



**Australian Government**

**Australian Radiation Protection and Nuclear Safety Agency**

## **Regulatory Impact Statement Public consultation draft**

### **Code of Practice**

## **Exposure of Human Subjects to Ionizing Radiation for Medical Research Purposes**

Comment on the Regulatory Impact Statement and draft Code of Practice should be forwarded by **26 March 2004** to:

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# Background

## Ionizing radiation and medical research

1. Researchers typically use ionizing radiation with human subjects to investigate medical conditions such as osteoporosis, cancer, Alzheimer's disease, deep vein thrombosis, coronary disease, diabetes, arthritis and chronic pulmonary disease. Although research usually involves volunteers with pre-existing conditions, such as those listed, there is often no known direct benefit to the volunteer from the research and it is not part of the medical management for the condition. In some instances the research may also involve the administration of ionizing radiation to healthy subjects.
2. Most medical research is carried out in teaching hospitals and universities in capital cities. The majority of studies involve bone density studies, extremity radiographs, the use of radiopharmaceuticals and Computed Tomography (CT) scans for screening and monitoring aspects of the research. Many research projects involve drug trials where the effects are monitored using ionizing radiation. Drug trials are often carried out on a multi-centre, worldwide basis.
3. Almost all sources (sealed and unsealed) of ionizing radiation used in research are also used in medical management of patients and are therefore regulated through licensing systems directed at the control of sources of radiation.
4. Although no published data is available on the number of research projects using ionizing radiation and human subjects, an estimate based on available Victorian data has been calculated by consulting the four main licensees<sup>1</sup> in Victoria. It was found that between three and seven per cent of total projects initiated in 2002 involved the exposure of human subjects to ionizing radiation and were referred to the Victorian regulator.
5. Limited data is available to quantify the economic impact of research projects specifically using ionizing radiation with human subjects. Estimates based on ethics committee or regulatory authority approval of the relevant projects is complicated due to simultaneous but mostly separate processes to access funding. For instance, some projects may obtain all the necessary regulatory approvals but do not proceed due to inadequate funding. In accordance with this finding, the Industry Commission acknowledged in 1995<sup>2</sup> that *'attempts to quantify economic impacts of R&D have been plagued by data problems, which are compounded by the complexity of the task.'* However, general figures for funding of medical research and Commonwealth funding of all types of research are available.
6. The Australian Bureau of Statistics (ABS) reports<sup>3</sup> that the Commonwealth was the source of 38.3% (\$3,923 million) of the total research and development (R&D)

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<sup>1</sup> Royal Melbourne Hospital, Austin & Repatriation Medical Centre, St Vincent's Hospital and Barwon Health

<sup>2</sup> Industry Commission Report 44, Research and Development, 1995

<sup>3</sup> ABS Report 8112.0 for 2000-01

expenditure of \$10,251 million across sectors<sup>4</sup>. In 2000-01, \$1,490 million was spent in Australia on R&D for the socio-economic objective of health<sup>5</sup>. Using the Victorian estimate that between 4 and 7 per cent of research projects involve the exposure of human subjects to ionizing radiation, it is estimated that the relevant research projects in Australia were associated with R&D funding of between \$59 million and \$104 million for 2000-01.

7. Human resources devoted to R&D are also available from ABS. In 2000-01, a total of 91,784 person years contributed to R&D in Australia. Researchers contributed 69% of this total, followed by 16% by technicians and 15% by other support staff. A total of 16,706 person years were used in research directed at the socio-economic objective of health. Using the Victorian estimate of the proportion of relevant research projects, between 669 and 1,170 person years were directed towards projects relevant to this impact analysis.
8. Although the proportion of Commonwealth funding directed towards the socio-economic objective of health is not available, grants from the National Health and Medical Research Council (NHMRC) for health and medical research<sup>6</sup> in 2001 totalled \$216 million. This represents 5.5% of total Commonwealth funding for R&D. The distribution of NHMRC funding approximately reflects the amount of medical research being carried out in Australian jurisdictions. In 2001, forty percent (\$87.2 million) of NHMRC funding went to Victorian researchers, twenty-four percent (\$51 million) went to NSW researchers and thirteen percent (\$28 million) went to QLD researchers, followed by 10.2% (\$22 million) to SA researchers, 8.7% (\$18.9 million) to WA researchers, 2.2% (\$4.8 million) to ACT researchers and just over \$2 million to researchers in NT and Tasmania combined.
9. The NHMRC reports<sup>7</sup> that '*Victoria receives more than 40% of NHMRC funding because it is home to four of the major medical research institutes and two of the largest and most active health research universities, each with a large number of active and high quality researchers*'. This pattern is reflected in the following details regarding regulatory approval of research projects that used ionizing radiation on human subjects.
10. During 2002<sup>8</sup>, the Victorian regulator approved 36 projects involving 20,543 human subjects (**Attachment A**). These human subjects were given effective doses between 0.002 and 13 millisievert (mSv) with 44% of human subjects from 14 projects receiving an effective dose of less than or equal to 0.1 mSv, and 52% of human subjects from 13 projects receiving between 1.0 to 4.9 mSv. In addition, an average of thirty projects a year using Dual Energy X-ray Absorptiometry (DEXA) scans are

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<sup>4</sup> Business, Commonwealth and State/Territory Government, Higher Education, Private non-profit

<sup>5</sup> The area of expected national benefit rather than the immediate objectives of the researcher. The SEO classification defines the main areas of Australian economic and social activity to which the results of research programs are applied. it describes the purpose of the research, ie why the research is being performed

<sup>6</sup> NHMRC Grants Book 2001

<sup>7</sup> NHMRC 'A Report on the Performance of the National Health and Medical Research Council 2000-2003

<sup>8</sup> In 2003, 31 projects were approved and nine projects were referred to the regulator that did not require approval.

conducted in Victoria. These projects are approved directly by the regulator without being reviewed by the Victorian Radiation Advisory Committee and involve the exposure of approximately 50 human subjects to between 0.002 to 0.15 mSv.

