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A CODE OF PRACTICE FOR USE IN BIOMEDICAL RESEARCH
INVOLVING THE IRRADIATION OF EMPLOYEES OF THE UKAEA

by

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ABSTRACT

Volunteers have been used in biomedical studies at Harwell since 1964. The procedures to be followed by investigators and the responsibilities of the Head of Environmental and Medical Sciences Division and the Chief of Medical Services were described in the minutes of the inaugural meeting of the Inhalation Studies and Approval Committee. Recently, these procedures have been reviewed and to make them readily available are summarised in this Code of Practice.

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Environmental and Medical Sciences Division
UKAEA Research Group
Atomic Energy Research Establishment
HARWELL

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COLLECTION Institutional Review Board
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FOLDER P.I.A. Anderson IRB No. 87-133
Whole Body Counting of Visitor from
AERE Harwell UK to Measure Residual
Activity from Ba-133 & Ra-226

INTRODUCTION

Volunteers have been used in biomedical research at Harwell since 1964. The purpose of the early experiments involving volunteers was to provide basic information on the fate of inhaled radioactive particles and vapours to enable more precise estimates of radiological dose to be made. Since that time, however, experiments in which radionuclides have been administered to volunteers have been conducted in order to investigate problems in the fields of medicine and of occupational and environmental health.

Experiments involving the use of volunteers at Harwell, were regulated initially by the Inhalation Studies Approval Committee (ISAC, later modified to INSAC). In 1970 INSAC was renamed the Tracer and Irradiation Studies Approval Committee (TISAC) to cover experiments involving the ingestion of radionuclides and the external irradiation of volunteers. This Committee includes medically qualified members with expert knowledge of radiation effects drawn both from the United Kingdom Atomic Energy Authority and other organisations.

The principles governing the use of volunteers were codified in 1964 by the Inhalation Studies Approval Committee in the minutes of the inaugural meeting (ISAC-2). In view of the important ethical considerations inherent in the use of volunteers and the fact that investigators may not be familiar with the procedures evolved at Harwell, it was felt desirable to review procedures and to prepare a code of practice covering the irradiation of volunteers, who are employees of the UKAEA, in which the principles to be followed are stated clearly.

OBTAINING APPROVAL FOR AN INVESTIGATION

INVOLVING THE USE OF VOLUNTEERS

Responsibilities of the investigator

- (1) An investigator must obtain the approval of the Tracer and Irradiation Studies Approval Committee before undertaking any investigation involving the use of volunteers.

... must provide information on the following points:-

- a) Justification for the proposed experiments including details of relevant animal studies.
- b) A summary of experimental procedures.
- c) Estimates of the likely radiological dose either to the whole body, or to the single organ which it is anticipated will receive the greatest dose, with information on how this was derived.
- d) Estimates of the number of subjects involved and whether single or multiple administrations will be used.

Terms of reference of the Tracer and Irradiation Studies Approval Committee

These are as follows:-

- a) To advise the Head of the Environmental and Medical Sciences Division on the suitability and safety of radioactive tracer experiments using human volunteers.
- b) To discuss and approve proposals for experiments.
- c) To review and comment on the results of the experiments.

RADIOLOGICAL DOSE

Responsibilities of the investigator

- (1) The investigator must ensure that the radiological doses incurred by volunteers are as low as possible, commensurate with obtaining the desired experimental information.
- (2) The investigator is responsible for calculating the radiological dose received. An independent assessment of radiological dose may be obtained from the Dosimetry Research Section of the Radiation Physics Group.

Limitations on radiological dose

In the minutes of the inaugural meeting, it was stated that the total dose to any volunteer should not exceed 1.5 rem per year (or the equivalent maximum

permissible organ dose appropriate to non-radiation workers) as a result of such (volunteer) experiments. Although the Medical Research Council have kept the question of dose limits for volunteer experiments under review, they do not publish specific dose limits on the grounds that these have the effect of removing responsibility from the investigator to ensure that the doses used are as low as possible.

