PROJECT FINAL REPORT

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Executive summary

With support from the European Commission, an international group of experts and advisors within the project "ARCH: Agenda for Research on Chernobyl Health" reviewed the health consequences of exposure to radiation from the Chernobyl accident and provided advice on the studies needed to be carried out in the future. The main outcome of the ARCH project is a proposal for a Strategic Research Agenda (SRA)[1], outlining a reasoned long-term plan for research into the health consequences of radiation from the Chernobyl accident.

The ARCH report concludes that there are many reasons why even now, 25 years after the accident it is important that a long-term coordinated research programme on the health effects of the Chernobyl accident be supported. Health effects from the accident continue and future effects are uncertain; past knowledge of radiation effects is largely based on atomic bomb studies, but Chernobyl involved a different type and pattern of exposure; assumptions on the risk of low dose exposure have been challenged by recent advances in radiobiology; estimates of deaths due to the Chernobyl accident vary widely.

The ARCH group of experts and advisors therefore recommended international support for the long term funding of a Chernobyl Health Effects Research Foundation (CHERF), for reasons similar to those that led to the creation of the Radiation Effects Research Foundation (RERF) some years after the atomic bomb exposures in Japan. The proposal is not to create a centre with dedicated research staff similar to the RERF, but to set up a mechanism to coordinate and fund studies that will enable assessment of the overall long-term health effects of this disaster. A key to the success of the ARCH recommendations is the creation, maintenance and follow-up of Life Span cohorts. These include already existing cohorts exposed to fallout as children in Belarus and Ukraine with detailed thyroid dose measurements as well as cohorts of liquidators. CHERF could be a virtual institute consisting of a Management Board with representatives of the funding organisation(s) and the countries most involved, both inside and outside the EU, and a Scientific Advisory Board which would help determine priorities for funding and advise the Management Board on projects that should be supported.

As well as suggesting the creation of the Chernobyl Health Effects Research Foundation, the ARCH group has highlighted the importance and prioritised a series of individual studies covering the main health consequences. Following a detailed review of current Chernobyl-related research findings, a list of proposals of major scientific and public health importance has been developed. During the development of these proposals stakeholders, including the general public, national and international bodies, were invited to contribute to the assessment of the proposed research on the better understanding of effects of radiation, particularly low dose and low dose rate radiation, and implications for public health decision making.

The proposed studies address the ongoing thyroid cancer problem, the apparent rise in breast cancer, inherited molecular-genetic alterations, and various cancers, cataracts and other non-cancer diseases in liquidators and in the general exposed population. Long-term studies of already existing groups with known radiation doses would provide invaluable information on the life-time risks of both external and internal exposure.

Unless coordinated studies are set up, together with a mechanism to ensure long-term funding, the long-term consequences of a nuclear accident involving the exposure of many millions of people to radiation will not be properly studied, speculation will flourish, and knowledge essential to assessing the risks of radiation exposure will be lost.

[1] http://arch.iarc.fr/documents/ARCH_SRA.pdf

List of Partners

International Agency for Research on Cancer (IARC), Lyon, France

Centre de Recerca en Epidemiologia Ambiental (CREAL), Barcelona, Spain

Dr Keith Baverstock, Bonn, Germany

Introduction

It is now 25 years since the Chernobyl accident, and, while a number of reviews of the health consequences of the accident have been made (*1-3*), there is controversy over its consequences to date, and considerable variability in the assessment of the potential consequences in the future (*4*) (*5, 6*).

There is general agreement on the importance of the demonstrated health effects to date, particularly thyroid carcinoma. Studies of the atomic bomb exposures in Japan show the importance of late and unexpected consequences of radiation exposure, particularly solid cancers, for which a significant increase was not established until more than 25 years after the bombs, and cardiovascular complications which were first recognised more than 40 years later (*7, 8*).

The reported rise in the incidence of other cancer and non-cancer diseases in areas of high fallout after Chernobyl suggests that other potential effects may occur in the future. The Agenda for Research on Chernobyl Health (ARCH) project was therefore created to advise on the scientific strategy needed for further research on the health consequences of the Chernobyl accident.