11. Only two of the Victorian research projects approved in 2002 used effective doses above 5 mSv. In other jurisdictions, 5mSv is the current NHMRC effective dose level before approval of the regulator is required. Most research exceeding 5 mSv involves the use of CT scans and radiotherapy techniques often with volunteers with cancer, where the research is being undertaken in addition to treatment for the disease. In Victoria, 140 human subjects received an effective dose of greater than or equal to 10 mSv.
12. In NSW, regulatory approval is only required where the effective dose exceeds 5 mSv. As a result of this approach, the regulator approved five research projects that used ionizing radiation on human subjects in 2002. In addition, data from a Sydney teaching hospital (**Attachment B**) over a 3-year period demonstrates a similar pattern to the data obtained for research in Victoria; most research involved human subjects receiving doses either less than 0.1 mSv or doses between 1.0 and 4.9 mSv. Research projects where 10 or more millisievert was used mostly involved CT scans to monitor cancer trials.
13. In 2002, 337 South Australian human subjects were exposed to ionizing radiation in 13 projects. About half of SA human subjects (174) were exposed to less than 5 mSv through their involvement in 6 projects. As elsewhere, higher exposures (> 10.9 mSv) involved human subjects with cancer. More than half the projects were drug trials involving diagnostic X-rays, Computed Tomography (CT) scans, Multiple Gated Acquisition (MUGA) scans and Dual Energy X-ray Absorptiometry (DEXA) scans to monitor the effects of the drugs being trialed. Projects included research with thrombosis, post-traumatic stress, gene therapy, Hunter syndrome, osteoporosis, diabetes and various types of cancer.
14. During 2001-2003, the West Australian regulator approved 6 projects using 101 human subjects. All of the projects used radiation for diagnostic purposes with effective doses between 1.7 and 72 mSv.
15. In Queensland, due to the absence of any project specific approval process, details regarding the number of human subjects and projects are not available. However, only a few institutions within the State are involved in research with human subjects.
16. Very few research projects involving human subjects have been carried out in Tasmania. No research using ionizing radiation on human subjects has been undertaken in the Northern Territory over the past two years. The Australian Capital Territory has had 3 clinical trials involving diagnostic radiation over the past two years (further details were lost during Canberra bushfires of 2002).
17. In Victoria, the regulator approved two projects using persons under 18 years of age in 2002. In total, these projects involved about 400 participants with each participant receiving an effective dose of up to 0.1 mSv. In 2001, six research projects were reviewed involving the exposure of 2893 human subjects under the age of 18 to between 0.01 to 0.4 mSv. Most of these projects involved bone density assessments.

18. A graph of the number of projects across jurisdictions above and below the regulatory limit of 5 mSv is at **Attachment C**. It should be noted that the graph is not entirely representative of research activity relevant to the subject of this analysis, due to the differences in regulatory requirements across jurisdictions. These differences are discussed below.

**Current regulatory processes**

19. In 1977, the World Health Organisation published Technical Report Series 611 *Use of Ionising Radiation and radionuclides on Human Beings for Medical Research, Training and Non-Medical Purposes* which divided research projects into categories depending on the radiation doses received by human subjects. This formed the basis for the 1984 NHMRC publication RHS 12.

20. In 1993, the International Commission for Radiological Protection (ICRP) modified the classification taking into account changes in the assessment of radiation risk and introduced a corresponding categorisation of the ‘level of societal benefit’ which can be considered as a basis for approval of the level of dose. The type or level of benefit that will result from the research, to subjects or society at large, is evaluated to justify the need to expose human subjects to ionizing radiation. The likely risk of harm to the human subjects is assessed based on the best quantification of doses available and also taking account of the characteristics (age, gender, health) of the subjects that may affect the risk from the proposed exposure. It should be noted that in the case of terminally ill patients, long-term risks of radiation are not relevant. The categories of risk and corresponding levels of benefit to society from radiation exposure is reproduced below:

<b>Level of Risk</b>	<b>Risk Category</b>	<b>Effective Dose Range (adults) (mSv)</b>	<b>Level of Societal Benefit Expected</b>
Minimal	Category I ( $10^{-6}$ or less)	< 0.1	Minor
Minor to intermediate	Category IIa ( $10^{-5}$ )	0.1-1	Intermediate
	Category IIb ( $10^{-4}$ )	1-10	to moderate
Moderate	Category III ( $10^{-3}$ or more)	> 10 <sup>a</sup>	Substantial

<sup>a</sup> *To be kept below deterministic thresholds except where therapeutic procedures involving radiation are being investigated.*

21. With Category I, where risks of total detriment<sup>9</sup> are of the order of 1 in 1 million, the level of benefit needed as the basis for approval of research with doses less than

<sup>9</sup> Sum of the probability of fatal cancers, the weighted probability of non-fatal cancers and the probability over all succeeding generations of serious hereditary disease resulting from the dose.

0.1mSv will be minor and will include investigations expected to only increase knowledge. With Category IIa, where the risks of total detriment are 1 in 100,000, the benefit is related to increases in knowledge leading to health benefit. With Category IIb, the risks of total detriment are 1 in 10,000, the benefit will be directly aimed at the cure or prevention of disease. With Category III, where risk of total detriment is 1 in 1,000 or greater, the benefit has to be substantial and usually directly related to the saving of life or the prevention or mitigation of serious disease.

22. Underlying the above assessment is the fundamental regulatory philosophy of regulators expressed in three principles based on the recommendations of the ICRP<sup>10</sup> which are summarised as follows:
  - *Justification*: human activities that cause exposure to radiation may be permitted only if they do more good than harm;
  - *Optimization of protection*: exposure to radiation from justified activities should be kept as low as reasonably achievable, social and economic factors being taken into account; and
  - *Limitation of individual dose*: doses must not exceed the prescribed dose limits.
23. In order to remain in step with developments, additional guidance for researchers and regulators was included in the NHMRC 1995 *Recommendations for limiting exposure to ionizing radiation* (republished as ARPANSA's RPS1).
24. In most jurisdictions, researchers are required to obtain advice and approval from internal and external sources for the use of ionizing radiation on human subjects. These sources include the institution's radiation safety committee, the institutional human research ethics committee, and, in some cases, the State/Territory regulator.
25. Some institutions have a radiation safety committee consisting of representatives from areas of the institution involved in the use of radiation, external radiation experts and the institution's radiation safety officer. These committees consider all radiation safety related issues including research projects that use ionizing radiation on human subjects. The committee's approval of the researcher's use of ionizing radiation may be required by the institution. In other institutions, the researcher is required to consult the radiation safety officer to verify the radiation dose described in documentation submitted to the human research ethics committee and regulator.
26. Each institution engaged in research with human subjects has a Human Research Ethics Committee (HREC). Researchers are required to seek approval for projects from the HREC within the institution. In almost all jurisdictions, the HRECs approval includes the consideration of the existing regulatory requirements of the jurisdiction.
27. Radiation protection regulators do not license HRECs. HRECs are required to operate in accordance with the NHMRC 1999 *National Statement on Ethical Conduct in Research Involving Humans* and must report to the NHMRC Australian Health Ethics Committee (AHEC) to ensure compliance with the *National Statement*. This

