspring of the British Nuclear Atmospheric test Program. *Epidemiology (sunnyvale)* 2014, 4:4 <http://dx.doi.org/10.4172/2161-1165.1000172>
- [10] Araneta MR, Schlangen KM, Edmonds LD, Destiche DA, Merx RD, Hobbs CA, Flood TJ, Harris JA, Krishnamurti D, Gray GC. Prevalence of birth defects among infants of Gulf War veterans in Arkansas, Arizona, California, Georgia, Hawaii, and Iowa, 1989-1993. *Birth Defects Res* 2003, 67(Part A):246-260
- [11] Kang H, Magee C, Mahan C, Lee K, Murphy F, Jackson L, Matanoski G: Pregnancy outcomes among US Gulf war veterans: a population-based survey of 30,000 veterans. *Ann Epidemiol* 2001, 11:504-511
- [12] Alaani S., Al-Fallouji M., Busby C., Hamdan, M. Pilot study of congenital anomaly rates at birth in Fallujah, Iraq, 2010. *Journal of the Islamic Medical Association of North America*, North America, 44, Aug. 2012. Available at: <http://jima.imana.org/article/view/10463>

[13] DoReMi. CURE: Concerted Uranium Research Report D5-17. Report on an integrated (biology-dosimetry-epidemiology) research project on occupational Uranium exposure. 2nd March 2015.

[19] DoReMi. CURE: Concerted Uranium Research Report D5-17. Report on an integrated (biology-dosimetry-epidemiology) research project on occupational Uranium exposure. 2nd March 2015.

4 Genetic effects in offspring of Test Veterans

4.1 I have been referred to two published reports of studies of the offspring of atomic test veterans. These are the 1998 study by Rabbitt Roff who carried out a questionnaire study of members of the British Nuclear Test Veterans Association (BNTVA) and the later 2007 case control study by Busby and de Messieres specifically of miscarriages in BNTVA spouses and congenital effects in their children and grandchildren [1, 2].

Taken together these provide persuasive evidence that the test veterans as a group shared some prior exposure to genotoxic stress which caused transmissible genetic or genomic damage. Their exposures to radioactivity at the test sites can be the only plausible explanation for such a group effect. Since it seems that the absorbed doses, as defined by the ICRP, received by the veterans were below natural background, the most probable explanation for the miscarriages, and the congenital conditions in their children and grandchildren is that the internal exposures they shared caused the effect and that the use of the ICRP concept of “absorbed dose” is unsafe for evaluating internal radiation exposures. This is the position of the Lesvos Declaration of the European Committee on Radiation Risk with which I agree. The matter of internal radiation exposure and its effects has been developed in a 2013 review by Busby [3]. One of the veterans in this case, Mr Battersby, very probably suffered from this effect as his wife gave birth to twins which were badly deformed and did not survive.

References Section 4

Rabbitt Roff S. Mortality and Morbidity of members of the British Nuclear Test Veterans' Association and the New Zealand Test Veterans' Association and their Families. *Medicine, Conflict and Survival* 1999; 15 Suppl. No 1

Busby C and de Messieres M. Miscarriages and congenital conditions in offspring of the British Nuclear Atmospheric Test Program. *Epidemiology (Sunnyvale)* 2014, 4:4 <http://dx.doi.org/10.4172/2161-1165.1000172>

Busby Christopher Aspects of DNA Damage from Internal Radionuclides, *New Research Directions in DNA Repair*, Prof. Clark Chen (Ed.) ISBN: 978-953-51-1114-6, InTech, DOI: 10.5772/53942, 2013. Available from:

<http://www.intechopen.com/books/new-research-directions-in-dna-repair/aspects-of-dna-damage-from-internal-radionuclides>

Witness Statement

I understand my duty to the court and the information in this report is to the best of my knowledge truthful and accurate. I do not know any of the clients in this case personally and have had no dealings with them prior to the referral of this case from the Appellants' representatives. I have received no fee for producing this opinion. I reserve the right to alter my opinion in the light of further evidence that may become available in the future.

Signed

A handwritten signature in blue ink, appearing to read 'P. Howard', with a horizontal line underneath the name.

Professor Charles Vyvyan Howard
MB. ChB. PhD. FRCPath.