Science and values in radiological protection

by T. Lazo*

The NEA Committee on Radiation Protection and Public Health (CRPPH) has been investigating the involvement of stakeholders in decision-aiding and decision-making processes for over a decade. A key conclusion that has resulted from this work is that while the vast majority of radiological protection decisions are informed by science, most decisions concerning public health and safety, or environmental protection, are taken based on broader value-judgement grounds. A relevant corollary to this conclusion is that, in general, the most sustainable decisions tend to be those that clearly reflect and articulate the social values on which they are based.

While these conclusions may seem to be relatively straightforward, applying them to real situations can be anything but. The CRPPH has therefore continued its study of decision making, focusing on case studies of the relationships between scientists and their scientific studies, which can often be uncertain and incomplete, and regulators and their regulatory needs. The objective of this work has been to better understand how, in the face of various levels of scientific uncertainty, value judgements are made and expressed in taking regulatory decisions.

The first step as part of this work was the organisation of the 1st Science and Values in Radiological Protection Workshop, held in January 2008 in Helsinki and sponsored by the Finnish regulatory authority (STUK). The main results of this workshop will be presented here, and have inspired the preparation of the 2nd Science and Values in Radiological Protection Workshop, which will be held from 30 November to 2 December 2009, near Paris, France.

Objectives and approach

There is a constant need for radiological protection policy makers, practitioners and other stakeholders to better understand the evolving interactions between science and values in the development of radiological protection policy and its practical application. Existing radiological protection principles may be challenged by observations of novel or emerging scientific phenomena such as bystander effects, genomic instability, adaptive response and others. Based on this new evidence, attempts are often made to suggest a revision of existing principles or to propose a new paradigm in radiological protection. At the same time, there is also a need for the radiological protection scientists studying these emerging phenomena to better understand the broad processes of radiological protection decision making and to better interact with these processes in terms of furnishing input coming from their research.

In order to explore decision making, and the interactions between scientists and regulators, the objective of the workshop was to initiate a process of reflection and dialogue among the research community, policy makers and other stakeholders that would, in the longer term:

- improve understanding in both the research and policy communities;
- contribute to the development of a more shared view of emerging scientific and societal challenges to radiological protection;
- identify research that will better inform judgements on emerging issues;
- identify elements of a framework that is better suited for the integration of new scientific and

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technological developments and socio-political considerations in radiological protection; and

- identify the most appropriate next steps in this process.

To achieve the above objectives, selected examples of emerging radiological protection issues were addressed in the workshop. Some of the key scientific issues identified in the NEA report on *Scientific Issues and Emerging Challenges for Radiological Protection* (OECD/NEA, 2007) were used as examples in the workshop, namely:

- non-targeted effects;
- individual sensitivity; and
- cardiovascular diseases.

Moderated discussions adopted a "what if" approach, assuming that particular scientific conclusions would be reached by research (e.g. that individual sensitivity can be easily measured and that individual risks can be considerably higher for sensitive individuals). Regulators and researchers then discussed the likelihood of such "what if" situations, and their possible repercussions for RP regulation and practice.

Non-targeted effects

Non-targeted effects refer to those effects that occur in cells not directly hit by ionising radiation. In particular, what are called bystander effects are effects that occur in cells that were not traversed by radiation and are induced by signals from irradiated cells. Another significant not-targeted effect occurs in the genetic offspring of the irradiated cell, where an increased rate of genomic alterations is seen in the progeny of irradiated cells.

Currently there is much that is unknown with regard to these two aspects of non-targeted effects. For example, in the area of bystander effects, what are the chemical messengers that result in damage being manifest in non-irradiated cells? Why does damage only occur in some cells in the vicinity of the irradiated cell? In the area of genomic instability, why does this instability occur irregularly in the family of progeny cells? More generally, it is not known whether these effects are linked to the later appearance of diseases, such as cancer, leukaemia, or cardiovascular diseases, and thus it is not known how these effects may affect the shape of the dose/response curve or the overall model of radiation-induced damage.

Why are non-targeted effects a relevant topic?

