MEMORANDUM

DATE: September 24, 1998

TO: Tom Bell, Mohandas Bhat, Frank Hawkins, Ruth Neta, Joe Weiss, and Libby White

FROM: Barrett Fountos

SUBJECT: Status of the Chernobyl Cooperative Research Program Between the United States and Belarus and Ukraine Presented at the 107th Meeting of the National Cancer Advisory Board

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On September 10, 1998, I attended the Chernobyl Studies session of the 107th Meeting of the National Cancer Advisory Board (NCAB) in NIH Building 31, Conference Room 10. This memorandum is to summarize the presentations by Bruce Wachholz, Chief, Radiation Effects Branch, National Cancer Institute (NCI), and Geoffrey Howe, Principal Investigator, Columbia University. Copies of the meeting agenda and overheads from both presentations are attached.

Summary of Status of the Chernobyl Studies:

- Of the 15,000 Belarussian cohort, 7,500 current addressees have been identified, 5,000 letters have been mailed, 3,500 contacts have been confirmed, and 2,869 have been screened.
- Of the 80,000 Ukrainian cohort, 20,000 have been randomly selected, 4,800 current addressees have been identified, 1,300 letters have been mailed, 800 contacts have been confirmed, and 529 have been screened.
- No leukemia study status report was presented.

Specific Highlights:

Presentation by Bruce Wachholz:

Dr. Wachholz explained key events which lead to NCI's participation in the Chernobyl health effects studies:

- 1986 Chernobyl accident
- 1987 Reagan/Gorbachev Summit

- 1988 Formation of the Joint Coordinating Committee for Civilian Nuclear Reactor Safety (JCCCNRS) headed by the Nuclear Regulatory Commission (NRC) with DOE participation

- 1989 Two DOE Subcommittees:

    - Environment
    - Health

        - Thyroid cancer and disease in children
        - Leukemia in liquidators

- 1990 DOE/NCI Interagency Agreement whereby funding is provided by DOE, NCI, and NRC for NCI to:

    - Develop research protocols for the long-term follow-up of thyroid cancer in children in Belarus and in Ukraine (those who were 0-18 years old at the time of the accident)

    - Develop research protocols for the long-term follow-up of leukemia in Ukrainian liquidators

Interim data as of 9/10/98 indicate that thyroid cancer incidence is higher in Belarus: there were 700 thyroid cancer cases in Belarus and 560 in Ukraine among those aged 0-18 years. The number of cases has increased continuously since 1986; the rate of increase has decreased. In 1996 and 1997, cases of thyroid carcinoma diagnosed in those currently aged 0-18 years appear to have decreased. However, these data do not yet include those older than 18. These data will be included when the chief pathologist has verified the diagnoses. Furthermore, there is no baseline of thyroid cancer incidence in those over 18.

The risk of thyroid cancer in Chernobyl affected populations is from I^{131}. For comparison, consider the following I^{131} releases from civilian reactors:

- 1957 Windscale, England - 20,000 Ci
- 1979 Three Mile Island - 15 Ci
- 1986 Chernobyl - 30×10^6 Ci

Also, consider the I^{131} releases from U.S. nuclear weapons production facilities:

1944-1972 Hanford - 0.7×10^6 Ci
1951-1970 Nevada Test Site - 1.5×10^8 Ci

The objectives of the thyroid cohort studies are to:

- Identify dose and time-related structural and functional changes in children exposed to radioactive materials released from Chernobyl;
- Develop risk estimates for cancer and nodules as a function of dose in relation to sex and age in 1986; and
- Compare the relative effectiveness of I^{131} with x-ray and gamma irradiation.

The Belarus cohort is to consist of 15,000 and the Ukraine cohort greater than or equal to 30,000 individuals who were in utero at the time of the accident and for whom direct thyroid measurements were made in 1986. The annual/biennial thyroid examinations include ultrasound, palpation, laboratory tests, and fine needle aspiration. Dose reconstruction is based on 1986 thyroid measurements, exposure history, and environmental data.

Direct thyroid measurement data are available for 32,011 in Belarus and 76,155 in Ukraine. Most (42% in Belarus and 60% in Ukraine) have an estimated thyroid dose between 0 and 0.3 Gy. 13,000 in Belarus and 46,000 in Ukraine.

