COINCIDENCE OF NEEDS IN RADIOLOGICAL AND TOXICOLOGICAL PROTECTION

R.V. Osborne

Manager, Environmental Research Branch
Chalk River Nuclear Laboratories
Chalk River, Ontario

The theme of my presentation is that research needs for radiological protection and the research programs that have evolved to meet these needs parallel closely those in the chemical toxicological field. I am going to comment on the similarity of the needs - at least as perceived from the radiological side, reflect on the framework for radiologically-related research and outline the research programs and facilities at CRNL that have developed within that framework. In AECL with its broadened mandate, we have the opportunity to turn more to research relevant to protection against chemical toxic agents. We see this workshop as a very valuable input into ensuring that we exploit our resources effectively and usefully.

In the introductory notes on the program we included what is, in effect, a statement of faith; namely, that quantitative assessment of risks from toxic agents, together with economic and political considerations, is a sound basis for making decisions to safeguard health and, at the same time, promote needed technologies.

Some argue that attempts at such assessments are almost futile; estimates are so uncertain that they tend to confuse and confound, so that fewer and fewer people can understand and be involved in decisions made to protect health. The undigestable size of environmental impact statements allows one to have some sympathy with this view. Rather than despair, we should recognize that there is a need for synthesis of information on impact. This certainly applies in radiological protection; I believe it does in toxicological protection.

It may be that we can never achieve a consensus on the relative significance of risks to health across all activities and agents. Quantitative comparisons of the risks from low levels of radiation, cigarette smoking, mountain climbing, driving cars or just living at home are so confounded by social and perceptual issues that they are generally not persuasive. Nevertheless, within a single field - risks from toxic agents for example - it seems worthwhile to strive for quantification, to have internal consistency. A desirable end is that an effluent limit placed on chemical X from industry A is logically consistent with the concentration limit placed on chemical Y in waterbody B, and on the limiting concentration of chemical Z in air at workplace C.

Obviously, it is difficult to do this - and I expect some of the speakers during the workshop will note these difficulties. But without quantification of risk, it is difficult to get any coherence into regulation of safety - or even to justify non-zero limits on effluents for example. This is particularly so for genotoxic agents for which it seems reasonable to assume that any increment in level carries a concomitant

increment in probability of deleterious effect. Since "zero" means "not detectable" such limits ratchet down as detection sensitivities improve.

For carcinogenic and genetic effects there are similarities in our concerns with ionizing radiation and chemical toxic agents in relation to the natural environment. Our concern is with anthropogenic sources which add to a natural background level. There are novel chemicals, just as there are novel radioactive isotopes but when regarded in the light of fundamental genotoxic mechanisms and repair processes, the impact of the "new" agents may be most appropriately regarded as incremental insults on a background of naturally-occurring damage.

In radiological protection we are evolving an internally-consistent framework for protection that can be linked, now, to estimates of probabilities of deleterious health effects.

The principles followed are quite general. One is to ensure that individual members of the population are not subjected to unacceptable harm or probability of harm. Specifically, we want to ensure that severe effects that have a threshold (so-called nonstochastic effects) are avoided completely and that the probability of deleterious effects that do not have a threshold (stochastic effects) is below a lower limit of unacceptability for risks to the individual. A second is to ensure that any potential detrimental health effects in a population from any given toxic agent are reduced to some low level. A third is to ensure that the potential detrimental effects are justified by the benefits of whatever practice was giving rise to the effects.

The phrase "potential health effects" is used deliberately. Based on internationally-accepted estimates of risk per unit dose, the probability of any detrimental health effects resulting from acceptable limits on radiation exposure is so low that these potential effects cannot be detected by direct epidemiological observation of exposed populations of workers, let alone of the general population. It is a reasonable but unprovable assumption that even very low doses of radiation produce a very low risk of producing some effect, even when we cannot observe these effects. The same concept is probably true for certain chemical agents.

To limit harm in an individual from a variety of toxic agents necessitates devising some way of comparing different effects from different agents. For radiological protection the combining is done at the tissue level through the surrogate measurable quantity "energy absorbed" (called dose). A limit on dose can therefore be used as a way of limiting risk from all radiations and radionuclides in organs and tissues provided that we can quantify:

(a) the shape of the dose-effect relationships,

(b) variations in the sensitivities of different tissues and organs to a given dose, and •

(c) variations in doses of different radiations to produce the same effect.