The precise nature of radiation-induced damage and the mechanisms that lead to detrimental effects (diseases) are not fully understood. However, it is assumed, for radiological protection purposes, that detriment is proportional to dose. If, however, effects in cells beyond those that are directly hit by ionising radiation influence the genesis of radiation-induced diseases, this would suggest that detriment is not as directly proportional to dose as we currently suspect. If so, the dosimetric criteria on which we currently base protection decisions would need to be revised.

What do we know now about non-targeted effects?

There is a substantial and growing body of knowledge in the area of non-targeted effects, and much research continues in this area. Bystander effects have been induced in unirradiated cells by ionising radiation, as shown in *in vivo* experiments in a human skin cell model, in mouse experiments, and in experiments with blood samples from irradiated humans. Bystander effects are thought to be mediated by cell-to-cell gap junction communication, and they are seen at low doses (on the order of a few mGy). Genomic instability, another type of non-targeted effect, is also known to occur as a result of irradiation. Here, progeny cells which have not been irradiated, and that may be several generations beyond the originally irradiated cell, manifest an instability in their genomic makeup.

What are the scientific issues?

There are many scientific issues that still remain unknown with respect to non-targeted effects, and considerable research is under way in this area, including studies of the nature of the signal-generating bystander effects, and the interaction of that signal with the bystander cell. Other more general questions are also being studied. For example, bystander effects seem to be dose-related only up to a certain low dose, and is primarily a low-dose phenomenon, with higher doses not resulting in further effects. In this context, it is also not fully understood whether targeted and non-targeted cells respond differently.

What are the regulatory issues?

In addition to these scientific questions, the issue of non-targeted effects also raises a series of significant regulatory questions. Broadly, at our current state of knowledge it is not clear whether non-targeted effects amplify the detrimental effects of radiation, and if so, how we would build non-targeted effects into radiation risk estimates.

What approach(es) should be followed to address the scientific issues raised above?

In order to better understand the nature of non-targeted effects, mechanistic studies are essential,

focusing on such things as DNA repair at low doses and low dose rates, at differences between the effects of high and low linear energy transfer (LET) radiation, and using new technologies, for example focusing on the significance of foci formation. Genetic susceptibility should be studied, using appropriate model systems, focusing on genetic and epigenetic components, and studying individual differences.

Likely evolution

Better understanding of non-targeted effects would very likely not affect the overall level of risk, but rather would better explain from where the risk originates. Thus, it would not be necessary, based on our current, incomplete understanding, to change the current approach.

Individual sensitivity

Individual sensitivity refers to the tendency of some individuals to be more or less sensitive than other individuals to radiation-induced damage. Such hypersensitivity or hyposensitivity can result from genetic differences, but can also be affected by living conditions (i.e. environmental exposure to other toxic substances) or lifestyle choices (i.e. smoking). The significance of this to the management of radiological protection is that the current system of protection is based on a broad, averaged approach that applies equally to all exposed or potentially exposed individuals. As such, decisions regarding justification, optimisation or limitation will not inherently account for variability in sensitivity, and thus may pose greater risks to some individuals than to others.

Currently, much remains scientifically unknown in this area, for example, the size of the potentially hypersensitive population and the magnitude of their hypersensitivity, the range and types of exposures likely to trigger such hypersensitive reactions, the mechanisms that produce hypersensitivity that may be linked to other environmental factors, etc. However, the fact that such populations may exist can pose ethical and regulatory issues that should be considered so as to avoid the need for hasty and insufficiently considered reactions by regulatory authorities should scientific discoveries arise confirming relevant hypotheses.

Why is individual sensitivity a relevant topic?

It is known that, at the high doses to which radiation therapy patients are subject, about 5% of cancer therapy patients are hypersensitive to radiation and express skin lesions much more frequently than other cancer therapy patients. This sensitivity is thought to be driven due to genetics, but it is not clear whether increased sensitivity to high exposures would also result in increased stochastic effect risks in humans, although this has been seen in animal studies.

In addition, it has been known for some time that, on average, women are twice as sensitive to radiation-induced stochastic effects (mostly breast cancer) than men, and that, again on average, young children (about five years and under) are roughly five times as sensitive to radiation-induced stochastic effects as adults. While it is generally true that risk differences of less than an order of magnitude are well within the statistical uncertainty of our current level of knowledge, stakeholders may not feel that differences of a factor of two or five should be dismissed as a statistical noise.

