

**SUPPORT AND MANAGEMENT FOR THE PROJECT:
"EFFECTS OF THE CHERNOBYL ACCIDENT ON THYROID CANCER AND LEUKEMIA/LYMPHOMA"
CONTRACT BETWEEN NATIONAL CANCER INSTITUTE AND THE TRUSTEES OF
COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK
QUARTERLY PROGRESS REPORTS, SEPTEMBER 30, 1999 - DECEMBER 31, 1999**

I. INTRODUCTION

This report covers activities carried out during the first quarter of the third year of the contract between the National Cancer Institute (NCI) and Columbia University for the support of studies of thyroid cancer in children in Belarus and Ukraine and leukemia and lymphoma in clean-up workers in Ukraine.

With regard to the thyroid studies, the focus has been on recruitment of study subjects and the maintenance of the subjects in the screened cohort. Establishment of a more adequate data management system in both countries has been of high priority since this is critical in terms of monitoring progress and assuring quality control. Quality assurance and control continue to be of high priority on the clinical side together with the evaluation of which procedures will be necessary for the re-screening examination.

With regard to the study of leukemia and lymphoma in the clean-up workers in Ukraine, emphasis has been placed on the compilation and finalization of the report on Phase I of the leukemia study together with the formulation of a protocol for a possible Phase II study. Work on dose assessment continues to be of high priority.

II. OUTLINE OF MAJOR ACTIVITIES

1. Thyroid Studies:

A. Bi-national Advisory Committee Meetings in Minsk, Belarus, October 11-12, 1999, and Kiev, Ukraine, October 14-15, 1999:

Members of the Columbia team (Drs. Howe, Brill, Fink, Mitchell, and McConnell) met with the Bi-national Advisory Committee together with colleagues from NCI, Belarussian and Ukrainian thyroid studies to review on-going study procedures and progress to date in the two thyroid studies.

B. NCI/Columbia Joint Meeting at Columbia University, November 5, 1999, Regarding Data Management Issues:

Members of the Columbia team (Drs. Howe, Heitjan, Zablotska and Professor Burch and Ms. Simakovsky) met with NCI (Drs. Beebe, Brenner, Luckyanov, Ron and Thomas) to formulate a strategy to institute a more efficient data management system in the data control centers of the two thyroid studies in order to better monitor the on-going progress in those studies, assure quality control, safeguard the storage and retrieval of study forms and to ensure the smooth transition from present screening procedures to re-screening.

C. NCI/Columbia University/Ukrainian and Belarussian International Meeting, Bethesda, Maryland, November 8-10, 1999.

Members of the Columbia Team (Drs. Howe, Brill, Fink, Greenebaum, Heitjan, McConnell, Zablotska, Ms. Hodgson, Ms. Simakovsky and Professor Burch) attended meetings with NCI and colleagues from the Ukrainian and Belarussian thyroid studies to review study progress to date. Although the meetings were formal in nature, with presentations from our Ukrainian and Belarussian colleagues, it did afford all personnel on the studies to meet one another and informally discuss problems and possible solutions and fostered closer collaboration between the Belarussian and Ukrainian thyroid investigators.

D. Individual Trips by Columbia Team Members:

A number of Columbia team members made trips to Belarus and Ukraine during the quarter and detailed reports for these trips have been forwarded to NCI. Copies of these trip report are available upon request. The following trips were made:

- ▶ Dr. Howe and Professor Burch: November 22-23, 1999, Minsk Belarus; November 25-26, 1999, Kiev Ukraine
- ▶ Drs. Fink, Greenebaum and McConnell: November 29-30 1999, Minsk, Belarus; December 2-3, 1999, Kiev, Ukraine.

Please see Appendix A for a brief summary of these trips.

2. Leukemia/lymphoma Study:

A. Leukemia Working Group: Drs. Howe and Finch attended meetings of the Leukemia Working Group at NCI on October 19, 1999 and November 15-16, 1999 to review the work done in the Phase I study with the possible aim of proposing a full cohort study (Phase II).

B. International Dosimetry Group: Dr. Howe attended a meeting of this group in Lyon, France on October 25-26, 1999 to review dosimetric calculations and the inter-comparison of the various methods for dose assessment.