For dose-effect relationships there are some data to support quantitative estimates of carcinogenic risk and thresholds for other health effects from medical experience, from the consequences of the nuclear explosions in Japan and from the underground mining of radioactive materials. Similarly there are some human data for chemicals - combustion products for example. For genetic effects from radiation we have to rely entirely on animal data; no significant genetic effects in human populations have been detected in the children of persons exposed to high radiation doses. In all cases we have to use data from animal experiments to supplement any human data available. Meeting these needs has resulted in research at the molecular, cellular, tissue and whole animal level at Chalk River as elsewhere.

Secondary limits - on concentrations in air, water, food, or effluents - should be consistent with the primary limit on harm. To ensure this in the case of radioactive materials we need quantitative relationships between:

(a) the dose in tissues and the amounts of material ingested, inhaled, or absorbed through the skin, and

(b) the concentrations to which people may be exposed as a result of release of given amounts of material from any particular source.

Meeting these needs has stimulated research studies on the biokinetics and metabolism of radioisotopes in many different chemical forms, including radiopharmacenticals, and on the dispersion and fate of such materials in the environment.

Ensuring that detrimental effects in a population from any given toxic agent are reduced to some reasonable level has come to be known (in radiological protection) by the acronym ALARA meaning "as low as reasonably achievable, economic and social factors being taken into account". Implementation imposes further needs on research. Assessment of total impact entails environmental predictions that extend spatially and temporally. How far into the future, how distant, and below what small increment in individual risk can overall impact be neglected are questions that are not easily answered. The need here is to be especially cautious in applying predictive models to scales (time and distance) way beyond their validity. Accounting for the improbability of exposures to toxic agents from particular sources is another need in any coherent protection system but one which, again, is not easily accomplished. It is worth noting that the differences in approach to protection against non-degradable toxic chemicals in contrast to degradable toxic chemicals are similar to those between long-lived and short-lived radionuclides.

Because of the importance of "ALARA" there is a continuing need to explore ways of improving protection economically. Therefore to complement the research on processes and the development of assessment models, there

is a need to develop instruments, protective clothing, methods of transportation and analytical methods.

For those of you in the chemical toxicological field, I expect the general needs that I have outlined above are familiar. Issues and judgements needed sound similar. An important aspect of the set of needs is that they are a set. The importance of any one can only be determined in the context of the overall set. For example in the radiological field the highly toxic effects of a particular radionuclide if inhaled are unimportant if conditions are such that that particular radionuclide is in a form that it is virtually impossible for it to become airborne.

The research programs here at Chalk River have evolved to meet these general needs in radiological protection. We have had the advantage of being multidisciplined both within the groups here and through the collaborations with staff from various universities and agencies.

We are also able to take advantage of the expertise and facilities of the more than 300 scientists and engineers throughout the laboratories here at Chalk River (Figure 1). A brief look at some of the activities and facilities will illustrate the point. The research in health sciences is all related to assessing the risk to health; of being able to make the link quantitatively between source and effect through all the steps as shown in Figure 2. There are three aspects to the work, aspects that I believe are common to chemical toxicology and radiological toxicology.

The first is the common need for research to understand the processes that affect the dispersion in the environment and determine human exposures, the metabolic and biokinetic processes that determine what happens to contaminants after exposure, and the cellular and molecular processes that determine the biological consequences. The second is the research and development needed to allow contaminants to be measured in the environment, including the workplace environment, to allow exposures to be measured, and to allow the distribution and fate of contaminants in humans to be measured. The third is the link that needs to be made between the first two; the knowledge of processes and the results of measurements. They need to be complementary; the results of measurements at any stage need to be usable in predictive models built on the knowledge of processes; the predictive models have to be designed to be used with measurable quantities. I will show how the program here fits into this framework, starting with the biological research.

A general model for biological effects is shown in Figure 3. High doses of radiation result in acute lethal effects but the greater concern is with genotoxic effects where the processes have much in common with those associated with chemical genotoxicants. Much of the work here has been concerned with repair processes and has involved experiments with microorganisms, animals, and human cell cultures. In passing, I note that studies with microorganisms have been aided by the development of a colony counter (Figure 4), an example of where expertise from elsewhere on site has been enlisted into the health sciences area.