What do we know now about individual sensitivity?

Individual sensitivity is known to be expressed at high doses, that is, levels experienced by patients undergoing radiation therapy, and may be expressed at low doses, for example, exposure levels experienced by occupationally exposed workers and by the public in general. With respect to radiation therapy patients, as previously stated 5% are hypersensitive to radiation, and of these, 5% (or 0.25% of all therapy patients) are very hypersensitive. Importantly, it is also suspected that there are some people who are hyposensitive to radiation, but the size of this group is not known.

What are the scientific issues?

High-dose considerations are particularly relevant because they are known to exist in radiation therapy patients. In particular, the link with specific genetic characteristics is being used to develop predictive tests that would indicate whether or not an individual would be likely to be hypersensitive to radiation. However, for such tests to be truly useful in helping to define an individual's treatment strategy, it is important to better understand the mechanisms and consequences of effects caused by hypersensitivity and their applicability, that is, at what range of exposures they might occur, what effect age at exposure may have, etc. Of course, any predictive tests would need to be suitably validated for accuracy and precision.

What are the regulatory issues?

In addition to these scientific questions, the issue of individual sensitivity also raises a series of significant regulatory questions. For example, since hypersensitive individuals are included in the exposed populations that have been used as the basis for the estimation of radiological risk,

in particular the populations of Hiroshima and Nagasaki, does this sufficiently take into account the risks of hypersensitive individuals? In fact, is most of our current risk estimate actually due to risks in these individuals? If so, would it be appropriate to re-evaluate our current approach to radiological protection, either identifying a new dose limit to best protect hypersensitive individuals and another for "normal" individuals, or keeping a single dose limit but setting it as a function of risks to hypersensitive individuals. In addition, if hypersensitivity is an issue (with individuals being at two or more times the "normal" risk) there would be a need to explore several other regulatory aspects, including protection of emergency response workers, and, depending on the relevant level of exposure perhaps protection of the public (sensitive groups) in emergency situations (implications for the current approach to planning emergency response optimisation for women, pregnant women and children).

What approach(es) should be followed to address the scientific issues raised above?

Given these types of scientific questions, credible strategies should include single-cell models and animal models, although the relevance of these to organs and humans need to be evaluated. To move forward, there is a need to develop research priorities, requiring an active dialogue between researchers and the regulatory and broader radiological protection community. A key aspect in the prioritisation of research will be to clearly agree on how to judge the likelihood of these studies to deliver answers, and to consider whether risk-modifying factors (age, diet, lifestyle, etc.) influence sensitivity.

Likely evolution

An important challenge posed by our current level of knowledge is the need to assess what changes would need to be made in our current radiological protection approach as knowledge evolves. Adopting a "what if" approach, several changes can be foreseen once the sensitive population has been more sufficiently characterised (i.e. what fraction of the population, how hypersensitive they are, how do age and sex influence sensitivity, etc.). Based on this level of understanding, it is likely that radiological protection changes would be considered for both high- and low-dose situations.

However, based on our current level of knowledge, and in particular on our understanding of the probable levels of increased risk should large populations of hypersensitive individuals exist, there seems to be no need to radically modify the current approach to radiological protection. No specific changes are recommended for occupational protection, protection of the general public, or for public screening programmes (i.e. medical screening or medico-legal screening).

A key aspect of this issue is the reflection of living with scientific uncertainty, and being prepared to react in an appropriate fashion should new evidence arise. Hence, and again based on current knowledge, it is suggested that in emergency exposure situations, medical diagnosis situations and medical therapy situations, some consideration should be given to refocusing protective actions taking individual sensitivity into account.

Cardiovascular diseases

It has been generally accepted that high dose (several Gy) radiation exposure to the heart or other parts of the circulatory system result in long-term increases in cardiovascular disease risks. Over the past 10-15 years, evidence has been emerging from the long-term follow-up of atomic bomb survivors and other populations that relatively low dose acute exposures (< 2 Gy) are also associated with increased cardiovascular disease risks.[1] Although the estimated relative risks are smaller than for cancer, it is clear that radiation-associated cardiovascular disease deaths will account for a substantial fraction of the total radiation impact on mortality in the atomic bomb survivors. However, those epidemiological data do not, and probably cannot, provide definitive evidence of increased cardiovascular disease risks following low dose (e.g. 0.005 to 0.5 Gy) exposures. Despite this uncertainty, these findings have increased interest in efforts to identify mechanisms for long-term radiation effects on the circulatory system and prompted the re-examination of cardiovascular disease risks in other populations.

