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Bulletin

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Introduction

This Bulletin presents a summary of accomplishments and highlights in the Idaho National Engineering Laboratory's (INEL) Boron Neutron Capture Therapy (BNCT) Program for June 1991. This bulletin includes information on the brain tumor and melanoma research programs, Power Burst Facility (PBF) technical support and modifications, PBF operations, and animal data charts.

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Principal Investigator's Highlights

A. BRAIN TUMOR RESEARCH

1. Project 1: Supporting Technology Development

Task 1: Gross Boron Analysis

A new filter wheel has been ordered for the ARL Model 3520 ICP-AES. A significant number of samples were processed on the ARL-3410.

Task 2: Borocaptate Sodium (BSH) Purity Determination

The first real final-dosage-form BSH packaged at Ben Venue Labs was analyzed and compared with samples from Callery and Centronic Ltd. The BSSO content of the Ben Venue product just meets the 0.4% SSO specification. The sample from Centronic Ltd clearly appeared to be most free of contamination and oxidation products.

Task 3: Active Form Identification

Further detailed investigation into albumin binding of BSH continues. Results are pending.

Task 4: Subcellular Analytical Development

Subcontracts with Atom Sciences (SIRIS) and Charles Evans and Associates (SIMS) were renewed July 23, 1991.

Task 5: Noninvasive Boron Quantification

MRI spectroscopy hardware upgrade will be installed at UofU by August 4,

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MASTER

1991. Dr. Gary Glover at Stanford is testing acquisition of boron spectroscopic information with a different imaging sequence. This offers the potential for boron resolution with 0.75 cm/pixel.

Task 6: Measurement Dosimetry

Neutron and gamma measurements in the HFR epithermal-neutron BNCT beam were made. These included: (1) neutron spectrum in the beam, (2) neutron and gamma measurements in the lucite beagle-head phantom, and (3) neutron and gamma measurements in the lucite cylindrical phantom. A detailed report is in preparation.

Task 7: Analytical Dosimetry

Development of the database management system continued at WSU, including preliminary testing of remote access from INEL and MSU.

2. Project 2: Treatment Protocol Development
Task 1: Large Animal Studies

Current status of six spontaneous brain-tumor dogs is reported. No additional normal-tissue experiments were conducted.

Task 2: Pituitary Tumor Treatment Evaluation Studies

ORSU reactor appears to be the best choice for the pituitary tumor experiments. Initial steps have been taken in the production of MoAbs against the CRF receptor.

3. Project 3: Human Pharmacokinetics

No activity to report.

4. Project 4: Drug Interaction and Toxicity

No activity to report.

B. MELANOMA RESEARCH

1. Project 1: Boron Localization Screening

Growth of BL6 in low phenylalanine/tyros medium is significantly suppressed compared to controls on exposure to BPA. This observation has consequences for the interpretation of the BPA dose-response curve. Further study of BPA biodistribution in B16-BL6 melanoma in BDF mice will begin in August 1991. The initial screening of liposome BNCT compounds will also begin in August 1991.

2. Project 2: Biodistribution, Pharmacology, and Toxicity of Boron Delivery Agents

Task 1: BPA/Molecusol/DEA Solubility and Availability Study

Studies of two column technologies using BPA (aqueous) standards suggests there may be an advantage with the Supelco column.

Task 2: Toxicity of Boron Delivery Agents

No activity to report.

3. Project 3: Large Animal Model Studies

These large animal experiments are on hold awaiting availability of the appropriate compounds.

4. Project 4: Melanoma Detection and Boron Quantification by Scintigraphy

See Project 3 above.

5. Project 5: Boronated Low Density Lipoproteins and Amino Acid Development and Evaluation

The route of synthesis of carboranyl alanine has been altered from that previously described.

6. Project 6: Boronated Liposome Development and Evaluation

UCLA researchers are encapsulating $\text{p-B}_{20}\text{H}_{18}^{2-}$ into liposomes for use in baseline murine experiments.

D. PBF TECHNICAL SUPPORT AND OPERATIONS

Selection of work packages for completion that are applicable to both inactivation and the BNCT Program has begun.

C. ADMINISTRATION

A draft Memo of Understanding has been prepared containing details of a possible working agreement with Georgia Institute of Technology. Proposed cost-sharing BNCT subcontracts with the European Collaboration on BNCT have also been prepared. The DOE-ER Peer Review of the INEL BNCT Program will be held September 11-12, 1991 in Idaho Falls, ID.

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Principal Investigator
INEL BNCT Program

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A. BRAIN TUMOR RESEARCH

Project 1: Supporting Technology Development

Task 1: Gross Boron Analysis

Samples received	155
Samples prepared for analysis (plus Quality verification)	40
Samples analyzed	487
Backlog:	
Awaiting preparation	115
Prepared, awaiting analysis	202

The ARL Model 3520 inductively coupled plasma-atomic emission spectrometer (ICP-AES) has been in limited service this month because of poor stability caused by irreproducible positioning of the filter wheel. Many attempts to repair the wheel were made as a new filter will cost approximately \$6 K. Only minor improvements were made in attempts to fix the wheel and a new one has been ordered. As it is, this instrument is still only useful for single channel analyses or analyses where the filter does not need to be changed.

Instrument time on the ARL 3410 was expanded and a significant number of samples were processed. There were 36 samples prepared for analysis, 144 samples submitted by Project 1, Task 3, and 111 samples submitted July 31, 1991 from ISU researchers.

Task 2: Borocaptate Sodium (BSH) Purity Determination

Analysis was performed on the first real final-dosage form BSH packaged at Ben Venue Laboratories. Data were collected with a variety of high performance liquid chromatography (HPLC) conditions to enhance certain aspects of the chromatograms. The chromatographic column was a new ET 300/8/4 Nucleosil[®] 10 C₁₈, reversed-phase column from Machery-Nagel. The mobile phase consisted of a methanol:water mixture with either 2.5 or 5 mM tetrabutylammonium sulfate (TBAS), ion-pairing reagent (Altech low ultraviolet (UV) PICA reagent) flowing at 1 mL/minute. Mobile phase methanol concentrations ranged from 48-53% and pH was maintained at 8.1. At methanol

concentrations of 48% with 5mM TBAS, the BSSO anion eluted as a broad peak at > 45 minutes, making these chromatograms useless for quantitation. However, they were useful for comparing the less well-retained components that normally elute very early. Changing the pH to 7.9 and 8.3 did not affect the quantitative or qualitative results. Injection volumes were 50 μ L and detection was performed with a Waters UV-Vis photodiode array detector set to collect a scan from 200-300 nm every three seconds at 2-nm resolution. Quantitation was obtained by averaging the weight percent results calculated from both the areas and heights at 215 and 225 nm.