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<sup>10</sup> adopted by Australia in ARPANSA's *Recommendations for limiting exposure to ionizing radiation (1995)*, and *National Occupational Health and Safety Commission (NOHSC) National standard for limiting occupational exposure to ionizing radiation (1995)* (Radiation Protection Series 1, (RPS 1))

compliance reporting is focussed on overall operation of the HRECs. The NHMRC AHEC also provides advice, guidance and support to HRECs through handbooks, bulletins, workshops and an ad hoc advisory service.

28. The NHMRC 1999 *National Statement on Ethical Conduct in Research Involving Humans* requires researchers and Human Research Ethics Committees to follow relevant State and Territory legislation, consult the ARPANSA *Recommendations for Limiting Exposure to Ionising Radiation (1995)* (RPS1) and seek additional advice from ARPANSA.
29. In 1984, the NHMRC published, as part of its Radiation Health Series, an '*Administration of Ionizing Radiation to Human Subjects in Medical Research (1984)*' (RHS 12). The statement is widely used by regulators. NHMRC handed responsibility for the Series to ARPANSA. However, RHS 12 was rescinded by NHMRC at their 141<sup>st</sup> session in March 2002.
30. The ICRP system of radiological protection adopted in Australia in ARPANSA's *Recommendations for limiting exposure to ionizing radiation (1995)*, and *National Occupational Health and Safety Commission (NOHSC) National standard for limiting occupational exposure to ionizing radiation (1995)* (Radiation Protection Series 1, (RPS 1)). This publication is used by State, Territory and Commonwealth governments to form the basis of the radiation protection requirements adopted in legislation, regulations and/or conditions of licence.
31. In 1995, the NHMRC *Recommendations for limiting exposure to ionizing radiation* (now re-published as ARPANSA RPS 1) supplemented RHS 12 through:
  - the description of doses as constraints;
  - the addition of a 5 year averaging period constraint consistent with RPS 1; and
  - a cumulative effective dose constraint of 5 mSv for children to 18 years.
32. Regulators have different approaches to applying the guidance and constraints documented in the NHMRC RHS 12 and the ARPANSA RPS 1:
  - (a) In Victoria, due to incidents arising from a lack of sufficient regulatory control over individual researchers in the 1959 regulations, licences at both the researcher and institutional level were introduced in 1984. As a result, all medical research projects involving exposure of human subjects to ionizing radiation must be submitted to the Victorian Radiation Advisory Committee (RAC) before an approval is given by the regulator. In order for the RAC to consider approval, researchers must provide:
    - copies of the research protocol,
    - the participant information sheet, that includes an explanation of the risks
    - estimates of radiation doses to participants,
    - evidence of approval by the institution's ethics committee,
    - evidence of the approval of their institution's Human Research Ethics Committee.
  - (b) In NSW, only those projects exceeding the constraints in the ARPANSA RPS 1 (greater than 5mSv) require the approval of the NSW Radiation Advisory

Council. The institutional HRECs oversee adherence to the dose constraints for projects where the effective dose does not exceed 5 mSv.

- (c) Regulatory approval in South Australia is required for any research involving the exposure of human subjects to ionizing radiation which would not have been received but for the purpose of research. An exemption under s. 44 of the *Radiation Protection and Control Act 1982 (SA)* can be granted that provides approval on an institutional basis, so that the regulator does not review individual research projects. However, all research projects involving the exposure of human subjects to ionizing radiation must be reported to the regulator. Exemption from regulator approval includes all research except:
- where the effective dose to the volunteer in any one year exceeds 5 mSv;
  - where the volunteer is less than 2 years of age and the effective dose in any year is more than 0.1 mSv; and
  - where the volunteer is between 2 and 18 years of age and the effective dose in any year is greater than 0.5 mSv.
- (d) In Queensland, there is no specific approval for the conduct of research on humans; rather any person who intentionally irradiates a person is required to hold a licence permitting such a practice. The licence permits use of the radiation source for a specific purpose and in accordance with an approved radiation safety and protection plan. Section 9 (1) (c) of the *Radiation Safety Regulation 1999 (QLD)* makes it a condition that a person using an ionizing radiation source for conducting health-related research on persons must comply with the NHMRC RHS 12. Institutions are also licensed and any additional regulatory guidance, such as what information should be presented to ethics committees and who should prepare the information, is exerted through this avenue.
- (e) In Western Australia, in addition to the NHMRC RHS 12, regulation 1 (3)(a) of Schedule 1 of the Regulations under the *Radiation Safety Act (1975) (WA)* also applies so that regulator approval for projects in Western Australia involving the exposure of human subjects to ionizing radiation is required where:
- the effective dose exceeds 5 mSv;
  - the effective dose to children or other persons incapable of giving informed consent exceeds 0.5 mSv;
  - the effective dose to infants, babies or foetuses exceeds 0.1 mSv; and
  - the radiation dose to any individual in any 5 year period exceeds an effective dose of 1 mSv per year.
- (f) In Tasmania, there is no formal process for assessment of research projects involving the use of ionizing radiation on human subjects. However, licence conditions require compliance with RPS 1 *Recommendations for limiting exposure to ionizing radiation (1995)*, and *National standard for limiting occupational exposure to ionizing radiation*.

- (g) In the ACT, where exposure is not part of 'the normal clinical practice' of a licence holder, approval to vary the licence and conditions related to the research may be required by the ACT Radiation Council.
- (h) In the Northern Territory, research of this nature requires a licence from the Chief Health Officer.