Why are cardiovascular diseases a relevant topic?

Cardiovascular diseases are currently not specifically addressed by the radiological protection system. The ICRP recognises the existence of this problem, but notes that experimentally observable dose-associated effect is at high doses, around 1 Gy.[2] There are still uncertainties regarding the shape of the dose response at low doses and whether these effects have a threshold at around 0.5 Gy or not at all. In general, the ICRP accepts that available data do not allow for their inclusion in the estimation of detriment following low radiation doses less than 100 mSv. This also agrees with the conclusion of the 2008 UNSCEAR report which found little evidence of any excess of risk below 1 Gy.[3]

The 2008 UNSCEAR report includes an annex on this topic and it seems inevitable that the ICRP

and other groups involved in the formulation of regulatory guidelines will have to address the question of how to incorporate potential cardiovascular disease risks into the evolving system of radiological protection.

Regulatory issues and likely evolution

If potential changes in radiological protection principles are made based on available Japanese risk estimates and the linear no-threshold (LNT) hypothesis considering risk for cardiovascular diseases, there will be a need for significant revision. Current dose limits would need to be lowered by 30-50%, with strong emphasis on optimisation. In such a case, the application of the precautionary principle should include not only the change in detriment but also the cost and other consequences associated with this change. If this is the case, the current radiological system will be significantly challenged. However, workshop participants also recognised that any potential change should be made in the light of evolving science and serious value judgements, and thus further research and dialogue is needed.

Moving forward

The 1st Science and Values in Radiological Protection Workshop was the first in the intended series of CRPPH workshops addressing emerging scientific issues and questions on the potential need to revise and/or to amend existing radiation principles and radiological protection criteria. It sought to initiate a discussion on the universality of the current fundamental radiological protection approaches and how it may be challenged by novel scientific issues. It aimed to provide insights into how agreement is reached regarding a "tipping point", that is, when the scientific and social aspects considered by policy makers and regulators hold sufficient weight to "tip" the scales towards a new regulatory approach or paradigm. It was felt that the discussions at the workshop, briefly summarised above, were a good beginning to better understanding various aspects of this important scientific and social question.

The CRPPH agreed that the second science and values workshop should re-emphasize that radiological protection is a combination of science and value judgements, and should focus on radiological protection issues that are currently being faced and continue to pose challenges. As such, the second workshop has been designed to address a series of current radiological protection issues from the standpoint not of "What if?", but rather, "What now?". This workshop will examine the social and scientific challenges posed by radon, by growing medical exposures, and by emerging radiological risks of cardiovascular diseases.

In these three areas chosen for the workshop, current approaches to radiological protection have not fully yielded the desired results (i.e. radon and medical exposures), or there is a perception that there is insufficient scientific evidence to warrant change in the current approach (i.e. cardiovascular diseases). Thus, while the objective of this workshop is not to develop detailed recommendations as to new approaches, it is expected that:

- Stakeholders in each area will present and exchange experience related to their viewpoints and relevant values, increasing their levels of mutual understanding to facilitate development of common approaches.
- Participants will discuss social and scientific rationale and justification of the need to adopt new approaches to radiological protection in each of these areas (tipping point).
- Practical approaches to improving radiological protection in each area will be discussed based on national experience.
- Participants will identify possible needs for further research and/or analysis in order to better understand the challenges and how they may be accommodated.
- Process and framework elements that could enhance radiological protection in these three areas by better integration of social and scientific aspects will be identified.

It is hoped that this workshop will result in a better understanding of how these judgemental decisions can be made in an increasingly transparent fashion, making clear their bases and their assumptions. It is also hoped that the discussion of these topics will provide participants with different national and institutional views of how to best address the challenges posed in these areas. A report summarising the results of this workshop will be published by the NEA in 2010. ■

References

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