In 1972 the World Health Organisation and the International Atomic Energy Agency assembled a group of consultants from several countries which considered the question of dose limits when ionizing radiation is used on human beings for medical research and training. The report of this Committee (1972) has been circulated as a consultative document, but not as a formal publication. The recommendations, therefore, have no legal standing. A summary of this document has been published by the British Institute of Radiology (1975). Among the proposals are that research projects be categorised, corresponding to the level of dose equivalent involved according to the following scheme:-

Category of project	Limits of dose equivalent (rem)	
	Total body	Single organs
I	<0.05	<0.25
II	0.05 - <0.5	0.25 - <2.5
III	0.5 - <5	2.5 - <25
IV	5 - 10	25 - 50

In Category I, the total body radiation permitted would be within the variations of natural background radiation received by the subject annually (i.e. $\sim 10^{-2}$ rem). In Category II, the total body radiation permitted would be of the same order as that received annually from natural sources (i.e. $\sim 10^{-1}$ rem). In Category III the total body radiation permitted to a subject is of the same order of magnitude as the annual limits of radiation permitted by the ICRP for

occupationally exposed persons.

The dose limits proposed by the WHO/IARC for projects will be taken as annual limits for volunteers resulting from all investigations at Harwell. The Head of the EMS Division has formal delegated authority to approve investigations in Category I, subject to minutes decisions of TISAC. Investigations in Category II must also be approved by TISAC and in addition, the Head of the EMS Division must consult the Director of the Atomic Energy Research Establishment, Harwell.

OBTAINING VOLUNTEERS

Responsibilities of the investigator

- (1) An investigator must not ask people directly to participate in experiments.
- (2) Volunteers may be obtained by advertising.
- (3) Pregnant women or people below the age of 18 years must not be used as volunteers.
- (4) No financial inducement shall be offered to volunteers except to ensure that there shall be no loss of earnings as a result of taking part in an investigation.

By advertising in the Harwell Bulletin, the Inhalation Toxicology Group of the EMS Division has obtained a panel of people who, in principle, are willing to participate in investigations. Members of this panel are circulated with details of specific experiments and asked if they will volunteer. At the same time, it is made quite clear that they may withdraw from the experiment at any time if they change their mind. One advantage of this system is that, as many of the volunteers are not members of the EMS Division, the problem of special relationships between investigator and volunteers is reduced.

In the event of a query by a volunteer's superior officer or manager, the Head of the EMS Division will send the relevant Division Head the letter shown in Appendix I, with a copy to the volunteer's superior officer or manager.

Responsibilities of the Chief of Medical Services (or Medical Officer nominated by him)

- (1) The Chief of Medical Services is responsible for ensuring that volunteers are medically fit to participate in the proposed investigation. A note to this effect will be made on the volunteer's medical record.
- (2) The Chief of Medical Services is responsible for obtaining informed consent from volunteers and must also satisfy himself that such consent has been given freely.
- (3) The Chief of Medical Services is responsible for completing the Volunteer Consent Form shown in Appendix II and for ensuring that it is signed both by the volunteer and by himself.

Responsibilities of the investigator

- (1) The investigator is responsible for preparing the necessary volunteer consent forms (see Appendix II) and filling out the details of the investigation which must include (a) the purpose (b) the appropriate TISAC paper reference (c) the method of administration (d) the radionuclide(s) involved (e) the approximate total activity administered (f) the estimated total dose to the relevant critical organ(s) and (g) whether single or multiple administrations are involved.