Sets containing standards and samples from Callery Chemical Company, Ben Venue Laboratories, and Centronic Ltd. were prepared for analysis on three different dates. Analysis of each set was performed as many as four times with slightly differing chromatographic conditions. The samples analyzed and the results are shown in Table I. The results for the Ben Venue Laboratories packaged product are listed in Table II. The samples were prepared in deionized water and underwent slight oxidation as they sat in the laboratory. Samples were handled under a nitrogen purge and all resulting solutions were purged with nitrogen. Close examination of Table II indicates that an additional 0.05-0.1 weight percent of BSSO anion was potentially formed in the sample solution over the course of three to four days. Even with the additional BSSO, a significance test at $P = 0.05$ (i.e., 95% C.L. using a one-sided student t-test) indicates that the BSSO content is less than 0.4 weight percent. Quantitation of BSS anion is generally difficult as it not always a well-defined peak and is often overlapped with other minor components that further skew the peak shape and resulting integration data. The BSS anion quantitation difficulties can be noted by the larger relative standard deviations.

A comparison of chromatograms of Na₂BSH product from Callery (BNCT-202), Callery/Ben Venue (BNCT-217), and Centronic Ltd. (BNCT-313) is shown in Figure 1. The excessive BSSO content of the product processed by Ben Venue Laboratories is readily apparent; however, it just meets the 0.4% specification. The late eluting peaks present in the material from Callery have apparently been fairly effectively removed. The Na₂BSH product purchased from Centronic Ltd. appears to be almost entirely free of contaminants and oxidation products.

Table I. Summary of Purity Analysis by HPLC.

Inventory Number	Sample Description	Weight % BSS Anion	Weight % BSSO Anion
202	Natural abundance Na ₂ B ¹⁰ SH from Callery (received 3/26/91) Lot #1890-146-3[2351-24-1]	0.7 ± 0.3	0.14 ± 0.05
217	Na ₂ ¹⁰ B ¹⁰ SH from Ben Venue Labs Lot #MJG060191	0.3 ± 0.2	0.38 ± 0.03
264	Na ₂ ¹⁰ B ¹⁰ SH from Ben Venue Labs Lot #MJG060191 (different vial) ^b	0.12*	0.34*
295A	Na ₂ ¹⁰ B ¹⁰ SH from Centronic Ltd. Batch #H245 (courtesy of Dr. Detlef Gabel)	0.07 ± 0.08	0.01 ± 0.01
313	Na ₂ ¹⁰ B ¹⁰ SH from Centronic Ltd. Batch #H363 (purchased by INEL)	0.11*	0.02*
<p>* Standard deviations not reported because n = 2.</p> <p>^b Sample was part of a group that was to be sent to WSU, but never left INEL because of a mixup. All samples were at room temperature for 1-2 days.</p>			

Table II. Summary of Ben Venue Laboratories Product Analyses.

Sample	Prep	Run	Approx. Hrs. After Prep	Weight % BSS Anion*	Weight % BSSO Anion*
217	1	1	8	0.286 ± 0.034	0.382 ± 0.004
217	2	1	13	0.343 ± 0.034	0.347 ± 0.008
217	2	3	54	0.532 ± 0.029	0.407 ± 0.009
217	2	4	67	0.393 ± 0.074	0.437 ± 0.01
217	3	1	11	0.119 ± 0.003	0.352 ± 0.020
217	3	3	32	0.187 ± 0.025	0.375 ± 0.025
264	1	1	11	0.062 ± 0.002	0.332 ± 0.024
264	1	2	32	0.182 ± 0.022	0.348 ± 0.020
Mean				0.263	0.372
Standard Deviation				0.156	0.035
BSSO ≥ 0.4% at P = 0.05 (One-tail t test)				N/A	No
<p>* Means ± one standard deviation calculated from both peak areas and peak heights at 215 and 225 nm.</p>

Figure 1. Comparison of chromatograms of Na_2BSH from Callery, Callery/Ben Venue, and Centronic Ltd.

Samples of all products listed in Table I were also submitted for carbon, hydrogen, nitrogen, and sulfur elemental analysis by combustion in a Carlo Erba Instruments EA 1108 Elemental Analyzer. Results from these analyses are summarized in the first three columns of Table III. Of note in Table III are the carbon and nitrogen results for BNCT-202 and the two samples from Centronic Ltd. The chromatograms for BNCT-295A contained at least two peaks that could possibly be attributed to organic contaminants. Normalized chromatograms for a 183- μg injection of BNCT-295A (Centronic Ltd. Batch #H245) are shown in Figure 2. The unknown component at ~ 4.75 minutes has an absorbance maximum at ~ 260 nm and the component at ~ 19.25 minutes peaks at ~ 240 nm. Neither of these components were readily apparent in BNCT-313 (Centronic Ltd. Batch #H363).

Since the sulfur analyses with the combustion method are typically poor for Na_2BSH , sulfur, as well as boron and sodium were quantitated by ICP-AES. A sample originally prepared for HPLC analyses and a second sample prepared by a different scientist were appropriately diluted with deionized water. In both cases, the raw material was han-

dled under nitrogen. Results from the two samples were very consistent so all results for replicate measurements of each sample were averaged and these averages are shown in the last three columns of Table III.

Hydrogen content for the BSH products should be in the 5.7-6.2% range for water content of 0-10%, respectively, for ^{10}B -enriched compound. Some excess water may have been picked up while weighing of the sample and loading the auto-sampler for the combustion analysis and may account for some of the excess hydrogen. The expected percent values for Na, boron, hydrogen, and sulfur are also listed in Table III. These values assume that the compound is 100% Na_2BSH and need to be adjusted for the actual water content of the samples. Water content, as determined by the difference from Na_2BSH that had been calculated from the boron content (52.6%) by Centronic Ltd. of the Batch #H363 (BNCT-313), was 8.1%. Water content in Batch #H245 was determined by Centronic Ltd. to be 5.8% by the difference from the Na_2BSH determined from the sodium content (20.53%). INEL elemental analyses suggest a slightly lower water content. Sulfur content would

Table III. Result of Elemental Analyses of Various Na₂BSH Samples.