Objectives

Given that any investigations will take place against a background of claims and counterclaims from individuals and organizations that have a vested interest in either exaggerating or downplaying possible health effects from the Chernobyl accident, it is necessary to devise a strategy for further Chernobyl research that takes these problems into account. This strategy was developed on the premise that any future research should address the following important objectives:

- health improvement in those exposed to Chernobyl or to future nuclear accidents;
- a realistic assessment of present and future health consequences to aid health planning for those exposed after Chernobyl, and after future accidents; and
- improved understanding of radiation effects and direct future radiation protection measures.

These are wide-ranging objectives and to achieve them ARCH built on existing reviews, new results and the knowledge and experience of experts. With the help of the Expert Group and Advisors, the ARCH Core Group outlined a practical strategy combining epidemiological studies using large-scale surveillance with studies focused on specific issues.

Issues that were addressed by ARCH include:

- are there sufficient grounds for health monitoring aimed at detecting currently unrecognised effects of radiation?
- what investigations, if any, might provide sufficient information to corroborate or alter our current understanding of radiation effects, including germ-line effects?

It is with this background that ARCH assembled a group of experts with knowledge on the health consequences of the Chernobyl accident that is dispersed throughout Europe and among the three most affected countries. The main objective of the conducted 'scoping study' was not only to advise

on future needs for research but also on its potential value for public health decision making in the affected countries.

Description of work

To meet the aims for which ARCH was supported by the Commission the work was carried out by a Core group and a Group of Experts and Advisors.

Core group

The Core group was composed of those who conceived the proposal to the Commission. They were responsible for the overall organisation of the study, for writing the documents, in collaboration with members of an Expert group and advisors (see the description below), for modifying them in the light of the comments of the experts and advisors, and then, when priorities had been agreed by the Expert group, making final changes to meet the comments of the external reviewers (see also the description below).
The Core group consisted of the following members:

- Keith Baverstock, radiobiologist, University of Eastern Finland
- Elisabeth Cardis, epidemiologist, CREAL, Barcelona
- Ausrele Kesminiene, epidemiologist, IARC, Lyon
- Dillwyn Williams, pathologist, University of Cambridge.

Expert group and advisors

The Expert group included leading experts with considerable experience in the follow-up of the health consequences of the Chernobyl accident and representing the essential complementary disciplines: epidemiology, radiation biology, medicine (in particular endocrinology), dosimetry, pathology. The names were approved by the EC. They were chosen to cover all health aspects of the consequences of radiation exposure and included representatives of the three most affected countries and the EU. Members:

- Keith Baverstock, University of Eastern Finland (radiobiology and public health)
- Dmitryi Bazyka, Radiation Research Centre, Ukraine (epidemiology)
- Elisabeth Cardis, CREAL, Spain (epidemiology)
- Vadim Chumak, Radiation Research Centre, Ukraine (dosimetry)
- June Crown, UK (public health)
- Yuri Demidchik, Belarusian Medical Academy of Postgraduate Education, Belarus (thyroid treatment)
- Yuri Dubrova, University of Leicester, UK (genetics)
- Victor Ivanov, MRRC, Russia (epidemiology and risk assessment)
- Ausrele Kesminiene, IARC, France (coordination, epidemiology and medicine)
- Semyon Poliakov, RSPC MT, Minsk, Belarus (cancer registration and public health management)
- Christoph Reiners, University Wurzburg, Germany (thyroid treatment)
- Margot Tirmarche, IRSN, France (epidemiology)
- Klaus Trott , Gray Cancer institute, UK, (medicine, non-cancer effects)
- Dillwyn Williams, University of Cambridge, UK (pathology and mechanism of cancer)

Scientists with significant experience in radiation research were also included as **advisors** to ensure harmonization with other existing or planned activities around the world:

- André Bouville, NCI, US (dosimetry)
- David Brenner, Columbia University, US (radiobiology)

- Vladimir Drozdovitch, Belarus, currently at NCI, US (dosimetry)
- Ian Fairlie, UK, (environment)
- Bernd Grosche, Federal Office for Radiation Protection, Germany (epidemiology)
- Sisko Salomaa, STUK, Finland (radiobiology)
- Richard Wakeford, University of Manchester, UK (epidemiology)
- Shunichi Yamashita, University of Nagasaki, Japan (thyroid diseases),

as well as the UNSCEAR secretary, Malcolm Crick and Zhanat Carr, WHO, Geneva.
The members of the Expert group and advisors met on three occasions. They reviewed and completed, when appropriate, in their area of expertise, draft position papers and documents prepared by the Core group and agreed on the priorities.