Some of the work on mechanisms of initiation and promotion of cancers has involved agents other than radiation, necessitating our development of carcinogen handling facilities (Figure 5). Later in the meeting Dr. Norman Gentner will be describing his group's studies of the variation in individual sensitivities to carcinogens, work that is being carried out with human cell cultures. It has been inevitable that much of our understanding of the relation between exposure and effect has come from studies with animals although it is realised that interspecies extrapolation can only be tentative with radiation just as with chemical agents. Causation of long-term effects in mammals is particularly difficult to study. The experiments need facilities for handling many animals for a long time. Examples of studies that we are currently completing are of the acceleration of mammary tumours by different radiation types (which needed individual metabolic cages such as shown in Figure 6) and of the induction of myeloid leukaemia in mice. The latter, which is involving 5300 mice for 3-4 years, is particularly interesting since there have been very few cancer induction studies with tritium in mammals.

Like many organizations involved with particular toxic agents we have looked at the health of our own work force. Specifically we have looked to see if there is any evidence for an effect from occupational radiation exposures on the causes of death. On the basis of current risk estimates we would not
expect to observe any effect and this appears to be the case. Figure 7 shows some of the results from this study.

I am turning now to studies of the relation between exposure to a toxic agent and the "dose" that is actually delivered to a particular organ, tissue or cell. We have been involved for at least three decades in developing biokinetic and metabolic models for predicting the fate of inhaled, ingested and percutaneously-absorbed materials, and for estimating the contents in particular body tissues from direct measurements (which are possible with some radionuclides) and from measurements of concentrations in excreta. An example of such a model currently being revised by us is shown in Figure 8.

The experimental work to support these modelling activities involves tracer studies with animals and humans. One recent study (with hairless rats) has been of the percutaneous uptake from surfaces contaminated with tritiated hydrogen an occupational concern in any future fusion industry. The autoradiograph in Figure 9 shows the distribution of organically-bound tritium within the skin layers some days after exposure. The model developed from this study relates the observed excretion of tritium in urine to the amount and variation in time of the organically-bound tritium.

Complementing the studies of the processes that lead to doses from exposures is the development of ways and means of measuring and of reducing exposures. Protective clothing to reduce the hazard from airborne contaminants has been tested here: indeed one of the first studies I carried out at Chalk River Nuclear Laboratories was of the protection

afforded by protective suits when worn by different individuals. Figure 10 shows suits used today.

For radionuclides and radiation there are obviously specific detectors but the general principles of sampling and monitoring in the workplace and in the environment are of general application. The emphasis in the developments in the health sciences areas at Chalk River Nuclear Laboratories has been in designing for stringent workplace applications and rugged environmental conditions. One of many devices is shown in Figure 11.

I turn now to the environmental part of the program. We have a 4000 hectare protected area around the laboratories (Figure 12) that for over three decades has provided the setting for detailed hydrological, hydrogeological and meteorological observations and many contaminant tracer experiments in air, water, and the sub-surface. The scope of the experimental work is best described in the framework of a simple compartment model of the biosphere as shown in Figure 13.

Our interest is in movement of contaminants within the compartments, and between the compartments. The models needed connect a source of contamination in any of the compartments to the exposure that would result to an individual in any of the compartments. Developing and refining such models, and building confidence in their validity, depends on understanding the processes that occur. This is the drive behind our environmental program. I will mention a few examples of current activities.

For the atmospheric compartment we have recently completed a study of the dynamics of the rise and dispersion of a heated contaminant plume. We have a cleared area, 300 metres in diameter (shown in Figure 14) for this kind of local dispersion experiment. The same area has been the site this summer of a tracer tritiated hydrogen dispersion experiment to investigate the interaction between the dispersing plume and plants and soil. The interest covers the micrometeorology, diffusion of gases in soils and the chemical and microbiological interactions very much a multidisciplined endeavour. This particular experiment brought scientists from Europe, the USA and Japan to participate. Some of the setup is shown in Figure 15.

The Perch Lake basin (shown in Figure 16) also within our experimental area has been the site of many of the hydrological and hydrogeological investigations. Currently, in collaboration with scientists from the Universities of Toronto and Trent, we are studying in part of this basin the infiltration of precipitation through forested terrain, trying to improve our understanding of the changes in chemical fluxes through the forest canopy, litter layer and unsaturated zone, and the generation of stream flows, with a view ultimately to being able to understand the effect of acidity changes in rain.