Sample	Weight % Carbon ^a	Weight % Hydrogen ^a	Weight % Nitrogen ^a	Weight % Sulfur ^b	Weight % Boron ^{b,c}	Weight % Na ^b
202	0.77 (0.09)	7.9 (0.1)	0.02 (0.03)	13.6 (0.2)	61.0 (1.0)	20.0 (0.4)
Expected ^d	0.00	5.5	0.00	14.6	59.0	20.9
217	0.00	6.0 (0.2)	0.00	15.8 (0.6)	60.3 (1.2)	21.5 (0.2)
264	0.00	5.8 (0.1)	0.00			
Expected ^e	0.00	5.74	0.00	15.2	57.3	21.8
295A	1.6 (0.2)	6.1 (0.6)	0.22 (0.05)	12.6 (0.7)	50.7 (1.9)	22.3 (0.3)
313	0.25 (0.06)	6.83 (0.09)	0.02 (0.03)	14.5 ^g	55.6 (1.0)	19.5 ^g
Expected ^f	0.00	5.74	0.00	15.2	57.2	21.8

Values in parentheses represent the standard deviation.

^a Determined by CHN combustion analysis.

^b Determined by ICP-AES. Each number represents replicate analysis on a sample prepared for HPLC and a second sample prepared by a different person.

^c Values have been corrected for isotopic abundance.

^d Assumes sample is 100% Na₂BSH and all boron is natural abundance.

^e Assumes sample is 100% Na₂BSH and all boron is 95% ¹⁰B.

^f Assumes sample is 100% Na₂BSH and all boron is 95.8% ¹⁰B.

^g Only two measurements on one sample. No sample prepared for HPLC was available at the time.

Figure 2. Normalized chromatograms of Centronic Ltd. Na₂¹⁰BSH, Batch #H245 (BNCT-295A).

be expected to be > 13% (w/w) for > 90% pure Na₂¹⁰BSH.

Because of the very hygroscopic nature of Na₂BSH, any analytical results concerning the elemental composition of these solid samples will be suspect unless the sample-handling procedures are known and well controlled. For instance, it has been noted at INEL that any Na₂BSH powder that visibly remains on a spatula will, if left open to the atmosphere, absorb enough moisture to become a paste within 20-40 minutes.

Task 3: Biochemistry of BSH and Its Oxidation Products

Experiments to confirm the previous BSH to albumin binding data using equilibrium dialysis were continued. Experiments using canine whole plasma and BSH to determine the major binding protein fractions are also still in progress. ICP-AES analytical results for many of these experiments are still pending and the results will be summed. Some new nuclear magnetic resonance data was also obtained this month concerning model reactions between BSH, BSS, and BSSO with cysteine, cystine, and albumin.

Task 4: Subcellular Analytical Development

The subcontracts with Atom Sciences and Charles Evans and Associates were renewed July 23, 1991.

Task 4A: Secondary Ion Mass Spectrometry (SIMS)

No reportable progress this month.

Task 4B: Sputter-Initiated Resonance Ionization Spectroscopy (SIRIS)

No reportable progress this month.

Task 4C: Alpha Track-Etch

ISU researchers are performing track counting analysis of ¹⁰B tissue standards and dog liver specimens received from WSU researchers using cellulose-nitrate film. The films being used are fabricated from nitro-cellulose formulas that the WSU researchers have used before. They will also

provide ¹⁰B-containing dog-brain tissue for track-etch analysis. The ISU reactor was not operating for two weeks in July and delayed progress somewhat; however, the reactor is scheduled to be back in operation by the end of July 1991.

Task 5: Noninvasive Boron Quantification

University of Utah (UofU): The spectroscopy hardware upgrade is being installed in stages to minimize interference of patient scheduling and will be completed by August 4, 1991. Final checkout will consist of a series of tests required by GE, phosphorus spectroscopy sequences and a chemical shift imaging sequence of BSH in 4% bovine albumin. Canine imaging will be delayed two weeks after the start of the UofU contract award.

Northwest Imaging (NWI): Boron magnetic resonance imaging (MRI) hardware and software for NWI is scheduled to be installed during August 1991.

Stanford University: An additional set of MRI coil hardware was sent to Dr. Gary Glover at Stanford to test the potential of acquiring boron spectroscopy information with a different imaging sequence. Initial tests using this sequence were performed using proton frequencies. Indications are that boron data will be obtainable in a matrix of 32 x 32 pixels for a 24-cm field of view with a slice thickness of 0.75 cm. This will provide boron resolution with 0.75-cm/pixel.

Task 6: Measurement Dosimetry

Program participants made the following neutron and gamma measurements in the High Flux Reactor (HFR) epithermal-neutron BNCT beam in Petten, The Netherlands:

1. Neutron spectrum in the beam using the same foil activation method used for the Brookhaven Medical Research Reactor (BMRR) at Brookhaven National Laboratory (BNL) - July 1, 1991.
2. Neutron and gamma measurements in the lucite beagle-head phantom using gold-copper foils and Thermoluminescent dosimeter (TLD)-400 dosimeters - July 2, 1991.
3. Neutron and gamma measurements in the lucite

cylindrical phantom (12.7-cm diameter by 18-cm long) using the same methods - July 3, 1991.

Foils were counted by the Petten Gamma Spectrometer Laboratory staff. The TLDs were sent to the INEL for readout. Readout of the TLDs at the INEL Radiological and Environmental Sciences Laboratory (RESL) has been partially completed. Some problems were encountered in the operation and an optical filter used on the TLD reader must be replaced. The TLD readouts should be completed by the latter part of August 1991.

Preliminary neutron analyses were performed at Petten by Program participants. Values of saturated foil activity from the neutron spectral measurements were obtained and neutron reaction rates for the two phantoms were calculated. This data was given to European Collaboration on Boron Neutron Capture Therapy (ECBNCT) personnel with the earlier results for the same foils/phantoms irradiated at the BMRR. These measurements provided ECBNCT with a basis for a decision to perform dog irradiations scheduled for the week of July 8, 1991.