C. NCI/Columbia University/Ukrainian International Meeting, Bethesda, Maryland, November 15-16, 1999. Drs. Howe, Finch and Littlefield attended meetings with NCI and colleagues from Ukraine to review study progress to date in the Phase I study of leukemia in clean up workers in Ukraine and to discuss the compilation of the final report on Phase I together with the proposal for a possible Phase II study.

D. Members of the Columbia team (Drs. Howe and Finch and Professor Burch) together with colleagues from NCI and Ukraine edited and finalized the report on Phase I of the study of leukemia in clean up workers in Ukraine. The report was sent to NCI, on December 21, 1999.

E. Dr. Howe was asked by NCI to take the lead from the US side in preparing a proposal for a possible Phase II study of leukemia in clean up workers in Ukraine in collaboration with colleagues from NCI and Ukraine

III. UNIVERSITY OF UTAH SUBCONTRACT

This progress report covers the work on dosimetry performed under the subcontract with the University of Utah for the first quarter of the third year of the contract.

Intercomparison:

The power supply for the EPR spectrometer at the University of Utah has now been repaired and the final samples for the USCRM/UU intercomparison (see Q3 1999 progress report) are being analyzed. The goniometer has not yet been repaired however the samples are being analyzed using manual rotation of 90° at 5 minute intervals. Analyses should be completed by the 2nd week in February.

ICRU Biodosimetry Writing Group:

The ICRU biodosimetry writing group met at the University of Utah in December, 1999. The meeting was the last scheduled for the group. A section on EPR sample collection and documentation by Dr. Chumak has been added. Final changes to draft reports are due February 15th.

IAEA CRP on EPR Dosimetry:

The IAEA CRP on EPR Dosimetry has completed its first draft. The report will be a detailed compendium of all aspects of EPR dosimetry of tooth enamel. The draft report will be sent on request.

IV. OUTLINE OF ADMINISTRATIVE ACTIVITIES

The primary focus of the administrative team was processing the purchasing of requests from Belarus and Ukraine for their upcoming year. Each request was assessed in consultation with relevant members of the Columbia scientific team, consultants and NCI and vendor bids were assembled. The final review of purchase requests were made at the November 1999 International Meeting of NCI/Columbia/Belarus/Ukraine scientists in Bethesda, Maryland.

The secondary focus of the quarter was the hiring of a Russian-speaking computer programmer, Irina Simakovsky. Ms Simakovsky was introduced to NCI and Belarus/Ukraine scientific staff at the international meeting held in Bethesda, Maryland, in November 1999.

Other activities occurring during the quarter included completion of the Annual Report for Year 2 (submitted on October 27, 1999), and preparation for trips and meetings as well as ongoing translations. On December 13, Drs. Howe and Sohn and Ms. Hodgson attended a reverse site visit at NCI to review Year 2 and discuss Year 3 of the Contract. Ms. Hodgson indicated that the next financial report (2706), to be submitted in January, 2000, will reflect her projections for purchasing and indicate the need for additional funds.

Please see Appendix B for Table 1: Timeline for the First Quarter of Year 3

V. FUTURE ACTIVITIES

It is anticipated that future activities will center on the maintaining and increasing "on the ground" involvement of the Columbia team in the two thyroid studies and the leukemia study, should it be funded. Frequent visits by members of the Columbia team to Belarus and Ukraine will be necessitated by the need to monitor recruitment of study subjects and the maintenance of those already screened and to implement the establishment of a new data management system in the two thyroid studies.

Members of the Columbia team will continue input in order to assess on going quality control in the thyroid studies.

Plans for the next quarter include:

A. Finalization by Dr. Howe and others of the proposal for a possible Phase II study of leukemia in clean up workers in Ukraine in conjunction with colleagues from NCI and Ukraine. This will involve direct contact between Dr. Howe and the Ukrainian investigators during several visits to Kiev.