External peer review group

Members of the peer review group are recognised experts in epidemiology, biology (radiobiology) and public health but otherwise not involved in ARCH and not specifically linked to work on Chernobyl. They were therefore able to give an independent assessment of the quality of the SRA, and on the relevance of the proposals to radiation health effects generally. The candidates were nominated during the first meeting of the Expert group and advisors. They were sent the completed Strategic Research Agenda at the end of the project, and returned their comments and suggestions which were acted upon by the Core group. The Core group took into account their comments, suggestions and criticisms in drafting the final version of the Research Agenda.

Position papers and outlines of a Strategic Research Agenda, and a wide range of possible projects suggested by the Expert Group were prepared by the Core group. The members of the Expert group and advisors reviewed, completed, when appropriate, in their area of expertise, draft position papers and documents prepared by the Core group and agreed on the priorities.

The proposals and the prioritisation evolved during three meetings and by correspondence until overall agreement was reached on the SRA and on the projects and their prioritisation.

Main achievements

In more detail, the work consisted of:

- Overview of current knowledge, ongoing projects and existing research recommendations and preparation of list of research questions which could in principle be answered by studies of Chernobyl consequences

- Overview of list of research questions agreed by expert group (type and design of study, requirements in terms of dosimetry, follow-up, biological markers and statistical power) and preliminary prioritisation

- Identification of current ("fast-tracked") research priorities, i.e. research that is both urgent and of demonstrated feasibility (prepared as Deliverable 1 and submitted to the European Commission).

- Identification of medium- and long-term research priorities, i.e. important research areas where studies cannot be conducted at present either because they would not be sufficiently informative yet or because feasibility/pilot work is needed before they can start; these may be the object of a further funding application;

- Assessments of strategic resource needs, added benefits over existing work, expected outcomes, timelines, risks, key assumptions about external factors for success;

- Development of project proposals.

The proposals for inclusion in Deliverable 1 were prioritized based on the following criteria:

1) Study of high scientific and social importance which if funded could start shortly;
2) Valuable work in progress which would collapse without urgent support;
3) Infrastructure forming an important resource for current and/or future projects, including those requiring urgent political discussion rather than short term financial support.

The work under ARCH has resulted in two main documents:

- the Strategic Research Agenda (SRA) – Deliverable 2
- and the Technical report – Deliverable 3.

Strategic Research Agenda

The Strategic Research Agenda (SRA) is the main document developed within the project to ensure that the health effects, short and long-term, of the Chernobyl accident are comprehensively studied.

To meet the objectives outlined above, the Expert Group recommended with high priority a number of infrastructure projects, including lifespan cohorts and tissue banks.

The Expert Group recommended that the following Chernobyl lifespan cohorts should be supported:

a) Liquidator cohort. Their exposure was largely to the whole body, but at a much lower dose rate than after the atomic bombs. The numbers (over 600,000) are much greater than in the atomic bomb survivors Life Span Study (89,000), so that a large cohort with a wide range of low to moderate doses could be formed from existing liquidator cohorts, making it a population which is likely to be most informative, with great statistical power, for the study of cancer and non-cancer effects in adults at exposure. Liquidator registries are maintained in the three most affected countries and in the Baltic States; dose information is available for the majority but needs validation.

b) Children at exposure cohort. Millions of children were exposed to fallout after Chernobyl, but only for a minority is individual dose information available. However a cohort of approximately 25,000 children from Belarus and Ukraine with detailed thyroid dose measurements has been collected as part of the BelAm and UkrAm projects with the original intent of following thyroid diseases only (23;24). With the appropriate cooperation and support this cohort could provide the basis for a long-term study of the cancer and non-cancer consequences of exposure to radiation from fallout.

The Expert Group recommended that the feasibility of setting up other potentially important cohorts be evaluated: a cohort of offspring of liquidators so that inherited effects can be studied and a cohort of evacuees from the control zone (in particular children exposed directly or in utero) who were exposed internally to very high levels of fallout for up to 15 days.

The Expert Group also recommended that a tissue bank be created or the existing thyroid tissue bank extended, to keep tumour and normal tissue and blood samples from the cohort studies, and make these available for future research studies. The bank could also preserve nucleic acids and immortalized lymphocytes from families with exposed parents and unexposed children to allow study of inherited effects.