The neutron flux values have been derived for the two irradiated phantoms. A comparison of the HFR beam (45 MW) with the BMRR beam (3 MW) shows, at the same locations inside the beagle phantom, that the HFR-to-BMRR thermal-flux ratio is approximately 0.7. The ratio is approximately 0.5 for the central axis of the cylinder phantom.

A detailed report of the Petten trip is in preparation and analysis of the neutron spectral foil data of the HFR beam is in progress.

Task 7: Analytical Dosimetry

Task 7A: Dosimetry Software/Alpha 1 Software Development:

Work continued on validation of the radiation transport module for the treatment planning system. A journal article (*Nuclear Science and Engineering*), describing some of the novel analytical methods used in this module, is in preparation.

Task 7B: Canine Dosimetry Analysis

Because of the postponement of the planned irradiations at BMRR this month, there are no

reportable actions in connection with this task at BMRR.

Task 7C: Database Management System

Two INEL staff were at WSU in mid-July 1991 to assist researchers with development of the BNCT database management system, review the design, and programming. Most of the database tables and many of the user input screens are complete. Entry of descriptive information for dogs, owners, and referring veterinarians has been completed, and entry of summary information for dogs (i.e., summary charts included in Appendix A) is nearly finished. Preliminary testing of remote access to the database from INEL and Montana State University (MSU) has been successful.

All BNCT personnel requiring access to the database should contact Jay Weidner at WSU (509) 335-0812 (office) or (509) 335-0880 (FAX) and he will provide appropriate accounts and passwords. Some of the initial information that is needed are: (1) full name, (2) account name (i.e., "jpw" for Jay P. Weidner), (3) office location and telephone number, and (4) electronic mail (EMAIL) address. The database is currently accessed via INTERNET. Final details for access via modems are still being investigated. If possible, send access requests, via EMAIL, to "jpw@minivan.vetmed.wsu.edu" and "root@pgavin2.vetmed.wsu.edu". Otherwise, contact Jay at his office or by FAX and he will send instructions on using the database after the accounts are cleared through Arlene Ackermann in the INEL BNCT Program office.

Task 7D: Biophysics/Stochastic Model Development

No reportable progress this month.

Task 7E: Neutron Source Analysis

No additional calculations have been performed this month.

Project 2: Treatment Protocol Development

Task 1: Large Animal Studies

Spontaneously-Occurring Brain Tumors: "Zar" Walter (#35447-152) returned to WSU for repeat computed tomography (CT) and MRI scans and no changes were observed in the shape or size of the tumor mass. Radiographic and CT examination revealed a marked right deviation of the trachea at the level of the aortic knob. A water-dense mass surrounding the aorta at this level that occupied much of the anterior mediastinum was present. Differential diagnosis would be a heart base tumor or an aortic body tumor. Because of his poor prognosis, "Zar" was euthanized on June 26, 1991. A complete necropsy was performed and histological results are pending.

"Dudley" Fiset (#35447-151) still has not had any hair regrowth on the top of his head or on his legs. Otherwise, he appears to be a happy, chirpy dog.

"Sugar" Ellsworth (#35447-142) returned to WSU for her six-month checkup in mid-July 1991. She had been disoriented and bumping into things for approximately two weeks. Changes in CT and MRI exams were consistent with massive cerebral edema and periventricular contrast enhancement (indicative of vascular necrosis). These changes are similar to those in dose-tolerance dogs who received 38 Gy or more irradiation. With the owner's consent, she was euthanized and a full necropsy was performed on July 23, 1991. No significant gross lesions were observed in the brain. Histopathological analysis is pending.

"Muffy" Lower (#35447-140) is still on her prednisone dose of 2.5 mg every three days. When she returns to WSU for her six-month checkup in early August 1991, she will probably be weaned off the prednisone completely. "Muffy" appears to have returned to her "old self," as she was before the tumor.

"Too Wide" Marshall (#35447-129) is doing well, as is Brandy Hoff (#35447-94).

Normal Tissue Tolerance (Neutron Irradiation): Baseline data is still being collected on the control dogs, and histopathologic analysis of tissues from previously euthanized dogs continues. No additional dogs have been irradiated this month. BNL

irradiations, originally planned for late July 1991, had to be canceled because a heat wave forced airlines to refuse acceptance of dogs for travel. Possibilities of housing dogs at alternate approved facilities near BNL are being explored, so dogs can be shipped during times of favorable weather and held until the BMRR is available.

Pharmacokinetics: Samples from "Mokie" Elkin (#35447-154) were sent to INEL for boron analysis. No additional dogs have been infused.

The latest animal chart data from Project 2, Task 1 Large Animal Studies is summarized in Appendix A.

Task 2: Pituitary Tumor Treatment Evaluation Study

Oregon Health Sciences University (OHSU) researchers are confident that the reactor facility at Oregon State University (ORSU) in Corvallis, OR provides the best site for the pituitary tumor experiments, as well as for the long-term followup experiments on live animals (i.e., rodents). ORSU staff have designed cell culture tube holding devices for the "stringer port" for future pituitary tumor cell irradiation. Modification of the port to minimize gamma irradiation is currently underway. ORSU staff have also tested the culture media in which the tumor cells will be bathed to evaluate the residual radioactivity after neutron exposure and it appears that this radioactivity is minimal.

Binding affinity and capacity studies are underway at OHSU to determine these parameters in AtT-20 and GH-3 cells and in human pituitary tumor cells. Endocrine stimulation tests of these cells are also underway to establish good baseline data before actual neutron exposure experiments begin.

BALB/C mice have been injected with intact human pituitary human cells and with detergent extracts of tumor cell membranes as the first step in the production of monoclonal antibodies against the CRF receptor. AtT-20 cells will also be detergent extracted to isolate a crude fraction of CRF receptors for ultimate CRF affinity column purification and use as an antigen for monoclonal antibody formation.

Project 3: Human Pharmacokinetics

Task 1: Drug Distribution Center; Clinical Data
 Storage Center; Regulatory Affairs

The target date for initiation of the subcontract with ISU is August 1, 1991. Space and personnel at ISU have been identified and considerable effort has been expended to supply the information required for final subcontract negotiations. Limited renovation of laboratory space will be required to provide suitable space for these centers and non-binding arrangements for initiation of this work has been completed.