B. Several trips to Kiev by Dr. Howe to Kiev. A trip in January will focus on data management in the thyroid study and the leukemia Phase II proposal. During this trip Dr. Howe will also co-chair a meeting of the dosimetry groups from Belarus and Ukraine. A second trip in February will involve a workshop on cohort analysis using the EPICURE computer program (see below), data management in the thyroid study and the leukemia Phase II proposal. A third trip in March will focus on data management/epidemiology in the thyroid study and the proposal for a Phase II study of leukemia.

C. A trip by Dr. Howe in March to attend the International Dosimetry Group meeting in Lyon, France.

D. Establishing a subcontract with the University of Illinois to expedite the back log in data entry in the thyroid study in Ukraine.

E. A training workshop on cohort analysis using the EPICURE computer program in Kiev, Ukraine, February 14-18, 2000, with attendance of approximately 15 relevant individuals from the three cohort studies in Belarus and Ukraine, taught by Dr. Michael Vaeth who is an expert on analyzing radiation data using the EPICURE program. Dr. Vaeth is Chairman of the Department of Biostatistics, University of Aarhus, Denmark.

F. A trip to Minsk, Belarus, by Drs. Brill and Mitchell to set up the ultrasound image archiving, retrieval and distribution systems. Drs. Brill and Mitchell plan to coordinate the work with the Ukraine data control center so that the same systems will be in place based on a single investment in the tools rather than separate different implementations. The media generated will be used to transfer images in support of the ultrasound quality control scheduled for this year.

G. The clinical team (Drs. Fink, Greenebaum and McConnell) is planning to re-emphasize the need for in depth meetings between the endocrinologists, cytologists, sonographers, pathologists and surgeons in both Kiev and Minsk. The importance of having the mobile teams perform needle aspiration of palpable nodules will be reiterated in communication with the relevant personnel in both study areas together with the importance of monitoring patients taking thyroxine for suppression of nodular goiter. Belarussian and Ukrainian laboratory results will be continually compared on an ongoing basis.

H. Purchase orders for supplies and equipment for delivery to Belarus and Ukraine will continue to be assessed and finalized. In this regard, it is expected that Dr. Masnyk together with Ms. Hodgson and Dr. Fink will travel to Belarus and Kiev sometime in March to review purchasing procedures, local vendors and prepare for an equipment inventory.

APPENDIX A

SUMMARY OF INDIVIDUAL TRIP REPORTS

1. Dr. Howe and Professor Burch, November 22-23, 1999, Minsk, Belarus

A number of issues were discussed with colleagues in the thyroid study in Belarus with particular emphasis on the acquisition of upgraded hardware/software for the DCC, improvements in the storage and retrieval of study forms, preparation of documentation for quality control procedures, utilizing SAS programs to produce reports, the necessity for American colleagues to gain access to the database structure and the database itself, and the issue of the time frame for re-screening. In this regard it was agreed that re-screening will take place yearly for participants up to the age of 18 years and after that will be once every two years.

2. Dr. Howe and Professor Burch, November 25-26, 1999, Kiev, Ukraine.

Three major issues were discussed with members of the thyroid study. The first was the contracting out to the University of Illinois's unit at the Pediatrics Institute data entry in order to reduce the serious backlog in data entry. Specific guidelines for data management and data entry in order to ensure quality control and limit loss of data were outlined. Secondly, selection rules for a Phase II sample of the cohort were discussed with the anticipation that this will be complete in early 2000 with location procedures in place so that screening of the new selection can start by April 1, 2000. Lastly, meetings were held with staff of the Kiev International Institute of Sociology which has been contracted to carry out as soon as possible focus groups amongst study participants and non-participants in order to gauge awareness of the study and to evaluate invitation and screening procedures. It is anticipated that the focus groups together with the training of study recruiters in inviting potential cohort members for screening will be complete by the end of December, 1999. Results of this activity will be reported in the next quarterly report.

3. Dr. Fink, November 29-30, 1999, Minsk, Belarus

Dr. Fink's time was spent reviewing laboratory activities and quality control results. The need for a normal range study was stressed at the time of his visit. The issue of supplies was discussed with Dr. Petrenko and Stezhko together with clinical issues.