Finally, to fully profit from the Chernobyl experience, the Expert Group emphasized that coordinated and long-term efforts are urgently needed. Although 25 years have passed, it is still not too late to

form a 'Chernobyl Life Span Cohort' as many important diseases, both cancer and non-cancer, have such long latent periods that the outcomes are expected for years to come.

To meet the need for comprehensive long-term studies with similar aims to those of the RERF a Chernobyl Health Effects Research Foundation (CHERF) should be set up. CHERF could be a virtual institute consisting of a Management Board with representatives of the funding organisation(s) and the countries most involved, both inside and outside the EC, and a Scientific Advisory Board which can use the ARCH strategic agenda to help determine priorities for funding and advise the Management Board on projects that should be supported. Particular attention should be paid to long-term maintenance of the infrastructure projects needed to support a range of studies. CHERF should be subjected to quinquennial external review by international advisors in the field but not receiving grant support for Chernobyl studies. This review would take into account the dissemination of outcomes of the work supported and the adequacy of the research strategy.

The Expert Group recommends that the EC should take the initiative in creating CHERF, with the following aims:

(a) to initiate and support the conduct of comprehensive research on the health effects of the Chernobyl accident,

(b) to provide and disseminate an accurate unbiased assessment of the long-term consequences of the Chernobyl accident,

(c) to provide public health organisations with the information needed to mitigate the consequences in the event of any similar exposure to radiation,

(d) to deepen scientific understanding of the interaction of radiation with tissue, with special attention to internal exposures,

(e) to inform radiation protection organisations of the short and long-term consequences of the Chernobyl accident relevant to radiation protection standards.

ARCH Technical report

The ARCH Technical report is the document that complements and supports the SRA. It includes very detailed reviews of the state of the art and questions arising from Chernobyl, and motivated specific project proposals, including those for the formation of the life-span cohorts to facilitate both general surveillance of the consequences and the individual more focussed studies. The Expert Group felt that these proposals were essential for the short, medium and long-term to maximise the information that can be drawn about radiation effects from the Chernobyl accident. The report includes all projects identified at the first Expert Group meeting and assessed in terms of their feasibility, importance (scientific and social) and priority for implementation. Each project contains details on the proposed type and design of the study, requirements in terms of dosimetry, follow-up, biological markers and statistical power) and prioritization. The following research areas were suggested:

- Improvements of infrastructures - Chernobyl life span cohorts:
  - ✓ cohorts of children with measured thyroid activity
  - ✓ cohorts of Chernobyl liquidators
  - ✓ evacuees and offspring of liquidators and evacuees
- Tissue banks
- Inventory of dosimetric information for population groups most affected by the Chernobyl accident
- Thyroid cancer and thyroid diseases

- Leukaemia and lymphoma
- Other tumours than thyroid (benign and malignant)
- Radiation-induced cataracts
- Cardio-vascular and cerebro-vascular diseases
- Immunological effects
- Acute radiation syndrome survivors
- Non-targeted radiation effects in Chernobyl populations including preconceptional irradiation
- Mental retardation following in utero exposure as a result of the Chernobyl accident

In addition, recent advances in radiobiology and their relevance to the consequences of the Chernobyl accident have been considered by a subgroup of ARCH.

Potential impact

The main outcome of the ARCH project – the SRA proposes long-term strategy for Chernobyl health research. If implemented, this strategy will allow:

- better planning for health improvement of those exposed after Chernobyl,
- accurate information on the consequences of the Chernobyl accident to replace the present uncertainty,
- informed health planning for prevention and care for those exposed after future accidents,
- collection of information important for radiation protection measures and
- improved understanding of radiation effects, particularly the relationship between low dose exposures and health effects.

The unprecedented nature of the Chernobyl accident allows studies that can improve our understanding of the interaction of radiation with living tissue and the consequences that follow.

Clearly it is imperative that the public health consequences of the Chernobyl accident are fully known to provide the knowledge base for decision making in defining public health policies, radiation protection and the management of future accidents. Studies to date have already provided information of considerable value, but there are areas where studies have produced conflicting results. A generally accepted assessment of all health consequences for both the liquidators and the general population covering the first 25 years after exposure is lacking. Comprehensive studies are needed for the lifespan of those exposed, and studies with a negative result are important in defining risks.

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