## Problem

### Outdated information

- 33. The NHMRC RHS 12 draws on the 1977 Technical Report Series 611 by the World Health Organisation (WHO) *Use of Ionising Radiation and radionuclides on Human Beings for Medical Research, Training and Non-Medical Purposes*. Since the WHO report, the International Commission for Radiological Protection (ICRP) produced Publication 62 *Radiological Protection in Biomedical Research* in 1993 which categorised risk and corresponding levels of societal benefit from the exposure of human subjects to radiation in the course of research. Additional guidance for researchers was also included in the NHMRC 1995 *Recommendations for limiting exposure to ionizing radiation* (republished as ARPANSA's RPS1).
- 34. Understanding of the effects of ionizing radiation on specific organs and tissues has also increased since 1984, with the ICRP producing a much more extensive list of tissue weighting factors for the evaluation of the risks from exposure to radiation in Publication 60, *1990 Recommendations of the International Commission on Radiological Protection*.
- 35. The NHMRC RHS 12 was rescinded by the NHMRC in March 2002 and, as it is more than 10 years since it was published, it is due for a review. However, the NHMRC does not wish to continue publishing the Radiation Health Series (RHS) publications and has handed responsibility for the RHS publications to ARPANSA.
- 36. Members of the working group advise that there is confusion amongst researchers in some jurisdictions as to whether NHMRC RHS 12 applies to their research due to its age and brief nature.
- 37. In Victoria, the common application form used by researchers to make submissions to ethics committees does not include reference to NHMRC RHS 12 because it does not contain the most up to date guidance. Instead, researchers are directed to follow the recommendations of ICRP Publication 62 and ARPANSA RPS 1 in filling out the ionizing radiation form for module five of the application.
- 38. The NHMRC's 1999 *National Statement on Ethical Conduct in Research Involving Humans* refers to RPS1 and the radiation dose constraints in the NHMRC RHS 12 are not consistent with those in Part 2 of ARPANSA RPS1. See paragraph 36 for radiation protection impact of this disparity.

### Radiation Protection Issues

- 39. The NHMRC RHS 12 does not take account of the possible participation by human subjects in multiple projects. Although ARPANSA RPS1 included an additional

constraint of 10mSv over 5 years to address this potential exposure, there have been other research applications that the existing guidance does not address. For example, equivalent dose to individual organs of adults and persons under 18 years.

40. The NHMRC RHS 12 has a dose constraint of 0.5 mSv in any year for children and 0.1 mSv in any year for babies, infants and foetuses, whereas ARPANSA RPS1 has a cumulative effective dose constraint of 5 mSv to age 18 years. If the baby and infant stage is taken from birth to 2 years of age, then the 'baby-infant-foetus' period covers approximately 3 years and the remaining 'child' period covers 16 years. This means that the constraint in the NHMRC RHS 12 allows a maximum cumulative dose of 8.3 mSv to 18 years compared to the 5 mSv allowed in ARPANSA RPS1.
41. The application of the existing guidance for the use of ionizing radiation in research with human subjects has been inconsistent across jurisdictions. Variations appear to mostly arise due to uncertainty of the scope of the NHMRC RHS 12. The Victorian regulator relies on an advisory committee to decide what projects utilise ionizing radiation for research purposes rather than patient care. The NSW regulator also uses an advisory committee, however research projects are only considered if the 5 mSv constraint is to be exceeded. Further variations in the application of existing guidance are detailed in paragraph 29.
42. The NHMRC 1984 statement applies to 'any administration of ionizing radiation to human subjects for the purposes of diagnostic or therapeutic research involving either external irradiation of the administration of radionuclides,..'. There is some distinction made between the use of radiation to persons expected to benefit from the procedure and their management as patients, and use of radiation of persons not expected to benefit from the procedure and their selection as human subjects. However, the NHMRC RHS 12 does not provide clear guidance on how to define whether the administration of ionizing radiation to human subjects is only for the purposes of research and hence whether the constraints within the Statement are applicable. Consequently, as outlined in paragraph 29, regulators have developed different definitions to decide whether the use of radiation in research projects falls within the scope of the NHMRC RHS 12.
43. The NHRMC 1984 Statement does not specify whether its scope includes clinical trials. As a result, there has been inconsistent application of the existing dose constraints where ionizing radiation is used to monitor the effectiveness of such trials.
44. The NHMRC RHS 12 does not contain specific guidance on how to assess the risks of the radiation used against the societal benefits which is needed by researchers to seek the approval of ethics committees and to explain the risk to human subjects.
45. The NHMRC RHS 12 is ambiguous in terms of the role of human subjects, guardians, researchers, institutions, regulatory authorities and ethics committees.
46. Since 1984, developments in research techniques have resulted in the following impacts:
  - (a) Use of nuclear medicine by researchers has significantly increased and will continue to do so with studies comparing nuclear medicine with other diagnostic techniques. For example, when the Victorian regulator commenced reporting on the use of

radiation in research with humans, a total of 7 operator licences and 6 management licences were approved. This is in comparison to 47 operator and 15 management licences being approved in 2002.

- (b) The potential for higher skin doses than envisaged in 1984 has increased due to current techniques such as multiple CT scans and prolonged fluoroscopic screening.

### Uniformity

- 47. Uniformity of radiation controls has been identified as an issue requiring attention. In July 1998, Health Ministers asked that an uniformity panel, comprising representatives from the States, Territories and Commonwealth, be formed to progress national uniformity. The Australian Health Ministers Council agreed in August 1999 to a proposal arising from discussions of the National Uniformity Implementation Panel (Radiation Control) (NUIP(RC)) that all jurisdictions should jointly develop a National Directory for Radiation Protection, through the endorsement of the Radiation Health Committee. The Directory would take a 'dynamic' form, changing over time as new agreements were reached by jurisdictions, and would be used by all jurisdictions in making changes to existing legislation frameworks. The National Directory will facilitate the national adoption of codes and standards developed jointly by States, Territories and Commonwealth.
- 48. The application of the present guidance does not permit this goal of uniformity to be achieved. Variations in requirements across borders create impediments to professionals that move across borders or operate in more than one jurisdiction. Cross-jurisdictional projects such as multi-centre trials, are examples of where the different requirements of jurisdictions would impact on the conduct of trials.

### Information Asymmetry

- 49. Currently most human subjects are provided with explanations of risk developed by researchers. In some jurisdictions, these risk statements have been developed in conjunction with regulators. However, many statements do not appropriately categorise risk for fear of deterring human subjects from participating. This is due to a lack of understanding by most human subjects of the levels of risk from exposure and the corresponding benefit to society. The Victorian regulator has advised that many projects forwarded to the advisory committee for approval are required to make changes to the risk statements for subjects before they are approved.