Project 4: Drug Interaction and Toxicity

This subcontract is still in negotiation with ISU.

B. MELANOMA RESEARCH

Project 1: Boron Localization Screening

B16-BL6 Cell Growth Curve: Researchers at WSU have assayed growth of murine B16-BL6 melanoma *in-vitro* in normal and tyrosine/phenylalanine-limited media supplemented with boronophenylalanine (BPA). Statistical analyses (student t-test) have been completed and confirm initial observations. Growth in low-amino-acid medium is indeed significantly ($p < 0.05$) lower than that in normal medium. Additionally, BPA at concentrations up to 100 mg/L is not significantly ($p < 0.05$) toxic to BL6 since *in-vitro* growth does not appear to be suppressed by exposure to BPA in both normal and low phenylalanine/tyrosine media. However, there are indications that growth of BL6 in low phenylalanine/tyrosine medium is significantly suppressed when compared to controls. These results will have consequences for the interpretation of the BPA dose-response curve.

BPA Dose-Response Curve: WSU researchers have completed a dose-response curve of boron (BPA) uptake by murine BL6 cells. Pellets have been sent to the INEL for ICP-AES boron analysis.

Biodistribution of BPA: WSU researchers have ordered the supply of mice to repeat the biodistribution of BPA in mice fed a normal diet and a diet low in tyrosine and phenylalanine. It is planned to inject B16-BL6 melanoma subcutaneously into BDF mice (not nude mice) the first week of August 1991. After the tumor has reached approximately 0.5-1.0 cm in diameter (two to three weeks), the mice will be inoculated with BPA (either intraperitoneally or intravenously) and tissues will be sampled at a time interval to be determined later (approximately six hours postinoculation). Tissues will be frozen and sent to the INEL for boron analysis.

BPA Fluorescence (Uptake): WSU researchers have evaluated the feasibility of using fluorescent spectrophotometry to study uptake of BPA by BL6. The results with p-BPA and BPA-HCL are inconsistent and it was concluded that this technique is not feasible to study BPA uptake. The next approach will be to assess whether radiolabelled (^3H or ^{14}C tag) BPA is appropriate for studying BPA uptake.

Screening of Liposome BNCT Compounds: WSU researchers have ordered BDF mice for the *in-vivo* screening of the first set of liposome compounds that have been received from UCLA, and are scheduled for delivery on August 1, 1991. After receipt, the mice will be divided into six groups and injected subcutaneously with B16-BL6. After the tumors have reached approximately 0.5-1.0 cm in diameter (about two to three weeks), the mice will be inoculated intravenously into the tail vein with the liposome compound (approximately the third week in August 1991). Tissues will be sampled through time (up to 36 hours after inoculation), frozen, and sent to the INEL for boron analysis. WSU and UCLA researchers are completing the details to coordinate efforts to efficiently screen these compounds.

Miscellaneous: WSU researchers have a list of possible animal suppliers that may carry immune deficient animals (rats and rabbits) and will investigate the possibility of utilizing these suppliers. WSU researchers have been culturing bovine endothelial cells for Pacific Northwest Laboratories (PNL) and will provide a cryovial as soon as a sufficient numbers of cells is obtained.

Project 2: Biodistribution, Pharmacology, and Toxicity of Boron Delivery Agents

Task 1: BPA/Molecusol/DEA Availability Study

Biodistribution of BPA: ISU researchers have completed evaluation of the two column technologies using aqueous BPA standards prepared over the range of 1-20 $\mu\text{g/mL}$. The optimum mobile phase composition varied somewhat for each column. The mobile phase for the Nucleosil column was 0.5 M phosphate buffer:methanol (60:40) and 0.05 M phosphate buffer:methanol (75:25) for the Supelco column. In both cases, the phosphate buffer was adjusted to an acidic pH in the range of 4.1 to 4.5. Columns were maintained at 27°C and column effluent was monitored at 224 nm. Triplicate injections of each standard were made using a Hitachi AS-4000 autosampler. Results are summarized in Table IV and are indicated as mean response $\pm$ the standard deviation (% CV).

Table IV. Evaluation of Two Column Technologies.

Standard	Nucleosil C ₁₈	Supelco LC-HISEP
1 $\mu\text{g/mL}$	90,541 $\pm$ 4,202 (4.6)	35,009 $\pm$ 1,159 (3.3)
5 $\mu\text{g/mL}$	27,4870 $\pm$ 7,272 (2.6)	62,714 $\pm$ 753 (1.2)
10 $\mu\text{g/mL}$	52,9348 $\pm$ 7,412 (1.4)	110,502 $\pm$ 1,091 (1.0)
15 $\mu\text{g/mL}$	76,5649 $\pm$ 10,037 (1.3)	161,923 $\pm$ 627 (0.4)
20 $\mu\text{g/mL}$	1,017,011 $\pm$ 3,673 (0.4)	204,018 $\pm$ 907 (0.4)
regression equation	$y = 4.88 \cdot 10^4 \times 3.73 \cdot 10^4$	$y = 9.126 \cdot 10^3 \times 2.17 \cdot 10^4$
	$r^2 = 1.00$	$r^2 = 0.997$

The magnitude of the intercept value (b) in both regression equations is puzzling, since the chromatograms show a lack chromatographic interference in the region of interest. Investigations will continue for possible explanations, but, at this time, it would appear that either column would be useful for BPA analysis. The Supelco column offers the advantage of permitting direct injections of plasma/serum samples, while the Nucleosil column requires that BPA be isolated from the biological matrix prior to analysis. Evaluation of plasma standards continue using the Supelco column, since validation of this method would permit direct injection of dog plasmas for quantitation of BPA levels.

Project 3: Large Animal Model Studies

Potential patients for large animal studies continue to be identified by WSU researchers. Large animal studies of boron distribution are awaiting shipment of liposome compounds.

Project 4: Melanoma Detection and Boron Quantification by Scintigraphy

Large animal experiments are on hold until preliminary results with radiolabeled boron compounds are available from the small animal studies.