Status of Thyroid Studies as of 9/10/98		
Activity	**Belarus**	**Ukraine**
Peer review	✓	✓
IRB approval	✓	✓
Protocols signed	5/94	5/95
Operations Manuals	✓	✓
Equipment/supplies	ongoing	ongoing
Subjects Examined	2,869	529
Dose Reconstruction:		
• 1986 thyroid measurement	Initial data available; reanalysis in progress	Initial data available; reanalysis in progress
• Exposure history	2,869	529
• Environmental data	To be used to develop an independent method of dose assessment	To be used to develop an independent method of dose assessment
Binational Advisory Committee	✓	✓

Besides DOE, NCI, and NRC, participating agencies include the Department of Veterans Affairs (Veterans Affairs National Acquisitions Center) and the Environmental Protection Agency (Office of Radiation and Indoor Air).

Question: How well are the studies managed?
Answer: The studies started one year ago. Many years lapsed between first involvement and study initiation. It took a long time to get started for several reasons, including: different scientific ethical standards in the United States compared to countries of the former Soviet Union; language barrier; and lack of experience of foreign investigators in conducting epidemiological studies.

Presentation by Geoffrey Howe:

The contract with Columbia University is to provide scientific and administrative support for the thyroid and leukemia studies. Dr. Howe anticipated a greater role in the conduct of these studies.

Descriptive studies found a dramatic rise in thyroid cancer in both countries. However, by design, they have limitations. Dose and outcome measured from analytical studies. In Belarus, initial pathology findings indicated 30 thyroid cancers based on 1,981 examinations. Dr. Howe presented calculations on statistical power and sample size. These and other details are presented in the handout.

Question: Are patients diagnosed with thyroid cancer being treated?
Answer: No. The governments of Belarus and Ukraine are responsible for treatment of affected individuals. Ethically, the United States cannot interfere.

Richard Klausner, Director, NCI, concluded that he hoped that the risk of exposure to I^{131}, although not achieved from the Nevada Test Site study, would be possible to ascertain from the Chernobyl studies.

Attachments (3)

Revised: August 26, 1998

TENTATIVE* NCAB AGENDA

107th Meeting of the
National Cancer Advisory Board

Conference Room 10, C Wing, Building 31

WEDNESDAY, SEPTEMBER 9 - OPEN

I.	SUBCOMMITTEE MEETING - Planning and Budget (Meeting at the Hyatt Regency Bethesda - See Subcommittee listing)	Ms. Stovall Ms. Nichols

THURSDAY, SEPTEMBER 10 - OPEN

9:00 a.m. - 9:15 a.m.

II. CALL TO ORDER AND OPENING REMARKS — Dr. Bishop

III. FUTURE BOARD MEETING DATES

Confirmed:

December 7-9, 1998	Monday, Tuesday, Wednesday
February 8-10, 1999	Monday, Tuesday, Wednesday
June 7-9, 1999	Monday, Tuesday, Wednesday
September 22-24, 1999	Wednesday, Thursday, Friday
December 6-8, 1999	Monday, Tuesday, Wednesday
February 14-16, 2000	Monday, Tuesday, Wednesday
June 12-14, 2000	Monday, Tuesday, Wednesday
September 11-13, 2000	Monday, Tuesday, Wednesday
December 4-6, 2000	Monday, Tuesday, Wednesday

(Evenings of the first day are available for scheduling subcommittee meetings. Full Board meetings begin the next morning.)

9:15 a.m. - 10:15 a.m.

IV. REPORT OF THE DIRECTOR, NCI — Dr. Klausner

* Check online for the most recent version of the NCAB agenda:
http://deainfo.nci.nih.gov/ADVISORY/boards.htm

10:15 a.m. - 10:35 a.m.

V. REPORT OF THE PRESIDENT'S CANCER PANEL — Dr. Freeman

10:35 a.m. - 10:45 a.m.

VI. NEW BUSINESS - SESSION I — Members

10:45 a.m. - 11:00 a.m.

COFFEE BREAK

11:00 a.m. - 11:40 a.m.