## Objectives

- 50. To cost-effectively ensure that human subjects and ethics committees are accurately informed of the radiation dose and associated risks.
- 51. To indicate boundaries above which radiation doses from medical research are unlikely to be acceptable
- 52. To promote uniformity across Australia of radiation protection practices in the exposure of human subjects to ionizing radiation for medical research.

## Statement of possible options

53. Three options to address the identified problems have been considered:

- ❖ Option 1 - do nothing and leave the 1984 NHMRC Recommendations in place for use by each jurisdiction as is currently the case
- ❖ Option 2 – allow the researchers to set their own safety requirements and enforce them or allow Government to monitor compliance of an industry developed set of requirements
- ❖ Option 3 - review the 1984 NHMRC Recommendations and develop a Code of Practice with current radiation protection requirements and philosophies which can be adopted into the National Directory as mandatory requirements.

## Impact Analysis

### Affected Parties

54. The main stakeholder groups affected by the proposed Code are

- (a) Hospitals and universities that conduct medical research and as the responsible person will need to monitor application of the Code.
- (b) Ethics committees that approve research projects
- (c) Researchers using ionizing radiation in their research
- (d) Human subjects exposed to ionizing radiation in research
- (e) Regulators in Commonwealth, State and Territory governments that approve and licence the use of ionizing radiation in research.

### Option 1 – Do nothing - continue with the NHMRC RHS 12

#### **Benefits**

55. If no action were to be taken, there would be no cost to government in developing or implementing a new set of requirements. There would also be no change to any compliance costs currently incurred by researchers or research institutions.
56. Parties affected would not be required to change any of their procedures due to NHMRC RHS 12.

#### **Costs**

57. Costs associated with ambiguities in the application of the current guidance (e.g whether therapeutic trials are included) will continue. This will continue to impact on the workload of ethics committees and radiation protection regulators.
58. If no action were to be taken it is likely that radiation doses to subjects may be greater than necessary to achieve the aims of the research. Such higher doses would be likely to be due to:

- the inadequate assessment of the subject dose history by the researcher,
  - the inadequate quality assurance of the radiation apparatus used for research,
  - the inadequate assessment of the radiation aspects of the research proposal by the HREC,
  - the use of dose constraints that allow higher doses for children and infants, and
  - the inadequate understanding of the risks by the subject.
59. Inadequate assessment and understanding of the research proposals could result in information asymmetry between human subjects and researchers and provide a possible avenue for litigation. Reliance on the outdated information in the NHMRC RHS 12 could give rise to claims of inadequate standard of care in radiation protection aspects of research projects.
60. The inconsistency between the NHMRC RHS 12 and RPS 1 would contribute to less than optimal protection for human subjects and continued lack of uniformity across jurisdictions.
61. Researchers conducting multi-centre trials will continue to have to meet different requirements according to which jurisdictions the trials are being undertaken.

#### Option 2 – Self regulation by the industry

62. An example of industry based regulation is a guideline document prepared by the NSW Hospital and University Radiation Safety Officers Group (HURSOG) at the request of the NSW regulator. The guidelines were developed to assist researchers, radiation safety officers, radiation safety committees and Human Research Ethics Committees (HRECs). All ethics committees in NSW have adopted the guidelines. The guidelines have since been revised to reflect changes in NSW legislation
63. No formal evaluation of the effectiveness of the HURSOG guidelines has been conducted and responsibility for approval of projects using greater than 5 mSv continues to rest with the NSW regulator.

#### **Benefits**

64. The HRECs are one of the principle sources of control over researchers. If industry regulation could be enforced through this mechanism it would provide a short-term benefit to Government in not having to prepare or print revised guidance. Governments would also not need to rewrite or amend regulations to refer to revised guidance and resources would not need to be allocated to enforcement issues. A purely industry based solution could enable the industry to respond to problems through outcomes-based risk management approaches.
65. Although the guidelines supplement the NHMRC RHS 12 and reiterates the recommendations on age and dose constraints contained in ARPANSA RPS 1. The guidelines also provide advice on the selection of human subjects, approval procedures for diagnostic and therapeutic applications in clinical research, quality

assurance and review processes, and the appropriate statements of risk for different levels of effective dose.

## Costs

66. Members of Human Research Ethics Committees (HREC) vary according to the originating organisation, are usually not radiation experts and as a result are reliant on external guidance. Networking between HRECs in order to share information on issues such as radiation protection appears to be limited. In addition, although HRECs report annually to the NHMRC Australian Health Ethics Committee (AHEC), reports do not include review of decisions, approval processes for projects using ionizing radiation or compliance with codes of practice in radiation protection.
67. In a recent survey<sup>11</sup> of HRECs by AHEC, committee members advised that with respect to the advice and support function provided by AHEC '*AHEC was not providing an advice function as much as a referral service. It was suggested if AHEC was not in a position to provide more definitive advice to HRECs, it could at least provide some comprehensive lists of names and contact details of experts in different fields who might be able to provide more definitive advice on specific topics.*' Therefore enforcement of agreed standards in radiation protection would not appear to be possible via this network.
68. The HURSOG guidelines are not used by HRECs outside NSW and the NHMRC RHS 12 does not provide sufficient guidance with regard to what advice should be sought to evaluate the use of the ionizing radiation. In Victoria's case, researchers are not guided to NHMRC RHS 12 in preparing submissions to HRECs, so committee members themselves are unlikely to refer to the NHMRC RHS 12.
69. The HURSOG guidelines do not provide guidance for deciding whether exposures to ionizing radiation should be classified as normal patient management, in which case the exposure is not for the purposes of research and other requirements apply. This is distinguished from exposure to additional radiation specifically for the purpose of research, the conditions of NHMRC RHS 12 must be applied. To decide on such matters, ethics committees are still reliant on regulatory mechanisms such as the NSW Radiation Advisory Council. The use of radiation in clinical trials is also subject similar uncertainties.
70. Any short-term benefits to Governments are likely to be outweighed by the following considerations:
  - A self-regulation model requires pro-active behaviour by the industry to organise itself efficiently and effectively, and respond with suitable standards and/or codes of practice. In general, there has been little evidence of this occurring amongst professional bodies unless there is some legal requirement to do so.
  - A self-regulation model may not be effective as there is unlikely to be an adequate method of enforcing compliance.