Project 5: Boronated Low Density Lipoproteins and Amino Acid Development and Evaluation

The route of synthesis of carboranyl alanine has been altered from that previously described. Direct azidation of the carborane imide proved to be impossible; apparently because of degradation of the carborane cage under the reaction conditions. The alternate method, bromination of the imide and subsequent azide displacement, is being utilized instead. Literature precedent has used di-n-butylboron triflate as a Lewis acid complexing agent to enforce stereoselective bromination. University of California/San Francisco (UCSF) researchers have encountered serious difficulties with the quality of commercially available triflate, which were not entirely resolved upon synthesis of this reagent in the lab. This agent has the further disadvantage that it is pyrophoric, a serious potential drawback in large-scale experiments. Other potential Lewis acids that should be more practicable are being investigated.

Azide displacement of the bromide has proven to be straightforward and proceeds in high yield. Transesterification of the azide-imide system with metal alkoxides is also proving to be a high yield reaction. Initial results indicate that final hydrogenolysis of the azido ester proceeds to the desired amino acid without difficulty. The over-all route

promises high yielding and high stereoselectivity, both of which are desirable for the synthesis of ^{10}B -enriched amino acids.

Project 6: Boronated Liposome Development and Evaluation

University of California/Los Angeles (UCLA) researchers are encapsulating the sodium salt of the octadecahydroelcosoborate(2-) photoisomer (*i*- $\text{B}_{20}\text{H}_{18}^{2-}$) into liposomes. These liposomes will be sent to WSU for baseline murine experiments. Scheduling for the large-scale production of liposomes at Vestar, Inc. is in progress.

Development of the synthesis and chemistry of new boron species as candidates for liposomal delivery is continuing. Two isomers of $\text{B}_{20}\text{H}_{18}\text{OH}^{3-}$ have been synthesized and purified in sufficient quantity for liposomal experiments to begin. Current emphasis is placed on the amine-substituted derivatives $\text{B}_{20}\text{H}_{17}\text{NH}_3^{3-}$.

The compositions of $\text{B}_{10}\text{H}_9\text{CO}^{1-}$ and $\text{B}_{10}\text{H}_9\text{NCO}^{2-}$ have been confirmed by x-ray structural analysis. Investigations into the synthesis of other derivatives of $\text{B}_{10}\text{H}_9\text{CO}^{1-}$ are continuing.

C. ADMINISTRATION

Proposed National BNCT Program: The INEL BNCT Program Manager met with BNL staff July 29-30, 1991 to discuss the scope, focus, and research center roles for a National BNCT research and development program and the capabilities and roles of appropriate neutron sources.

BMRR: BMRR began operations at 3-MW power the week of July 15, 1991. The next canine dose-tolerance irradiations were scheduled for July 25 and 26, 1991, but were postponed to August 8-9, 1991, because dogs could not be shipped to BNL because of the hot weather.

Georgia Tech Research Reactor (GTRR): INEL participants met with Georgia Institute of Technology (GIT) administrative staff to establish interest and university commitment for modification of the GTRR for BNCT use. The INEL BNCT Program Manager also gave an INEL BNCT Program presentation at Emory University. There appears to be a strong desire from both institutions to participate in development. A draft Memo of Understanding has been prepared containing details of a possible working agreement with GIT and has been sent to the EG&G Legal Office for review. FY-92 work packages for preliminary physics design of the GTRR filter and treatment room internals are in preparation.

ECBNCT/Petten: On July 15, 1991, a proposed cost-sharing BNCT subcontract with the ECBNCT (beam time at Petten in exchange for dosimetry analyses performed at INEL for the European canine program) was transmitted to the EG&G Subcontracts Administration Office for approval. The subcontract is now undergoing OPSEC review and EG&G Legal Office review. A request for proposal (RFP) is expected in August 1991.

A separate cost-sharing subcontract is being generated with ECBNCT to gain access to a working copy of the Program's analytical dosimetry software in exchange for human BSH pharmacokinetic data.

Budget: A meeting was held July 1, 1991 with Program management and DOE-ID financial counterparts to improve communication of budget issues to DOE-HQ. Another meeting was held July

23, 1991 to review the direction of the INEL BNCT Program in light of DOE-ER's requests for a national, four-year plan and the recent release of the remaining money from the Congressional budget action for FY-91.

DOE-HQ sent DOE-ID a memorandum dated July 1, 1991 authorizing activities that "will support both the option to modify PBF for future BNCT research and the option to place the facility in a radiologically and industrially safe condition preparatory to transfer to the Decontamination and Decommissioning Program."

Plans are being developed to determine what portion of the \$7.6 M, which was just released to the Program, can be effectively utilized this fiscal year and what portion must be carried over to FY-92. A portion of this funding must be carried into FY-92 to supplement PBF standby funding in the FY-92 President's budget (\$3 M), since standby costs are approximately \$4.5 M/year.

DOE-ER Peer Review: The schedule for the DOE-ER peer review of the INEL BNCT Program will be September 11-12, 1991, in Idaho Falls, ID.

Boron Compound(s): Analysis of the BSH drug from Ben Venue Laboratories is not complete because of scheduling and equipment problems with the atomic emission spectrometers at INEL.

Personnel from Callery Chemical visited the INEL BNCT Program office the week of July 22, 1991. It is projected that the requirement for BSH for the next calendar year is approximately 2 kilograms ¹⁰B enriched and 500 grams natural boron. Production of this quantity could be a problem.

D. PBF TECHNICAL SUPPORT AND OPERATIONS

Restaffing of the facility and selection of those work packages for completion that are applicable to both inactivation and the BNCT Program has begun based on the release of an additional \$5.9 M funding for PBF.

Inspection of the PBF canal fuel storage racks for structural integrity and cadmium content will begin in August 1991. This inspection was scheduled to begin in late June 1991, and must be completed before April 1992 for PBF technical specification compliance. The inspection will require moving PBF fuel stored in the temporary fuel storage racks to the permanent fuel storage racks while the individual storage locations are being inspected. The detailed operating procedure (DOP) for this inspection is bulky and repetitive, and required changes in the wording of the PBF Technical Specifications and the PBF Standing Directives to ensure the procedure was straight-forward and could be implemented safely. The reviews and approvals for these changes and the DOP took longer than anticipated because key individuals were also engaged in DOE Tiger Team reviews.

