DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER
22201 23rd Drive S.E.
Bothell, WA 98021
(425) 486-8788

NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C.F. NUMBER
TO: Dana C. Matthews, M.D.	6/5-15/2001	
TITLE OF INDIVIDUAL: Principal Investigator	TYPE ESTABLISHMENT INSPECTED: Sponsor/Investigator	
FIRM NAME: Fred Hutchinson Cancer Research Center	NAME OF FIRM, BRANCH OR UNIT INSPECTED: Same	
STREET ADDRESS: 1100 Fairview Avenue North	STREET ADDRESS OF PREMISES INSPECTED: Same	
CITY AND STATE (Zip Code): Seattle, WA 98109	CITY AND STATE (Zip Code): Same	

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

1. There are no procedures in place for the prompt reporting of Serious Adverse Events (SAEs) to FDA and the IRB as evidenced by the following:

A) The following subjects experienced SAEs that were reported to FDA in IND ——— Annual Reports but were not promptly reported in SAE reports to the FDA, Subject ———————————

B) Subject ——— experienced an SAE on 6/23/99 and it was not received by the IRB until 11/3/99.

C) Subject ——— experienced an SAE on 5/18/96 and it was not received by the IRB until 1/7/97.

D) Subject ——— experienced an SAE on 11/20/99 and there is no documentation that it was reported to the IRB.

2. There are at least three data sets for the findings and experiences of IND ——— These data sets reside with the investigator, the study coordinator, and the Fred Hutchinson Cancer Research Center. FDA inspection team was not informed that the data set within Fred Hutchinson Cancer Research Center contained IND ———specific information until the 6th day of the inspection by the sub-investigator. There is no record of cross-validation of the three data sets. There is no documentation that any plan for verifying data integrity of the three data sets is in place.

3. In a review of 27 subject records, in possession of the study coordinator, the following subjects were hospitalized without any notification to FDA or the IRB of the occurrence of an SAE: Subjects ——————————— #s = 7

4. There are no procedures in place for the adequate monitoring, review, or quality assurance of the progress of any protocol under IND——— as evidenced by the following:

A) There is no documentation that case report forms (CRFs) for the protocols went through a review and approval process. The study coordinator changed the CRFs after informal discussion with the investigator without establishing the purpose and intent of the CRFs.

B) The CRFs are different from chart to chart and were changed during the course of each clinical investigation.

C) The cover CRF for each chart has a space for the investigator to sign as having reviewed and approved the data in the subjects' charts. The investigator did not sign the cover CRF in the majority of charts.

D) There are subjects' records and IRB correspondence where white-out was used to obliterate the original record. There is no documentation that the investigator commented on this practice.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Connie P. Rezendes	Carl A. Anderson, Investigator Connie P. Rezendes, Investigator	June 15, 2001

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
22201 23rd Drive S.E. Bothell, WA 98021 (425) 486-8788	9/17-28/2001
	FEI NUMBER 3034598

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Janet Eary, MD

FIRM NAME	STREET ADDRESS
University of Washington Medical Center	PO Box 356113
CITY, STATE AND ZIP CODE Seattle, WA 98195	TYPE OF ESTABLISHMENT INSPECTED Clinical Investigtor

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

In reference to your participation in protocols under IND [redacted]:

1. Subjects' case histories.

Subject case histories do not contain adequate information as evidenced by:

A. Inclusion into study. Prior to April, 1999 there is no documentation for inclusion into investigative procedures. After April 26, 1999 the form, Notice of Patient Inclusion, is used. The form is an advance notice predominantly signed by the study coordinator, not the investigator. This form does not have specific physician/investigator orders for subject inclusion into Iodine-131 BC8 antibody treatment.

B. There are no physician orders for the dosimetric dose of Iodine-131 BC8.

C. There is no documentation that the principal investigator approved the therapeutic doses of 131-Iodine-BC8 that the subinvestigator, Dr. Eary, calculated and prescribed for subjects based on dosimetry.

D. In 13 of 25 charts reviewed there are no signed physician orders for the therapeutic dose of Iodine-131 BC8 antibody treatment.

E. In all 25 charts reviewed there is no documentation that a physician authorized to administer radiolabled investigational products was present, or provided oversight, during the infusions.

F. For 15 charts reviewed for data regarding lungs and kidneys there are no source documents to verify the radiation absorbed doses for the kidneys, based on dosimetric calculations, that Dr. Eary reported to the principal investigator. For 7 of the same 15 charts there are no source documents to verify the radiation absorbed doses for the lungs.

G. There are numerous markovers and obscuring of original data in the subject charts. For example, the case history for subject [redacted] there is dosing information written in pencil with erasures of original data and replacement data filled in.

2. Informed Consent Form (ICF):

A. In protocol [redacted] subjects received more than the upper limit of [redacted] milliCuries of radiation administered in violation of the IRB approved ICF.

B. There are no scan reports for the images acquired after the diagnostic doses of 131-Iodine-BC8, or any other documentation that the sub-investigator or staff reviewed the images as required by the IRB approved ICFs for both protocols [redacted] and [redacted]

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Carl A. Anderson, Investigator	September 28, 2001

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
22201 23rd Drive S.E. Bothell, WA 98021 (425) 486-8788	9/17-28/2001
	FEI NUMBER 3034598

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Janet Eary, MD

FIRM NAME	STREET ADDRESS
University of Washington Medical Center	PO Box 356113
CITY, STATE AND ZIP CODE Seattle, WA 98195	TYPE OF ESTABLISHMENT INSPECTED Clinical Investigtor

3. Test Article:

Regarding batch production records for manufacture of 131-Iodine-BC8 that was the responsibility of Dr. Eary:

A. There is no documentation of the review and approval of the protocol (revised 1989 version) for the manufacture of the 131-Iodine-BC8 by the subinvestigator. In addition there are hand written changes to the protocol that are without approval of the subinvestigator.

B. There is a new protocol prepared September 10, 2001 that has not yet been used. This protocol, presented to FDA during the inspection, has not been reviewed or approved by the subinvestigator.

C. There is no documentation that microbiology tests that are part of the batch production records have been reviewed by the subinvestigator.

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		Carl A. Anderson, Investigator	September 28, 2001

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DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
22201 23rd Drive S.E. Bothell, Washington 98021-4421 425-486-8788	09/14/01 & 10/24-26/01
	FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Dana C. Matthews, M.D.

FIRM NAME	STREET ADDRESS
Fred Hutchinson Cancer Research Center	1100 Fairview Avenue North
CITY, STATE AND ZIP CODE Seattle, Washington 98109	TYPE OF ESTABLISHMENT INSPECTED Sponsor/Investigator

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

1. The sponsor has never performed quality control audits of the manufacturing operations of the investigational product (BC8) for studies conducted under IND [redacted] and of the manufacturing facility at Fred Hutchinson Cancer Research Center since the Spring of 1996.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	Linda S. Leja	Linda S. Leja, CSO	10/26/01