Also in the Perch Lake basin we have been able to exploit the distributions of small amounts of radioactive contaminants from the waste management areas to study the advection, dispersive and sorptive properties of the soils and sands. In some instances the importance of microorganisms

in facilitating transport has been very evident. Figure 17 shows the vertical profile in a plume of cobalt-60 that has developed in the aquifer beneath one of the waste management areas. Such detailed mapping enables us to estimate not only the fate of the particular contaminants in the areas observed but, by supplementing the observations with experimental work in those areas, allows us to develop more generally-applicable models. The field columns shown in Figure 18 are one means of varying geochemical parameters in a controlled manner in studying the kinetics of sorption of added radiotracers for example.

Radiotracers are used in many sites to examine physical, chemical and microbiological processes. Tracer studies at one particular site have already allowed us to develop and test detailed advection/dispersion models for movement in the sub-surface over 40 metres (see Figure 19). We are now preparing to extend the study to 200 metres and intend to include chemical as well as radioactive contaminants. These experiments provide an example of the application of computer technology to automating data collection in the field. The distribution of radionuclides vertically was determined by computer-controlled scanning (see Figure 20).

Another compartment is that of surface water. Our interest here is in being able to know enough about the interactions between the sediments and material in the water so that the long-term fate of contaminants can be predicted. We have been able to observe the behaviour of radionuclides in several of our lakes under natural and controlled conditions and, most recently, we have been using radiotracers for toxicologically-important metals.

In summary, I have illustrated the broad range of facilities and research disciplines at Chalk River that we have developed to support radiological protection. They span research on the processes underlying environmental transport from source to exposure, underlying biokinetics, and underlying biological effects. There are many common areas between our activities and those involved with protection from chemical toxic agents. The multidisciplinary nature of the groups have proved important, as has the possibility for a scientist to be involved in a broad range of problems - ranging from very basic to very applied research. All these research activities are finally synthesized in the assessment of risk from exposure to radiation. Some of us have also been involved in drafting documents related to regulation; another feedback to helping to set research priorities.

Now, with the opportunity to increase our efforts in research relevant to chemical toxicology, we want to maximize our effectiveness. We are looking for an increased involvement with university colleagues, we are looking for opportunities to work with other government agencies and we are hoping to contribute to resolving some of the long-term concerns of industry.

It was with these thoughts that we posed the questions for the workshop. Where are the gaps in our current knowledge? What research is needed?

Figure 1: Chalk River Nuclear Laboratories on the bank of the Ottawa River, about 200 km north-west of Ottawa.

Figure 2: The link from sources of a radioactive contaminant or radiation and the biological effects.

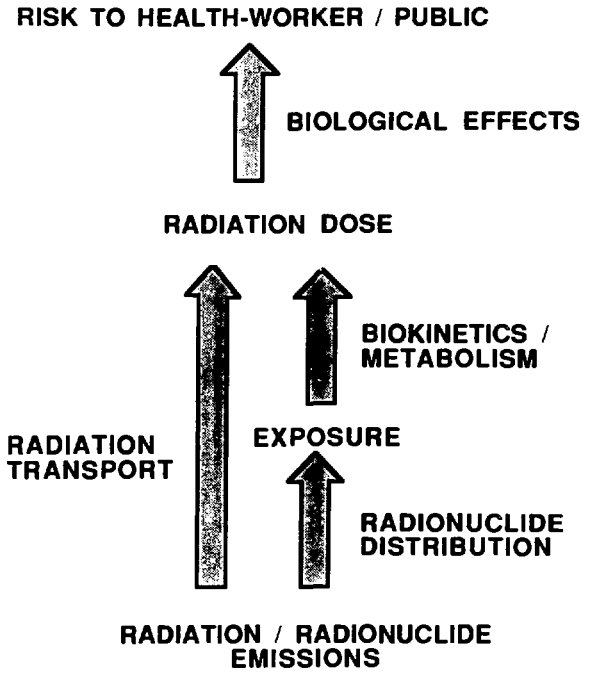

Figure 3: A model for the biological effects of radiation and other genotoxic agents.