VII. NCI PROSTATE CANCER PRG — Dr. Klausner, Dr. Scardino, Dr. Tindall

11:40 a.m. - 11:55 a.m.

DISCUSSION

11:55 a.m. - 12:30 p.m.

VIII. NCI BREAST CANCER PRG — Dr. Klausner, Dr. Davidson, Dr. Moses

12:30 p.m. -12:50 p.m.

DISCUSSION

12:50 p.m. - 2:35 p.m.

LUNCH AND CENTERS SUBCOMMITTEE MEETING

2:35 p.m. - 2:55 p.m.

IX. MEMBER'S PERSPECTIVE/INTERESTS — Dr. Bishop

2:55 p.m. - 3:40 p.m.

X. CHERNOBYL UPDATE — Dr. Rabson, Dr. Austin, Dr. Wachholz, Dr. Howe, Dr. Jackson

3:40 p.m. - 4:00 p.m.

XI. LEGISLATIVE UPDATE — Ms. Foellmer

4:00 p.m.

XII. ADJOURNMENT OF OPEN SESSION

4:00 p.m. - 4:15 p.m.

COFFEE BREAK

4:15 p.m. - Adjournment

CLOSED SESSION

This portion of the meeting is being closed to the public in accordance with the provisions set forth in section 552b(4) and 552b(6)(c), Title 5, U.S. Code and Section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2).

XIII. SPECIAL ACTIONS SUBCOMMITTEE — Dr. Li, Dr. Kalt

Consideration of informational updates; human subject, gender and minority subject, biohazard and animal welfare problems; foreign grants; MERIT Awards; appeal letter; staff recommendations; staff informational items; Board Members' concerns on current grants.

XIV. EN BLOC — Dr. Bishop

CONFIDENTIAL ISSUES REGARDING STAFF AND AWARDEES — Dr. Klausner

FRIDAY, SEPTEMBER 11 - OPEN

9:00 a.m. - 10:00 a.m.

XV. NEW TRAINING INITIATIVES — Dr. Wittes, Dr. Kimes

10:00 a.m. - 10:45 a.m.

XVI. CANCER INFORMATION SERVICE RESPONSE TO OFFICE OF THE INSPECTOR GENERAL REPORT — Ms. Hubbard, Ms. Thomsen, Dr. Wittes

10:45 a.m. - 11:00 a.m.

COFFEE BREAK

11:00 a.m. - 11:15 a.m.

XVII. SUBCOMMITTEE REPORTS AND NEW BUSINESS - SESSION II

11:15 a.m. - 11:40 a.m.

XVIII. INFORMED CONSENT REVISION INITIATIVE — Dr. Wittes, Ms. McCabe

11:40 a.m. - 11:55 a.m.

XIX. STREAMLINED REVIEW OF AMENDED P01s — Dr. Kalt

11:55 a.m. - 12:10 p.m.

XX. FUTURE AGENDA ITEMS

12:10 p.m.

ADJOURNMENT

CHORNOBYL
(Chernobyl)