The technical specifications were modified to recognize the 80-gram plutonium/beryllium (Pu/Be) neutron source as a fuel unit. Defining the source as a fuel unit in the terms of the technical specifications provided a known safety envelope for handling the source while moving fuel to the permanent fuel storage rack from the temporary fuel storage racks. Criticality analysis and independent analysis were performed to ensure criticality safety for removal of the permanent canal fuel rack "bumper," and to show inspection of the outside wall of the temporary fuel storage racks was not necessary to ensure a criticality hazard did not exist.

The Pu/Be neutron source is stored at the Advanced Reactivity Measurement Facility (ARMF) at the Test Reactor Area (TRA) at INEL. A minimal transport plan was developed and reviewed by the Transport Plan Review Committee and approved by DOE-ID for transporting the source from TRA to PBF.

The DOP for verifying the cadmium integrity pro-

vides for calibrating the source and the associated detector to known cadmium thicknesses and the calibrated detector readings are then compared to detector readings taken through the fuel storage rack walls for cadmium thickness determinations. A visual inspection of the rack for physical damage or degradation will occur while the fuel is relocated for the cadmium inspection. This inspection will require five to six weeks for completion of activity in the reactor building.

The scheduled preventive maintenance performed in the plant during the month included: (1) fire extinguishers, (2) control room air conditioners, (3) secondary chemical treatment pump, (4) emergency generator, (5) auxiliary air compressor, (6) gas stock monitor, (7) plant air compressor, (8) constant air monitors, (9) 5/15-ton overhead crane, (10) demineralized water storage tank, (11) cathodic protection, and (12) Halon systems.

Training conducted during the month included: (1) operations review of Quality Program Plan, (2) self-assessment training, (3) second-quarter Operations Standing Directives and Standard Practice change review, (4) emergency brigade orientation, (5) conduct of operations and conduct of maintenance craft training, (6) emergency brigade fire hose house equipment training, and (7) hazardous communication and introduction to PBF training for the crafts.

APPENDIX A

LARGE ANIMAL MODEL STUDIES

SUMMARY OF PATIENT DATA

INEL BNCT CANINE TUMOR TREATMENT STUDY

BORON DOSE													
ANIMAL	SEX/AGE	NAME OF DOG	BIOPSY DIAGNOSIS	BORON DOSE (mg ¹⁰ B/ kg bw)	DATE	START TIME ¹	DURATION MINUTES ²	CALCULATED DOSE (cGy)	¹⁰ B ESTIMATED AVG (ppm)	SURV.	DAYS	DEATH	
												DATE	CAUSE
35447-79	F/7	"Pugee" Krebs	Astrocytoma ³	50	07/07/89	375	77.8	1923	18.5	No	348	06/20/90	Urinary Distinction
35447-80	M/4	"Mugsy" Marshall	Astrocytoma	50	08/07/89	369	78.0	1722	21.6	No	12	08/19/89	Anesthesia
35447-83	M/11	"Rusty" Collins	Meningioma ⁴	50	08/25/89	430	68.5	1829	21.4	No	170	02/11/90	Focal Encephalomalacia
35447-87	M/1*	"Benji" Williams	Nasal meningioma ⁶	50	09/28/89	420	80.3	1653	20.6	No	140	02/14/90	Euthanasia- (recurrent clinical signs)
35447-93	F/6	"Brandy" Grudzinski	Oligoden- droglioma ⁶	50	10/30/89	310	68.1	1912	24.9	No	300	08/27/90	Neurologic deterioration
35447-94	F/5	"Brandy" Hoff	Meningioma ²	50	10/25/89	464	86.0	1887	14.3	Yes			
35447-95	M/6	"Godfrey" Beers	Meningioma ⁴	50	10/24/89	388	63.3	1743	24.5	No	0.5	10/25/89	Neurologic deterioration
35447-100	F/7	"Juno" Bagley	Meningioma ⁴	50	11/30/89	315	73.0	2185	28.9	No	43	01/12/90	Euthanasia
35447-108	F/4	"Trixie" Herklotz	Papilloma ²	50	02/16/90	225	49.0	1900	51.9(?)	No ⁵	(a)	06/??/90	Lost followup
35447-118	F/9	"Scuzzy" Jenkins	Astrocytoma ⁶	50	10/19/90	170	75.0	2300	85.3	No	158	03/26/91	Unknown
35447-129	F/6	"Two Wide" Marshall	Papilloma ²	50	10/18/90	210	116.0	2141	56.9	Yes			
35447-132	M/13	"Sarge" Smith	Meningioma ⁶	50	10/19/90	198	164.0	2300	34.5	No	54	12/12/90	Stomachsurgery complications (GDV)

¹ Time from start of boron injection to start of irradiation.

² Irradiation time in minutes.

³ Diagnosis from CT and/or MRI scans.

(a) Dog died sometime week of June 11, 1990, was buried without necropsy, owner did not return messages or communicate with WSU.

* "Benji" Williams age is unknown

GDV = gastric dilatation volvulus

⁴ Biopsy confirmed.

⁵ Did not improve neurologic status.

⁶ Postmortem histopathology report

INEL BNCT CANINE TUMOR TREATMENT STUDY

ANIMAL	SEX/AGE	NAME OF DOG	BIOPSY DIAGNOSIS	BORON DOSE		DATE	START TIME ¹	DURATION MINUTES ²	CALCULATED DOSE (cGy)	ESTIMATED ¹⁰ B AVG (ppm)	SURV.	DAYS	DEATH	
				(mg ¹⁰ B/ kg bw)									DATE	CAUSE
35447-134	F/8	"Peggy" Cunningham	Meningioma ⁶	50		10/29/90	198	190.0	1729	20.6	No	33	12/01/90	Neurological complications
35447-139	M/11	"Hobart" Felder	Meningioma ⁶	50		01/22/91	160	83.0	2300	57.5	No	13	02/04/91	Toxic shock ⁷
35447-140	F/3	"Muffy" Lower	unidentified	50		01/22/91	149	152.0	2300	40.3	Yes			
35447-142	F/6	"Sugar" Ellsworth	unidentified	50		01/23/91	168	105.0	2300	44.5	No	181	07/23/91	Brain necrosis
35447-147	M/9	"Bomber" Buck	Malignant meningioma ⁶	50		02/07/91	206	132.0	2300	37.1	No	102	05/21/91	Euthanasia: recurrent clinical signs
35447-151	M/6	"Dudley" Fiset	unidentified	50		02/28/91	211	69.0	2300	67.6	Yes			
35447-152	M/10	"Zar" Walter	Meningioma	50		03/19/91	204	78.4	2300	60.8	No	99	06/26/91	Euthanasia Metastasis in chest

¹ Time from start of boron injection to start of irradiation.