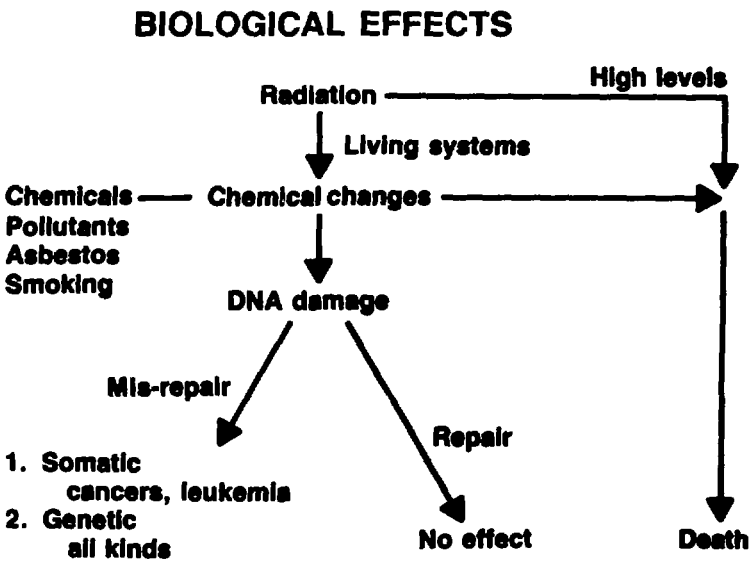

Figure 4: The colony counter developed at Chalk River Nuclear Laboratories. The device automatically counts and records the number of colonies grown on a culture medium. (Hall, D.S., Baker, J.C., Unrau, P. and Davis, R.S., Advances in Laboratory Automation Robotics: An Intelligent Colony Counter, pp. 591, Ed. by Janet R. Strimaitis and Gerald L. Hawk, Published by Zymark Corp., Hopkinton, Mass., 1986.)

Figure 5: Carcinogen handling facilities at Chalk River Nuclear Laboratories.

Figure 6: Metabolic cages have been used to study the excretion of tritiated water in rats and mice (Johnson, J.R., Myers, D.K., and Gragtmans, N.J., An Experiment Designed to Measure the RBE of Tritium for the Induction of Myeloid Leukaemia in Animals, AECL-9339, Radiation Protection Dosimetry, Vol. 16, No. 1-2, pp. 161-164 (1986); and Gragtmans, N.J., Myers, D.K., Johnson, J.R., Jones, A.R., and Johnson, L.D., Occurrence of Mammary Tumors in Rats after Exposure to Tritium Beta Rays and 200 kVp X Rays, Radiation Research 99, 636-650 (1984)) and to study the metabolism of inhaled uranium ore dusts and of other toxic agents. Other experiments in the Animal Facility have been concerned with interaction of different agents that influence the yeld of cancer (5 recent references are: 1. McGregor, J.F. (with revisions by Myers, D.K.), Enhancement of Skin Tumorigenesis by Cigarette Smoke Condensate Following ß-Irradiation in Rats, JNCI, Vol. 68, No. 4, April 1982.
2. Myers, D.K. and McGregor, J.F., Interaction of ß Radiation and 2-Anthramine for Induction of Skin Tumors in Rats, Radiation Research 90, 228-231 (1982).
3. Gragtmans, N.J. and McGregor, J.F., Effect of Hyperthermia on Epithelial Microneoplastic Cell Populations Induced by Irradiation of Rat Skin, JNCI, Vol. 70, No. 5, May 1983.
4. Mitchel, R.E.J., Morrison, D.P., Gragtmans, N.J. and Jevcak, J.J., Hyperthermia and phorbol ester tumor promotion in mouse skin, Carcinogenesis vol. 7, no. 9, pp. 1505-1510, 1986.
5. Mitchel, R.E.J., Morrison, D.P., and Gragtmans, N.J., Tumorigenesis and carcinogenesis in mouse skin treated with hyperthermia during stage I or stage II of tumor promotion, Carcinogenesis vol. 8, no. 12, pp. 1875-1879, 1987.

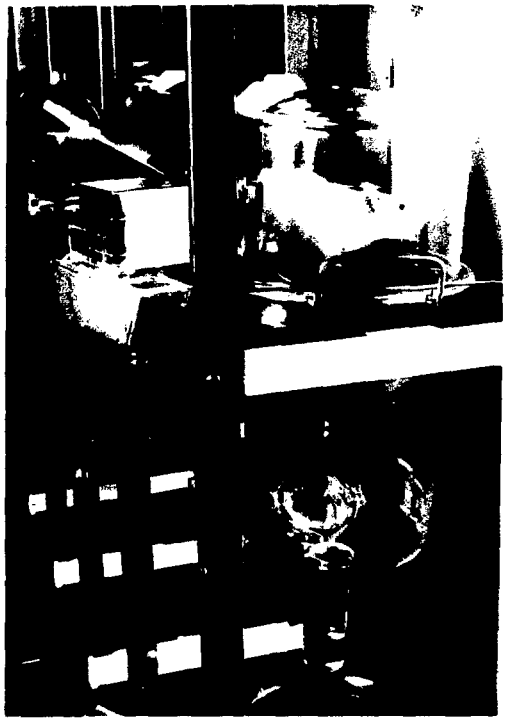

Figure 7: Causes of death in employees of Chalk River Nuclear Laboratories. (Werner, M.M. and Myers, D.K., Mortality among long-term Chalk River Employees, Atomic Energy of Canada Limited, Report AECL-9344, December 1986.)