Cooperative Research Program

between

The United States

and

Belarus and Ukraine

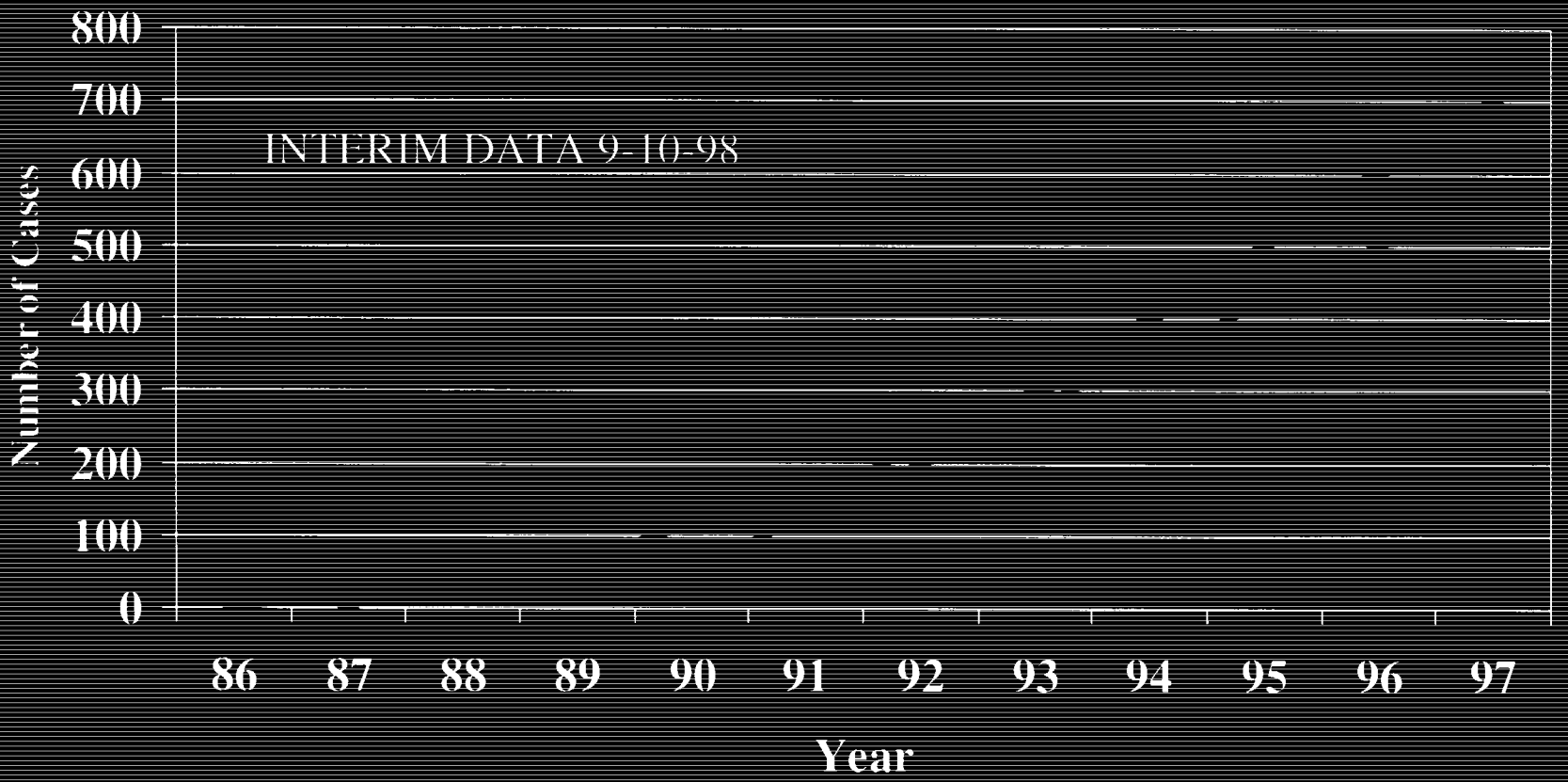
September 10, 1998

9/10/98

Background

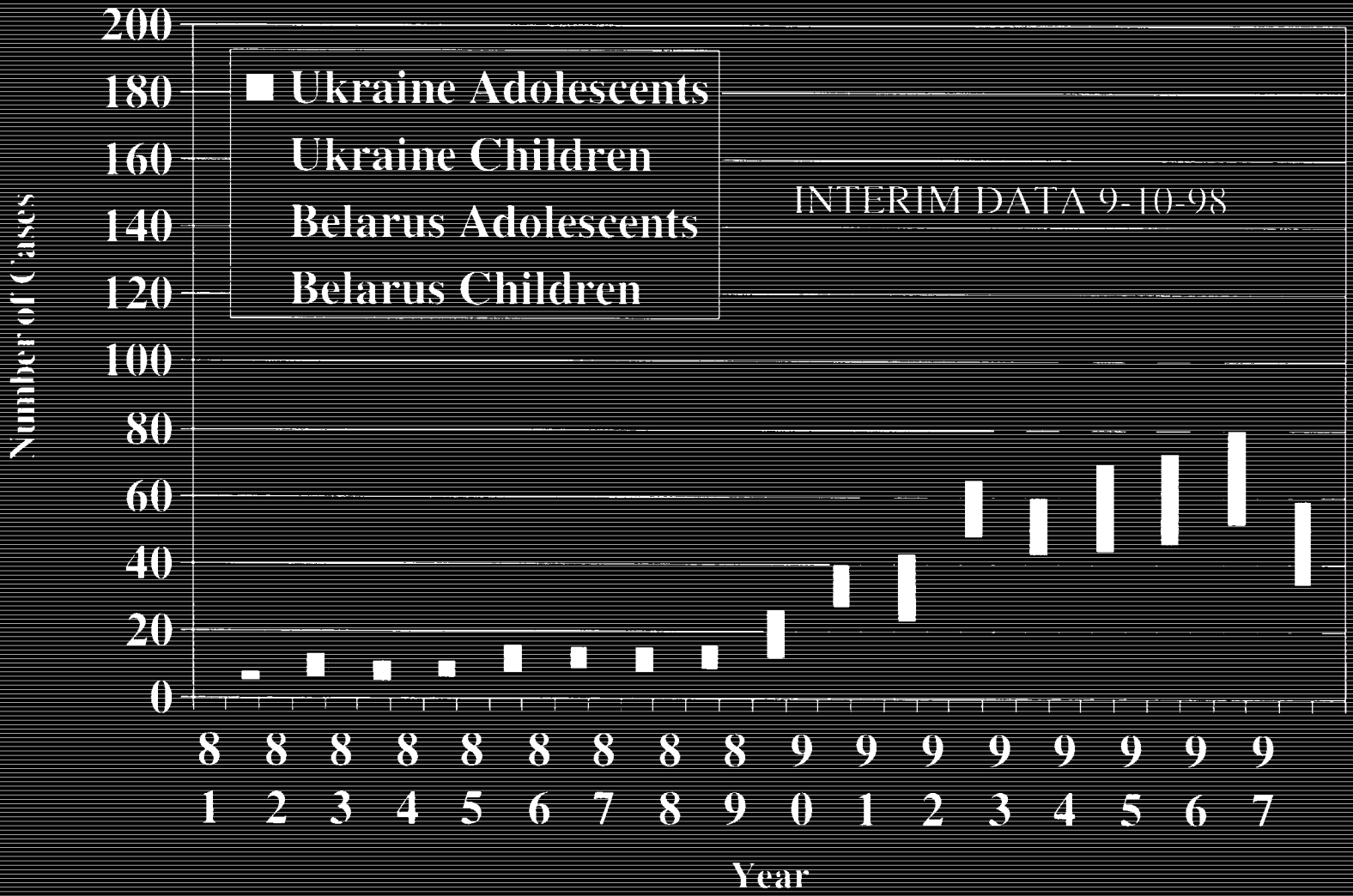
- Presidents Reagen and Gorbachev (1987)
- Joint Coordinating Committee on Civilian Nuclear Reactor Safety (1988)
  - Nuclear Regulatory Commission (NRC)
  - Department of Energy (DOE)
- DOE - Two Sub-Committees (1989)
  - Environment
  - Health
    - Thyroid Disease - Especially Cancer in Children
    - Leukemia - In Clean-up Workers
- DOE - NCI Interagency Agreement (1990)
  - Develop Research Protocols
    - Long-term Follow-up Studies of Thyroid Cancer in Children
    - Leukemia Among "Liquidators" (Clean-up Workers)
- Funding: DOE-NRC-NCI

Number of Thyroid Cancer Cases in and (Age 0-18 Years)



