Applicability of Radiation Response Models to Low-Dose Protection Standards

ANS / HPS Topical Meeting in Tri-Cities, WA

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Summary of the Meeting

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We have reached about the close of this great meeting. I was asked to be on this spot at the end and I appreciate this challenge with gratitude. I promise to be brief and to the point.

You all agree, I am sure, that the meeting reached its goal – that of open exchanges of facts, views, interpretations, hypotheses and theories and of their consequences for optimization of radiation protection with the best possible outcome in the service of society.

There would today probably be no discord in in radiation protection if the Nobel Laureate Herrmann Josef Muller many decades ago had not suggested that the proportionality between dose and mutation incidence, (in fact chromosomal damage incidence, observed at high doses was also observed at low doses –a claim without research backing. The LNT model was born and stayed.

Our meeting now interlocked – openly for the first time - deep rooted complexities of approaches, interpretations and recommendations for optimization of radiation protection - in view of what we know to-day.

All aspects of the complexities were presented and discussed spanning all relevant disciplines - in plenary sessions and panels – and also in personal contacts at social functions. Clearly, the development and adoptions of regulations is of great societal value and depends on public perception, policies and legislation. And these are informed by but not determined by scientific evidence.

Focal issues were the present applications of recommendations in radiation protection at the national and international levels. The intellectual sources of these

recommendations derived from epidemiology, biology, physics and mathematics, modeling of risk against dose, informing the public in the effort to alleviate unwarranted fears, and the need to consider application of low doses in medicine and industry.

The interdisciplinary composition of the experts was optimal beyond expectation and responded to a wide range of questions, as they came from the fields of epidemiology, system biology, cell biology, molecular biology, biochemistry, biophysics, health physics, mathematics, model makers, legal socio-economists, physicians, decision makers, and administrators as well as practitioners of radiation protection – a gathering as never before. Indeed, the stakes were high against a background of controversial disputes, misunderstandings, stakeholders, bias and public fear bordering on panic. How dangerous are low doses and low dose-rates?

After three days of deliberations, Panel 7 brought together in a focus the arguments for a common denominator of the multitude of presentations of facts, interpretations and suggestions - with visions to apply them to be accepted rigidly based on science by what serves best for the public.

Regarding science, it appears that one may summarize the presentations at the meeting being voiced by three groups of opinions.

The first and oldest group holds the LNT model to be the unconditionally best for the practice of radiation protection. This alliance is maintained despite the acknowledgment of a lack of proof that the LNT model applies. For this reason the scientific dogma of this group has been questioned regarding the use of the LNT model for predicting numerically health risks from low doses and low dose-rates. With this constraint, this group advocates for the continued use of the LNT model for practical administrative and executive reasons. The group does not consider low-dose-induced changes in cellular mechanism of adaptive protection. Public fear of low doses and economic burdens brought on by the LNT model must be addressed within the balance of risks and benefits to society.

The second group of voices judges the risks of any health effects from low doses and low dose-rates to be negligibly small supporting the abandonment of the LNT model in favor threshold model. The strength of this argument is the lack of evidence of an increase in cancer incidence at low doses (below about 100 mGy).

All acknowledge that the health risk at this dose level is very small compared to the risk from other toxic exposures, especially from endogenous toxins such as reactive oxygen species and hydrogen-peroxide. Another advantage here is the continued applicability of the conventional dosimetry.

The third group of voices began to assemble 40 years ago after the discovery of low-dose-induced changes in cell signaling with delayed responses. This group found increasing attention through the emerging evidence that low-doses induce cellular signal changes, which with a delay of hours can lead to stress response type metabolic alterations. These include adaptive responses in terms of protection against damage accumulation. Accordingly, appropriate risk models must include the probabilities of multiple responses after low-dose exposures. There is the risk of radiogenic damage, for instance to the DNA, and of the radiogenic protection mainly against radiomimetic damage irrespective of the origin of this damage. The resulting multiple response models, thus, take into account individual cell biology mechanisms under genetic control and potentially brings such a degree of damage prevention that it balances radiogenic damage production. In this latter case, the exposed system will have a dose threshold. If radiogenic damage prevention outweighs radiogenic damage production a benefit results (i.e., the system experiences a hormetic effect). This approach by group three has the advantage of integrating all response patterns in system elements into a holistic response. Research data now support the concept that oxidative metabolism during evolution has led to the emergence of protective pathways essential to life and also shielding against detriment from low doses of ionizing radiation. In this context one may appreciate low doses to be essential to life.

These three voice pools as they came together at this meeting are now ready to interact in a creative manner and be supported by basic and applied research on low-dose effects. The study on mechanisms that operate after low-dose exposure not only fortifies what we envisage today but also opens new research avenues of yet unforeseen dimensions, for instance, in therapeutic medicine.

The LNT model for dose-risk assessment at low doses is direct and relatively simple but is inconsistent with the complexities of biological systems. In fact, this model has not been validated in cell - and animal experiments. Moreover, the LNT model for radiation protection results in more harm than benefit to society.

To me, radiation protection needs additional models. Today, sufficient data is available to form a consensus to integrate dose limits into radiation protection, for instance in terms of a dose threshold below which risk cannot be comprehended. This consensus must include the plea for further radiobiology research.

A note of thanks: For having set the meeting to be an intellectual whirlpool, the chairman Alan Waltar who conceived the plan for the meeting together with the people in the magnificent committees for all functions deserve a most sincere applause as expression of thanks.

May everyone here have a safe trip back home.

THANK YOU!!