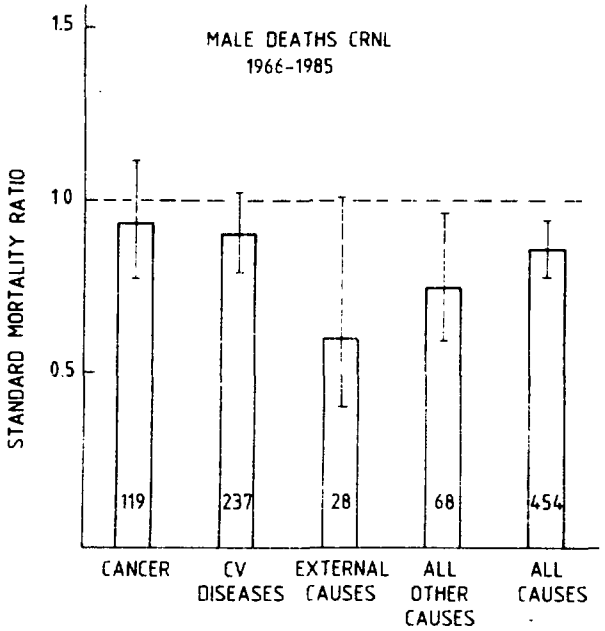

Figure 8: Model for the fate of inhaled materials. (Adapted from Johnson, J.R. and Meloncoff, S., A comparison of excretion and retention between the current ICRP lung model and a proposed new model, Proceedings of the 26th Hanford Life Sciences Symposium, Health Physics (in press).)

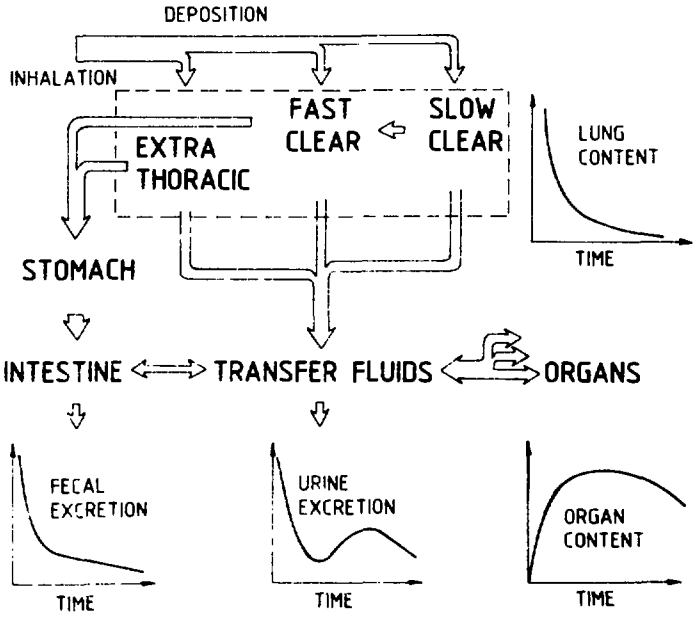

Figure 9: Distribution of organically-bound tritium in the skin of a hairless rat exposed to a metal surface contaminated with tritiated hydrogen. (Johnson, J.R., Lamonthe, E.S. and McElroy, R.G., Metabolism and dosimetry of tritium from tritium-contaminated surfaces, Proceedings of the 3rd Tritium Symposium, Tritium Technology in Fission, Fusion and Isotopic Applications, 1988 May, Toronto, Fusion Technology (to be published).)

Figure 10: Protective clothing for work in contaminated atmospheres.

Figure 11: A portable "sniffer" for airborne radionuclides. The unit shown was designed at Chalk River Nuclear Laboratories and is now available (as portable monitor 209) from Scintrex Ltd.(222 Snidercroft Road, Concord, Ontario).