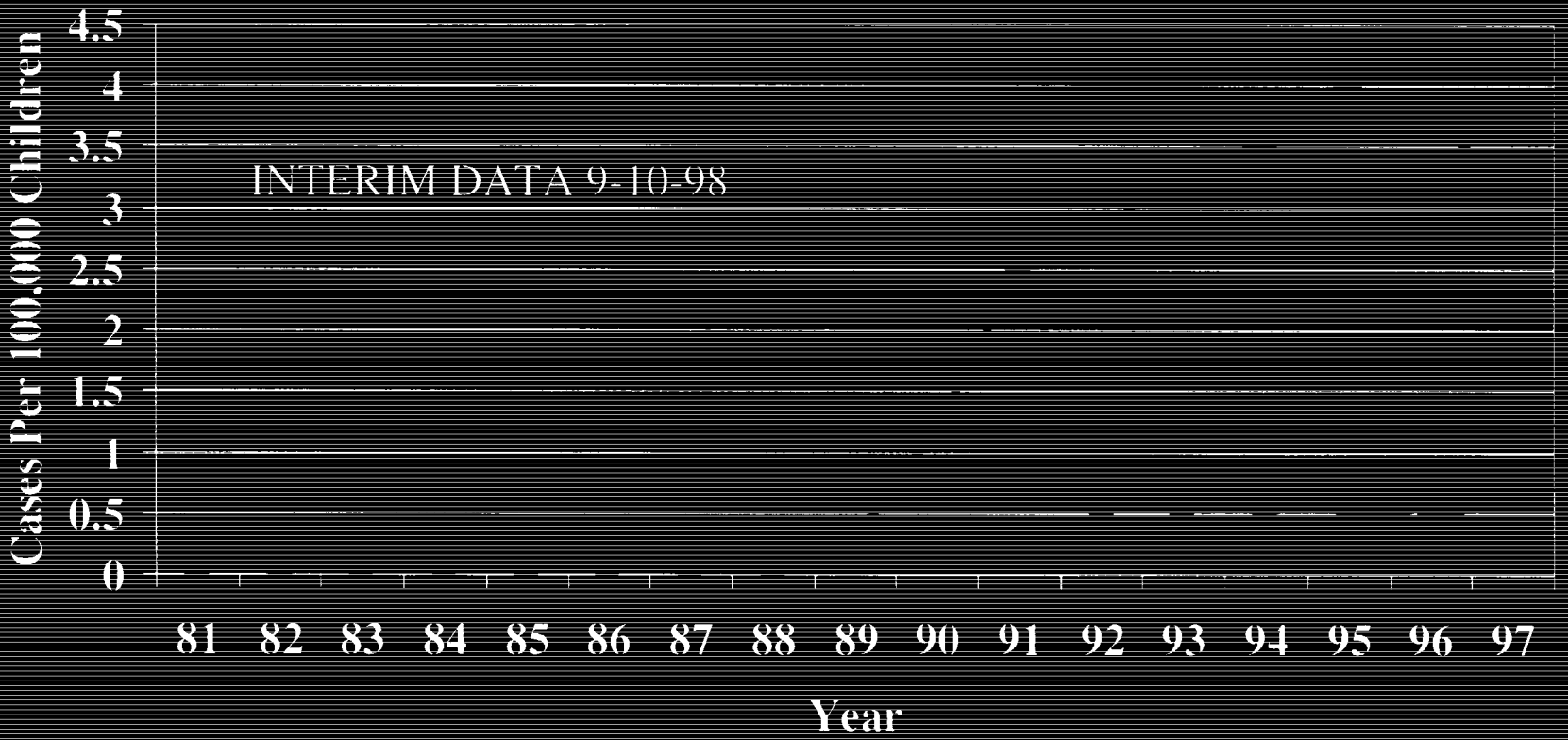
9/10/98

Cases of Thyroid Carcinoma Diagnosed in and in Children (Age 0-14) and Adolescents (Age 15-18) Before and After the Chornobyl Accident



9/10/98

Incidence of Thyroid Cancers in and Among Children (Age 0-14)



9/10/98

Thyroid Studies

- Risk of Thyroid Cancer from I-131
- I-131 Released from
  - Windscale, England (1957): ~20,000 Ci
  - Three Mile Island, U.S. (1979): ~15 Ci
  - Chornobyl, Ukraine (1986): ~30 x 10^6 Ci
    - > 10^6 Children Exposed
    - > 10^5 Children's Thyroids Measured
- U.S. Nuclear Weapons Facilities
  - Hanford, WN (1944-1972): ~0.7 x 10^6 Ci
  - Nevada Test Site (1951-1970): ~1.5 x 10^8 Ci

9/10/98

Thyroid Cohort Studies Objectives

- Dose-and Time-Related Morphologic and Functional Changes in Children Exposed to Radioactive Materials Released from Chornobyl
- Risk Estimates for Cancer and Nodules as a Function of Dose in Relation Both to Sex and Age in 1986
- Comparison of the Relative Effectiveness of I-131 with that of X-Ray and Gamma Irradiation