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<sup>11</sup> NHMRC Stakeholder Evaluation 2002 Human Research Ethics Committees

- Subjects may be less confident that radiation protection issues have been adequately addressed than if an independent regulator established the requirements and may therefore be reluctant to volunteer for research projects. In Victoria, the development of risk statements for human subjects has required a balancing of actual risks and the perception of risks associated with projects using ionizing radiation.
71. There is no single peak industry body that could organise itself to participate in the development of an industry standard. Researchers using ionizing radiation in research with human subjects belong to various professional bodies such as the Royal Australian and New Zealand College of Radiologists (RANZCR), the Australasian College of Physical Scientists and Engineers in Medicine (ACPSEM), the Australian Institute of Radiographers (AIR), the Australian and New Zealand Association of Physicians in Nuclear Medicine (ANZAPNM) and the Australian and New Zealand Society of Nuclear Medicine (ANZSNM). The professions these bodies represent may have inconsistent priorities with regard to radiation safety, which could in turn result in non-uniform standards.
72. Governments would have no direct control over exposure, dose limits and safety procedures. This could be detrimental to the health and safety of subjects and eventually the public if measures to minimise doses to subjects were to lapse.

### Option 3 - implement a revised national code of practice

73. ARPANSA, through its Radiation Health Committee, has developed a proposal for a Code of Practice for the Safe Exposure of Human Subjects to Ionizing Radiation in Medical Research. This proposal follows the review of the previous National Health and Medical Research Council's (NHMRC) Statement for the Administration of Ionizing Radiation to Human Subjects in Medical Research (1984) (NHMRC RHS 12) and addresses the problems outlined earlier in this analysis – outdated information, radiation protection issues, lack of uniformity and information asymmetry.
74. A code of practice would:
- have a set of constraints for specific organs and tissues in accordance with international developments in radiation protection;
  - be consistent with Part 2 and the dose constraints for children of ARPANSA RPS 1;
  - contain guidance material for the categorisation of risk and the corresponding contribution to societal benefit;
  - require researchers to take into account subjects exposure history;
  - clarify responsibilities and streamline current processes for researchers, regulators and ethics committees, and
  - provide a consistent reference for evaluation of risk and development of risk statements.
75. The Code provides a set of requirements that would be adopted by State and Territory regulators as part of their regulatory frameworks in controlling uses of ionizing radiation in research with human subjects.
76. The draft Code was prepared by a working party with representation from the South Australian Environment Protection Agency, the Royal Australian and New Zealand College of Radiologists (RANZCR) and the Australasian College of Physical

Scientists and Engineers in Medicine (ACPSEM), with a secretariat provided by ARPANSA. The draft therefore contains the views of those that would be regulated by such a code and those would use the code to regulate the relevant use of ionizing radiation in research.

## Benefits

77. The draft ARPANSA Code has the following benefits over option 1, retaining the NHMRC RHS 12:

<b>Draft ARPANSA Code of Practice</b>		<b>NHMRC RHS 12</b>
Code of Practice	Sets requirements designed to be used more readily by regulators	Mostly voluntary guidance in the form of 'should' statements
Clause 1.3	Scope includes therapeutic clinical trials	Not clear about exposures from the monitoring of therapeutic clinical trials
Table 1	Cumulative effective dose of 10 mSv over 5 years (in accordance with RPS1);	New constraint - no equivalent in RHS12
Table 1	Equivalent dose of 200 mSv to any organ or tissue, or a portion of any organ or tissue in any year	New constraint - no equivalent in RHS12
Table 1	Total cumulative effective dose of 5 mSv for children to age of 18 years (in accordance with RPS1)	New constraint - no equivalent in RHS12
Table 1	Total cumulative equivalent dose of 200 mSv for children to age of 18 years to any organ or tissue, or a portion of any organ or tissue	New constraint - no equivalent in RHS12
Table 1	Effective dose in any year to age 2 years of 0.1 mSv; and	New constraint - no equivalent in RHS12
Table 1	Effective dose in any year for age 2 to 18 years of 0.5 mSv	New constraint - no equivalent in RHS12
Section 2	Includes responsibilities for the researcher, the subject and the responsible person	Mostly directed at HREC
Sub-section 2.1	The responsibilities for the researcher include seeking the approval of the HREC, obtaining the informed consent of subjects, examine the past radiation dose history of subjects and maintaining records	New clause - no equivalent in RHS12
Clause 2.1.1	Requires the researcher to obtain the approval of the HREC and comply with the requirements of the regulatory authority and the Human Research Ethics Committee	Requires researchers to obtain the approval of the Human Research Ethics Committee (HREC), with responsibility for ensuring the requirements of the regulatory authority being mentioned but not assigned to anyone in particular
Clause 2.1.2	Guidance for researchers in preparing submissions for the HREC is provided	aspects of this guidance were directed at the review process of the HREC