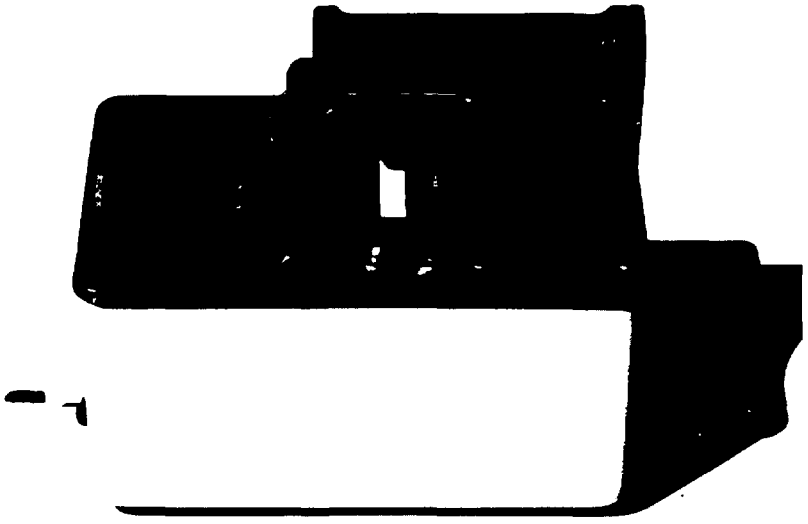

Figure 12: Part of the protected natural area around Chalk River Nuclear Laboratories.

Figure 13: Compartment model of the biosphere.

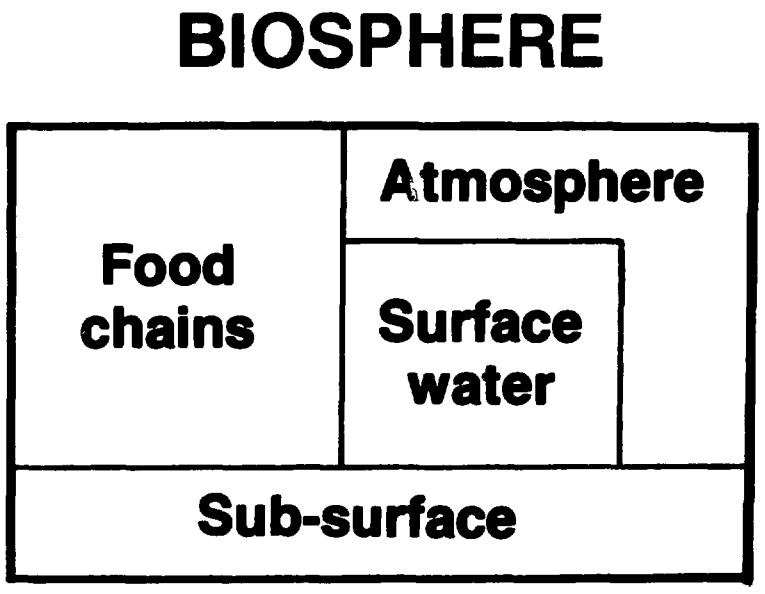

Figure 14: The experimental field at Chalk River Nuclear Laboratories.

Figure 15: Part of the sampling equipment distributed on the experimental field during the experimental tracer experiment with tritiated hydrogen.

Figure 16: Part of the Perch Lake basin at Chalk River Nuclear Laboratories.

Figure 17: Vertical section through a cobalt-60 plume on the sands down the hydraulic gradient from a waste management area. (Killey, R.W.D., McHugh, J.O., Champ, D.R., Cooper, E.L. and Young, J.L., Subsurface colbalt-60 migration from a low-level waste disposal site, Environ. Sci. and Technol., 18(3), pp. 148-157, 1984.