Thyroid Cohort Studies
Belarus and Ukraine

- Cohort (Belarus: ~15,000; Ukraine: ≥30,000)
  - In Utero - Age 18 at Time of Accident
  - Measurement of Thyroid in 1986
- Annual/Biennial Thyroid Examinations
  - Ultrasound
  - Palpation
  - Laboratory Tests
  - Fine Needle Aspiration (as indicated)
- Dose Reconstruction
  - 1986 Thyroid Measurements
  - Exposure History
  - Environmental Data

Thyroid Dose Distribution from the Chornobyl Accident Among Children with Thyroid Measurements

INTERIM DATA 9-10-98

Estimated Dose (Gy)	Belarus		Ukraine	
	Number	Percent	Number	Percent
0-0.3	13,418	41.9	45,938	60.3
0.3-1	10,381	32.4	19,293	25.3
1-2	4,101	12.8	5,684	7.5
2-5	2,901	9.1	3,698	4.9
5-10	794	2.5	1,012	1.3
>10	416	1.3	530	0.7
TOTAL	32,011		76,155	

9/10/98

Status Of Thyroid Studies

	Belarus	Ukraine
Peer Review	✓	✓
IRB	✓	✓
Protocols Signed	May, 1994	May, 1995
Operations Manuals	✓	✓
Equipment/Supplies (Ongoing)	✓	✓
Examination of Subjects	2,869	529
Dose Reconstruction:		
• 1986 Thyroid Measurement	Initial results available; reanalysis in progress	
• Exposure History	2,869	529
• Environmental Data	To be used to develop an independent method of dose assessment	
Bi-national Committees	✓	✓

9/10/98

Participants

(Agencies)

NCI

- Division of Cancer Biology (Faye C. Austin, Ph.D.)
  - Radiation Effects Branch (Bruce W. Wachholz, Ph.D.)
- Division of Cancer Epidemiology and Genetics (Joseph Fraumeni, M.D.)
  - Radiation Epidemiology Branch (Gilbert Beebe, Ph.D.)

DOE

- Deputy Assistant Secretary for Environment, Safety and Health (Paul Seligman, M.D.)
  - Office Of International Health (Frank Hawkins)

NRC

- Office of Executive Director of Operations (Joseph Callan)
  - Office of Research (Schlomo Yaniv, Ph.D.)

Department of Veterans Affairs

- Veterans Affairs National Acquisitions Center (Philip Naas)

EPA

- Office of Radiation and Indoor Air (Dale Hoffmeyer)

9/10/98

Participants
(Operations)

NCI

- Ihor Masnyk, Ph.D. - U.S. Project Director (DCB/REB)
- Gilbert Beebe, Ph.D. - Epidemiology (DCEG/REB)
- Andre Bouville, Ph.D. - Dosimetry (DCB/REB)

NIDDK

- Jacob Robbins, M.D. - Endocrinology

CONSULTANTS

- A. Bertrand Brill, M.D., Ph.D. - Nuclear Medicine, Ultrasound
- Stuart Finch, M.D. - Radiation Hematology
- Everett Mincey, Ph.D. - Biochemistry
- Herman Mitchell, Ph.D. - Data Management, Computer Science
- Paul Voilleque - Dose Reconstruction

CONTRACTOR

- Columbia University School of Public Health
  Geoffery Howe, Ph.D., Head, Division of Epidemiology, P.I.

SCIENTIFIC SUPPORT FOR THYROID AND LEUKEMIA STUDIES

1. **COLUMBIA UNIVERSITY:**

A. School of Public Health	Epidemiology Biostatistics Data Management
B. Faculty of Medicine (Cancer Center)	Endocrinology Ultrasonography Cytology Clinical Laboratory Management Hematology Pathology
C. Faculty of Medicine (Center for Radiological Research)	Radiology Biological Dosimetry