<b>Draft ARPANSA Code of Practice</b>		<b>NHMRC RHS 12</b>
Clause 2.1.2 (d)	An estimate from a medical physicist, of the radiation dose and estimated risk to be provided to HREC	New clause - no equivalent in RHS12
Clause 2.1.2 (e)	The possible benefits to society	New clause - no equivalent in RHS12
Clause 2.1.2 (f)	Statement confirming that an appropriate quality assurance program is in place and that any irradiating apparatus complies with regulatory authority requirements	New clause - no equivalent in RHS12
Clause 2.1.2 (g)	The precautions to be taken to minimise radiation exposure	New clause - no equivalent in RHS12
Clause 2.1.2 (h)	The information and consent form provided to subjects	New clause - no equivalent in RHS12
Clause 2.1.2 (i)	Dose monitoring and record keeping procedures	New clause - no equivalent in RHS12
Clause 2.1.3	Selection of subjects according to the prescribed criteria is now the responsibility of researchers	RHS 12 is not clear whether it is the responsibility of researchers or is overseen by the HREC
Clause 2.1.3 (b)	Selection criteria now include consideration of pregnancy in women of reproductive age and an assessment of the dose to the foetus	New clause - no equivalent in RHS12
Clause 2.1.7 (d)	Researchers must estimate the absorbed skin dose for multiple CT scans or prolonged fluoroscopic screening	New clause - no equivalent in RHS12
Clause 2.1.10	Requires researcher to provide HREC with advice from the regulatory authority where the radiation dose exceeds constraints included in the Code	RHS12 does not specify at what stage of the HREC process the researcher should seek the advice of the regulator
Clause 2.1.13	Requirement for adequacy and correctness of specific elements of the research proposal to be validated by regulator or medical physicist	RHS12 suggests that the HREC seek advice on correctness of the information provided
Sub-section 2.2	Subjects or their guardians are responsible for aspects of participation of human subjects <ul style="list-style-type: none"> <li>➤ Receiving an explanation of the nature and objectives of the project, full understanding of the risks and demonstration of consent.</li> <li>➤ Retaining records of participation and providing previous dose history to researchers</li> <li>➤ The right to terminate participation at any time.</li> </ul>	New clause - no equivalent in RHS12
Sub-section 2.3	The general role of the HREC and evaluation of proposals with attention to: <ul style="list-style-type: none"> <li>➤ Inclusion of verification of the estimated dose from the regulator or a medical physicist.</li> <li>➤ Advice from the regulator where doses exceeds the constraints in the Code</li> <li>➤ the arrangements for record keeping</li> </ul>	New clause - no equivalent in RHS12

	<b>Draft ARPANSA Code of Practice</b>	<b>NHMRC RHS 12</b>
	➤ legal requirements for use of ionizing radiation	
Sub-section 2.4	The responsible person is required to monitor observance of the Code and implementation	New clause - no equivalent in RHS12
Annex 1	Annex to explain assessment of risk and societal benefit to subjects	No equivalent

**Stakeholders are requested to provide information in relation to whether organ dose constraints for ages 2, and ages 2 to 18 also need to be specified (refer Table 1)**

78. The proposed ARPANSA Code would give clear guidance on radiation safety requirements to researchers, Human Research Ethics Committees and human subjects. The specification of responsibilities for researchers in a revised national code of practice may remove additional licensing requirements and therefore reduce the cost of research. For example, in Victoria, researchers are individually licensed. During 2002, 47 operator licences were issued in Victoria in addition to 15 management licences to the institutions where research with human subjects is conducted<sup>12</sup>.

**Stakeholders, particularly from private institutions, are requested to provide information in relation to the likely costs to comply with the requirements of the proposed ARPANSA Code of Practice**

79. The revised guidance would be published as part of the ARPANSA Radiation Protection Series (RPS) and form part of the National Directory. This process would result in a nationally agreed and up to date protocol and would provide national uniformity for relevant research. This would ensure that all stakeholders are aware of their obligations when operating in jurisdictions other than their home jurisdiction. A single, up to date source of guidance, such as would be provided by an ARPANSA code of practice, would enable a uniform approach across Australia to the use of radiation in research with human subjects.

80. The proposed ARPANSA Code refers to Australia's most recent radiation protection standards that in turn incorporate current international protection guidelines using dose limits in ICRP Publication 62 (1993). This includes a detailed description in Annex 1 of the categories of risk in relation to the effective dose and the corresponding level of societal benefit. There is benefit in researchers and ethics committees being able to clearly categorise the risks according to such guidance. This guidance would also reduce uncertainty for researchers seeking ethics committee approval.

<sup>12</sup> In 2003, 45 operator licences and 17 management licences were issued in Victoria

81. All jurisdictions would be able to collectively ensure that the Code is current, by review through the Radiation Health Committee, which includes representatives of all jurisdictions and has the development of national Codes and Standards as part of its role under the *Australian Radiation Protection and Nuclear Safety Act 1998 (Cth)*.

## Costs

82. Much of the proposed code of practice is a consolidation of current advice and best practice for the regulation of relevant research, so the costs would not be expected to increase significantly for the majority of research projects.
83. Implementation of a new code such as that proposed could result in therapeutic trials being regulated where previously they may not have been. This could contribute to the cost of research in this area where regulatory approval is required.

**Stakeholders involved with therapeutic trials, particularly researchers, are requested to provide information on estimated costs to apply, implement, administer or enforce the proposed ARPANSA Code of Practice.**

84. Regulators will incur some additional cost to update licence conditions. This would be a one-off cost and would vary according to the number of licences, particularly in Victoria where researchers as well as institutions are licensed.
85. The proposed changes to the information to be provided to HREC would result in additional work for researchers that could be enforced by the regulator as a condition of licence. This information is currently requested by the HREC based on current guidance. This would result in a shift in the workload from the HREC to the researcher and possibly the regulator. The Victorian Department of Human Services Human Research Ethics Committee advises that researchers would spend an average of one day per project preparing submissions for HREC or the Victorian Radiation Advisory Committee.

## Consultation

86. The proposed Code was developed by a working group of the Radiation Health Committee (RHC). The RHC includes representation of all Commonwealth, State and Territory radiation protection regulators, a person representing the interests of the public and members of medical and academic institutions. All RHC members participated in the development of the proposed Code via their membership of the Committee.
87. The draft Code of Practice has been released for a period of public comment from 11 February until 26 March 2004. Copies of the proposed Code are also available on the ARPANSA web site at [www.arpansa.gov.au](http://www.arpansa.gov.au). The following organisations have been advised of the availability of the proposed ARPANSA Code and this Regulatory Impact Statement and their comments have been requested:
- (a) Radiation Protection Regulators

- (b) Radiation Advisory Committees/Councils
- (c) NHMRC Australian Health Ethics Committee, State Govt Ethics Committees
- (d) University/Hospital: RSO's, HRECs registered with NHMRC
- (e) Professional bodies: RANZCR, ACPSEM, AIR, ANZAPNM, ANZSNM, RACP, the Australian Society for Medical Research

## Recommended Option

88. Option 1 would not meet the objectives as the NHMRC has decided to discontinue its RHS publications and the current NHMRC statement will not be reviewed or updated to be in accord with international guidelines or scientific findings.