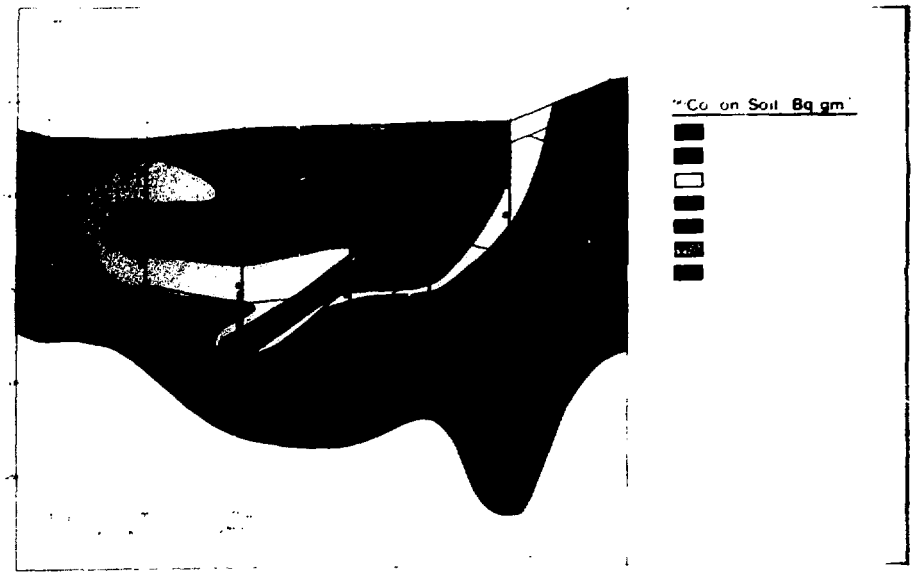

Figure 18: Field columns being installed in an aquifer in order to ensure that the geochemical conditions for studies of sorption kinetics are representative of field conditions. (Champ, D.R., Moltyaner, G.L., Young, J.L. and Lapcevic, P., A downhole column technique for field measurement of transport parameters, AECL-8905, 1986.)

Figure 19: The dispersion of a radioactive tracer in a natural aquifer at the tracer test site. (Moltyaner, G.L., and Killey, R.W.D., The Twin Lake tracer tests: Longitudinal dispersion, Water Resour. Res., in press.)

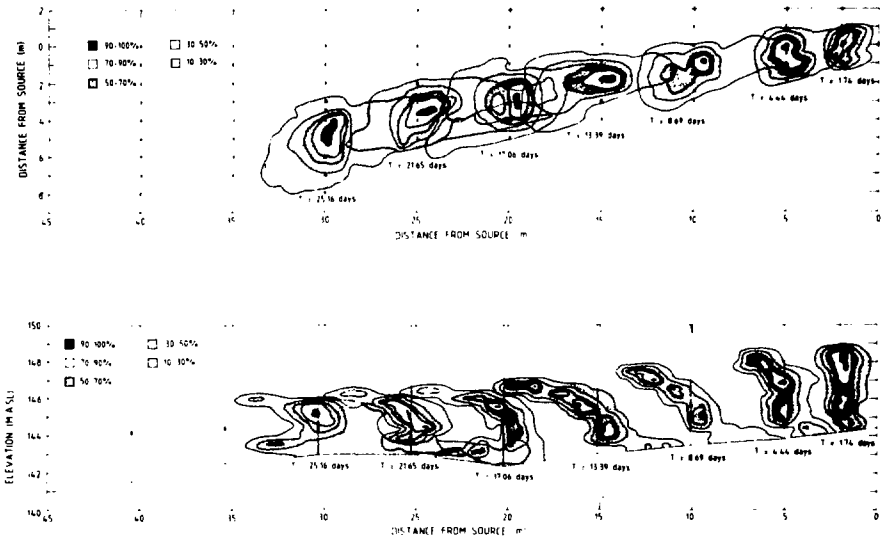

Figure 20: Automation of sub-surface data collection.

Discussion

D.K. Myers:

Part of your presentation dealt with acceptable and unacceptable levels of exposure. Could you tell us some more about these concepts? Who decides what is acceptable?

R.V. Osborne:

To answer your second question first; the responsibility for setting safety standards rests with our elected representatives. We, as scientists, can try to quantify to the best of our ability the relationships between amounts of toxic materials and the extent of, or probability of, harm to the health of individuals. We can compare the deleterious impacts on health of different toxic materials, of different occupations, even of different lifestyles. We can try to quantify the benefits that must stem from any activity, or use of a chemical, or use of radioactive materials, or adoption of an industrial practice. I say "must stem" because if there are no benefits in any particular instance then there is no justification for any risk to health in that instance. But deciding what level of safety -- what level of risk -- should be aimed for is very much a social decision made, ultimately, by the politicians. We have to make the technical issue as clear as we can.

The recommended approach in radiological protection is to set a lower limit to unacceptable levels of exposure from radiation. That is, exposures below such a limit are not necessarily acceptable. The acceptable level is reached when the exposures are as low as reasonably achieved -- the ALARA principle that I noted in my talk as being so important in protection.