2. **UNIVERSITY OF UTAH:**

Center for Applied Dosimetry	Physical Dosimetry

SCIENTIFIC SUPPORT FOR THYROID AND LEUKEMIA STUDIES: PERSONNEL

Epidemiology	G. Howe, Principal Investigator D. Burch
Biostatistics	D. Heitjan
Data Management	D. Heitjan G.R. Howe
Endocrinology	R. McConnell
Ultrasonography	(J. Fayter)
Cytology	E. Greenebaum
Clinical Laboratory Management	D. Fink
Hematology	R. Reiss
Pathology	(A. Matsushima)
Radiology	C. Medvedovsky B. Worgul
Biological Dosimetry	C. Geard T. Straume (Univ. of Utah)
Physical Dosimetry	E. Haskell (Univ. of Utah) T. Straume (Univ. of Utah)

Recruitment of Cohort in Belarus, Current Status

15,000 on 1986 Dose File

↓

7500 Current Addresses Identified:
Chernobyl Registry
Local Medical Records
Passport Office

↓

5000 Letters Sent

↓

3500 Contacts Confirmed

↓

2869 Screened

Recruitment of Cohort in Ukraine, Current Status

80,000 on 1986 Dose File

↓

20,000 Randomly Selected

↓

10,000 Current Addresses Identified:
Chernobyl Registry
Local Medical Records

↓

1300 Letters Sent

↓

800 Contacts Confirmed

↓

529 Screened

Examination Schedule

1. Examinations carried out in fixed centers and mobile units.

2. Schedule:

   palpation, laboratory tests (ionized calcium, thyroid stimulation hormone (TSH), urinary iodine), ultrasound, and epidemiology/dosimetry questionnaire.

3. Further evaluation:

   A. If nodule found, fine needle aspiration biopsy performed on all suspicious nodules >5 mm.

   B. If nodule suspicious for malignancy based on clinical, sonographic or cytologic findings, surgery performed.

Initial Pathology Findings, Belarus

Thyroid Cancer	30
Suspicious for Thyroid Cancer	1
Thyroid Adenoma	1
Nodular Goiter (solitary)	103
Multinodular Goiter	8
Diffuse Goiter	76
Combined Goiter	1
Autoimmune Thyroiditis	19

Based on 1,981 examinations

Initial Pathology Findings, Ukraine

Diffuse Goiter, Grade 1	48
Diffuse Goiter, Grade 2	3
Nodular Goiter, Grade 1	9
Multinodular Goiter, Grade 1	3
Autoimmune Thyroiditis	3

Based on 529 examinations

PARAMETERS OF LINERA RELATIVE RISK MODEL FOR THYROID CANCER
ACUTE EXTERNAL EXPOSURES TO GAMMA AND X-RAYS
BASED ON COMBINED DATA FROM 7 STUDIES (RON ET AL 1995)
AS PROVIDED BY DR. J. LUBIN, U.S. NATIONAL CANCER INSTITUTE
FEBRUARY 1996

Parameter		Estimate
Main Effect (β)		12.4 per Sievert
Age at Exposure, Years (multiplicative factor):		
	0-4	1.0
	5-9	0.6
	10-14	0.2
Time Since Exposure, Years (multiplicative factor):		
	<30	1.0
	≥30	0.3

OBSERVED AND "EXPECTED" EXCESS OF THYROID CANCER AMONGST CHILDREN EXPOSED TO ^{131}I

Expected Values Calculated From Risks Based on Studies of Acute Doses of External Radiation

Study	Observed	Expected[a]
Swedish diagnostic	0.9	20.3
FDA	2.6	19.0
Nevada Test Site	2.6	2.6
Marshall Islanders	4.8	17.5
Total	10.9	59.4

Estimated Relative Biological Efficiency $10.9/59.4 = 0.18$

[a]Excess Risk = $4.0/10^4$ person years gray

Power to Detect Statistically Significant Dose Response Relationship

	Belarus	Ukraine
Sample Size	15,000	50,000
Relative Biological Effect:		
1.0	99%	99%
0.33	84%	97%
0.16	64%	84%

Follow-up: 15 years
Linear excess relative risk model
α one-sided: 0.05

Ability to Discriminate Amongst Relative Biological Effectiveness Factors

	Belarus	Ukraine
Sample Size	15,000	50,000
Relative Biological Effect:		
0.33	0.1-1.6	0.13-0.83
0.16	0.0-0.9	0.06-0.46

Follow-up: 30 years
Linear excess relative risk model
Expected 95% Confidence Interval