89. Option 2 is not tenable for the following reasons:

- (a) The potential for exposure to unsafe levels of ionising radiation is neither a low risk event nor of low significance.
- (b) There is little evidence that the industry can organise itself for self-regulation with respect to radiation protection either through the existing arrangements with the NHMRC AHEC, between HRECs or through researchers professional organisations. Although the NSW HURSOG has developed guidelines in this area, the development was at the request of the regulator and were designed to supplement, rather than replace the national recommendations. The guidelines have not been used outside NSW.
- (c) Through the experience of particularly the Victorian regulator, governments have not found that they can fully divest their responsibility to monitor compliance and take action to remedy non-compliance in matters concerning health and safety, especially those that concern radiation health and safety.
- (d) A purely industry-based solution may enable industry to respond to problems through innovative outcomes-based risk management approaches. However, in the area of radiation safety, an approach that favours prevention of the effects of the potential hazards (exposure to a particular source has a long latency period of 10 to 15 years) would not be compatible with short-term priorities that could arise in competitive environments. The NCP Review of Radiation Protection Legislation did not in general support industry regulated systems due to these competing pressures.

90. On balance, the benefits of option 3 outweigh its costs for the following reasons:

- (a) The proposed Code should not provide any change in exposure of human subjects, as the specified levels of protection in the proposed Code are more specific than those in the NHMRC RHS 12, the proposed ARPANSA Code will ensure that there is no information gap when the NHMRC statement is formally withdrawn.
- (b) Option 3 would facilitate enforcement and monitoring as the code of practice will be incorporated into the National Directory for Radiation Protection, which will be adopted by radiation protection regulators in all States and Territories. This will contribute to uniform regulation of the practice.

- (c) Option 3 enables ARPANSA to be a common reference point for information, advice and clarification for HRECs and other affected parties and would therefore streamline current procedures particularly for cross jurisdictional activities.
- (d) ARPANSA has the resources to ensure that the Code is updated to reflect current international guidelines and scientific research.

91. It is recommended that the proposed *Radiation Protection Code of Practice for safe exposure of human subjects to ionizing radiation for medical research purposes* be incorporated into the National Directory for Radiation Protection.

## Implementation and Review

92. The proposed Code will be published by ARPANSA as a Radiation Protection Series publication. All regulators in the Commonwealth, State and Territory, who manage activities pertaining to ionizing radiation will be expected to adopt the Code by express reference in their regulations.

93. The Code will be reviewed through the ARPANSA Radiation Health Committee within 10 years of its commencement to ensure it is still relevant to the radiation protection needs of the community. Earlier review would be undertaken if there are problems in the implementation of the Code, if international or national radiation protection objectives change or if there is new information from international research.

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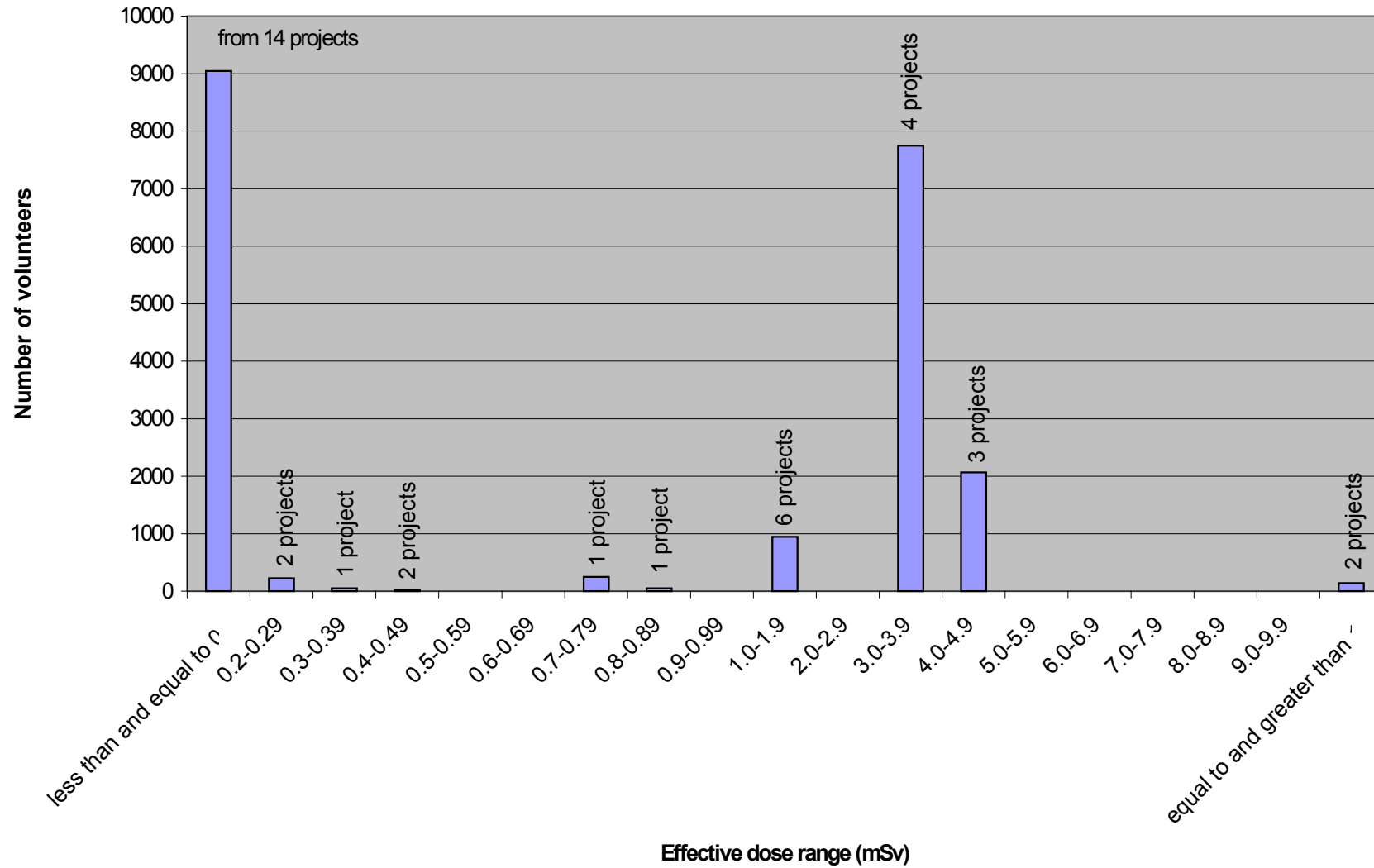
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