The general ethical principles involved in investigations on human subjects have been discussed in a statement by the Medical Research Council (1964). The distinction between procedures contributing to the benefit of the individual and those which have no direct benefit is carefully drawn. Investigations of the type carried out at Harwell generally fall into the latter category. The MRC, which had in mind the wide range of new treatments and investigations in present day medical research, pointed out that "the possibility or probability that a particular investigation will be of benefit to humanity or to posterity would offer no defence

in the case of legal proceedings. It is always necessary, therefore, to ensure that the true consent of the subject is obtained explicitly. By true consent is meant consent freely given, with proper understanding of the nature and consequences of what is proposed. Assumed consent, or consent obtained by undue influence, is valueless and in this latter respect, particular care is necessary when the volunteer stands in special relationship to the investigator. Written consent unaccompanied by other evidence that an explanation has been given, understood and accepted is also of little value."

RECORD KEEPING

Responsibilities of the investigator

- (1) The investigator must inform the Head of Medical Records of every experiment involving the use of a volunteer by completing the appropriate form (see Appendix III) and returning it within one week of the experiment.
- (2) The investigator must ensure that the subject's cumulative dose from all investigations in the current calendar year shall not exceed 50 mrem to the whole body, or 250 mrem to any single organ.

Responsibilities of the Head of Medical Records

- (1) The Head of Medical Records shall keep a register of all experiments involving the use of volunteers. The register will include (a) the name of the investigator and volunteer (b) the reference number of the appropriate TISAC paper (c) the radionuclide and activity retained and (d) the radiological dose to the critical organ.
- (2) The Head of Medical Records will also record the cumulative dose to the volunteer in the current calendar year and, if this exceeds 50 mrem to the total body, or 250 mrem to any single organ, he will notify the Chief of Medical Services.
- (3) The Head of Medical Records will enter details of dose incurred in

each volunteer's medical record at the end of the calendar year or, if a volunteer leaves the employment of the UNRISA, at the time of leaving.

The purpose of a central register of all investigations using volunteers is to ensure that, in cases where a volunteer is being used by more than one investigator, an accurate record of cumulative dose is maintained.

References

Report of a WHO/IAEA consultation on the use of ionizing radiation on human beings for medical research and training including the use of radioactive materials (1972) WHO/PRL 73.1. (This is an unpublished WHO document copies of which may be seen on request).

Irradiation of human subjects for medical research (1975) British Institute of Radiology Bulletin 1/2 p.4.

Responsibility in investigations on human subjects. Statement by the Medical Research Council (1964) Report of the Medical Research Council for the year 1962-1963, HMSO.

STAFF IN CONFIDENCE

Letter notifying a volunteer's Division Head and superior officer/manager that he wishes to participate in an experiment

A member of your Division Dr/Er, has volunteered to take part in an investigation involving the administration of a radionuclide. This investigation has been approved by the Tracer and Irradiation Studies Approval Committee (the AERE Ethical Committee). Management at Harwell has sanctioned the use of volunteers in biomedical research, provided that prior approval of the Ethical Committee is obtained.

Each volunteer is fully acquainted with the nature of the procedures involved and the associated risks and is given a thorough medical examination to ensure that he is fit to participate. A volunteer may withdraw his consent at any time if he so wishes.

I trust that you will agree to this volunteer's participation. Provision can be made for the time spent by a volunteer to be booked against the appropriate project number.

Appendix II

STAFF IN CONFIDENCE

Purpose of investigation

Authorisation

TISAC paper reference

Minute reference

Details of investigation

Radionuclide(s) administered

Likely number of administrations

Total activity administered

Anticipated total dose(s) to critical organ(s)

Name of investigator

Signed

Date

VOLUNTARY CONSENT

The nature of the study and its possible hazards have been fully explained to me by Dr I hereby consent to take part and to carry out the procedures outlined above. It is understood that I may withdraw at any time from participation in the study.

Name

Signed (Volunteer)

Date

I confirm that I have explained the nature of the investigation described above to this volunteer.

Name

Signed (Medical Officer)

Date

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Appendix III

STATE IN CONFIDENCE

To Head of Medical Records

Dose record for volunteer experiment

Name of Volunteer

TJSAC approval reference

Date of experiment

Radionuclide(s)

Activity retained

Critical organ(s)

Calculated dose to critical organ(s)

Name of investigator

Signed

Date