4. Dr. Fink, December 2-3, 1999, Kiev, Ukraine

Dr. Fink spent most his time in Kiev reviewing laboratory activities and quality control results. Patient results were reviewed and compared with results from Belarus which Dr. Fink had received from Dr. Petrenko. The need for a normal range study was stressed. In addition, the issues of supplies was discussed.

5. Dr. Greenebaum, November 29-30, 1999 Minsk, Belarus

Dr. Greenebaum together with her colleagues in Kiev finalized the cytology form. She reviewed the cytological results for number of selected cases and forms and found them to be accurate and complete. She did however determine that the proportion of "inadequate" FNA cases was high particularly in Aksakovchina and that slides have multiple identification numbers on them.

6. Dr. Greenebaum, December 2-3, 1999 Kiev, Ukraine

The cytology form in Ukraine was also finalized at the time of Dr. Greenebaum's visit. Cytological results for selected cases were reviewed and found to be accurate although forms from the data control center were not accessible.

6. Dr. McConnell, November 29-30, 1999 Minsk, Belarus.

The primary focus of Dr. McConnell's trip to Minsk was to ensure that the guidelines (which were established during the last quarter) for describing goiter size and for selecting patients for fine needle aspiration, biopsy and surgery were being implemented. This was reviewed in considerable depth with mixed results. The Belarussians had changed their Palpation Form using the current WHO criteria for goiter size, and amended the Operations Manual to sanction biopsy of nodules 5-10 mm in adults if there are suspicious ultrasound findings. A thorough chart review showed that quality control is taken seriously.

8. Dr. McConnell, December 2-3, 1999, Kiev, Ukraine..

As with his trip to Minsk, Dr. McConnell's primary focus in Kiev was to ensure that the guidelines for describing goiter size and selecting patients for fine needle aspiration, biopsy and surgery were being implemented. There still was no written criteria for needle biopsy of nodules smaller than 10 mm in size for referral to surgery. A thorough chart review indicated that quality control is somewhat lax in Ukraine where there are often gaps and uncorrected errors in clinical records.

APPENDIX B

Year 3 TIMELINE

September 30, 1999 - September 29, 2000

September 30, 1999	First Quarter of Year 3 Begins
October 11-12, 1999	Bi-National Advisory Committee Meetings In Kiev G. Howe, A. Brill, D. Fink, H. Mitchell and R. McConnell)
October 14-15, 1999	Bi-National Advisory Committee Meetings In Minsk G. Howe, A. Brill, D. Fink, H. Mitchell and R. McConnell)
October 19, 1999	Leukemia Working Group Meeting at NCI (Drs. Howe and Finch)
October 25-26, 1999	International Dosimetry Meeting in Lyon, France (Dr. Howe)
October 27, 1999	Year 2 Annual Report Submitted to NCI
November 5, 1999	NCI/Columbia Joint Meeting At Columbia Regarding Data Management (Drs. Howe, Heitjan, Zablotska and Prof. Burch and Ms. Simakovsky)
November 8-10, 1999	NCI/Columbia/Ukrainian and Belarussian International Thyroid Studies Meeting, Bethesda, Maryland (Drs. Howe, Brill, Fink, Greenebaum, Heijian, McConnell, Zablotska, Ms. Hodgson, Ms. Simakovsky and Prof. Burch)
November 15-16, 1999	NCI/Columbia/Ukrainian International Meeting on Leukemia Study Meeting, Bethesda, Maryland (Drs. Howe, Finch and Littlefield)
November 22-23, 1999	Data Management Trip to Minsk, Belarus (Dr. Howe and Prof. Burch)
November 25-26, 1999	Thyroid Study Data Management and Subject Response Trip to Kiev, Ukraine (Dr. Howe and Prof. Burch)
November 29-30, 1999	Clinical Laboratory Trip to Minsk, Belarus (Drs. Fink, Greenebaum and McConnell)
December 2-3, 1999	Clinical Laboratory Trip to Kiev, Ukraine (Drs. Fink, Greenebaum and McConnell)
December 6, 1999	Program Review Meeting in Bethesda (Dr. Finch)
December 13, 1999	Reverse Site Visit at NCI (Dr. Howe, Dr. Sohn and Ms. Hodgson)
December 21, 1999	Leukemia Phase I Study Report Sent to NCI