² Irradiation time in minutes.

³ Diagnosis from CT and/or MRI scans.

⁴ Biopsy confirmed.

"Penny" Bird, #35447-136: Health deteriorated too quickly for radiation treatment; received boron injection; moved to pharmacokinetics study.

⁵ Did not improve neurologic status.

⁶ Postmortem histopathology report.

⁷ Infection in rear leg.

INEL BNCT CANINE PHARMACOKINETIC STUDY

SUMMARY OF PATIENT DATA

BSH INTRAVENOUS INJECTIONS STUDY

ANIMAL	NAME OF DOG	EUTHANASIA DATE	MIN'	CASE SUMMARY	PATHOLOGY DIAGNOSIS	DOSE (mg/kg)	BLOOD SERUM AND URINE ANALYSIS		TISSUE ANALYSIS	CT		MRI	
										UNENH.	ENH	UNENH.	ENH
35447-1	"Muffy" Klugh	03/23/87	540	Yes	Pituitary adenoma	55	Yes		Yes	Yes		Yes	Yes
35447-2	"Stashi" Christensen	05/18/87	750	Yes	No tumor/positive boron control	57	Yes		Yes	N/P	N/P	No	No
35447-3	"King" Henry	05/18/87	Control	Yes	No tumor/negative boron control	0	Yes		N/P	No	No	No	No
35447-14	"Marsha" Despain	06/30/87	780	Yes	Invasive adenocarcinoma	62	Yes		Yes	Yes	Yes	Yes	Yes
35447-15A	"Amos" Vallangdigham	08/03/87	780	Yes	Invasive nasal carcinoma	59	Yes		Yes	Yes	Yes	Yes	Yes
35447-18	"Slim" Pozzobon	09/14/87	770	Yes	Invasive nasal adenocarcinoma	30	Yes		Yes	Yes	Yes	Yes	Yes
35447-20	"Mischief" Scott	11/02/87	90	Yes	Meningioma	55	Yes		Yes	Yes	Yes	Yes	Yes
35447-23	"Rocky" Christensen	11/13/87	780	Yes	Pituitary adenoma	55	Yes		Yes	Yes	Yes	Yes	Yes
35447-24	"Mariah" May	11/24/87	720	Yes	Subarachnoid cyst	55	Yes		Yes	Yes	Yes	Yes	Yes
36845-25	"Sandy" Frazier	01/26/88	780	Yes	Meningioma	53	Yes		Yes	Yes	Yes	Yes	Yes
35447-28	"Boots" Belisle	02/22/88	125	Yes	Regional demyelinative disease	55	Yes		Yes	Yes	Yes	Yes	Yes
35447-30	"Sunny" Seeley	03/01/88	420	Yes	Pituitary adenocarcinoma	55	Yes		Yes	Yes	Yes	Yes	Yes
35447-32	"Pip" Hahn	02/26/88	410	Yes	Meningioma	55	Yes		Yes	Yes	Yes	Yes	Yes
35447-33	"Coco" Pechtel	03/23/88	420	Yes	Nasal adeno carcinoma	56	Yes		Yes	Yes	Yes	Yes	Yes
35447-37	"Tucker" Reeves	04/14/88	420	Yes	No tumor/positive boron control	10	Yes		Yes	N/P	N/P	No	No
35447-39	"Fritts" Cogan	05/02/88	100	Yes	Meningioma	10	Yes		Yes	Yes	Yes	Yes	Yes
35447-40	"Rocky" Underwood	05/03/88	420	Yes	Fungal granuloma	30	Yes		Yes	Yes	Yes	Yes	Yes
35447-43	"Blue" Archer	05/23/88	420	Yes	Diffuse cortical astrocytoma	52	Yes		Yes	N/P	N/P	Yes	Yes
35447-49	"Jenny" Nelson	06/29/88	420	Yes	Diffuse astrocytoma	33	Yes		Yes	Yes	Yes	Yes	Yes
35447-50	"Caesar" Chenoweth	07/13/88	420	Yes	Meningioma	55	Yes		Yes	Yes	Yes	Yes	Yes
35447-54	"Licorice" Meyers	08/03/88	410	Yes	No tumor/positive boron control	55	Yes		Yes	Yes	Yes	Yes	Yes

¹ Euthanasia time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.

(P) Partial results

N/A Not applicable

N/P Not Performed

INEL BNCT CANINE PHARMACOKINETIC STUDY

SUMMARY OF PATIENT DATA

BSH INTRAVENOUS INJECTIONS STUDY

ANIMAL	NAME OF DOG	EUTHANASIA DATE	MIN ¹	CASE SUMMARY	PATHOLOGY DIAGNOSIS	DOSE (mg/kg)	BLOOD SERUM AND URINE ANALYSIS	TISSUE ANALYSIS	CT		MRI	
									UNENH.	ENH	UNENH.	ENH
35447-55	"Kelley" Langston	08/17/88	410	Yes	Diffuse astrocytoma	55	Yes	Yes	No	No	Yes	Yes
35447-57	"Rafferty" Reber	09/01/88	410	Yes	Meningioma (plasmapheresis)	50	Yes	Yes	No	Yes	Yes	Yes
35447-59	"Heidi" Boyer	09/12/88	180	Yes	Meningioma	55	Yes	Yes	No	Yes	Yes	Yes
35447-62	"Chester" Scott	10/09/88	180	Yes	Meningioma	55	Yes	Yes	No	Yes	Yes	Yes
35447-67	"Muffet" Hammel	11/01/88	180	Yes	Astrocytoma	55	Yes	Yes	No	Yes	N/P	N/P
35447-70	"Mac" Meyers	11/15/88	180	Yes	Fibrillary astrocytoma	55	Yes	Yes	No	Yes	Yes	Yes
35447-71	"Jake" Brede	01/04/89	180	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	N/P	N/P
35447-72	"Mandy" Ross	02/07/89	495	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-76	"Scotty" Klemm	05/28/89	410	Yes	Protoplasmic astrocytoma	55	Yes	Yes	No	Yes	Yes	Yes
35447-86	"Brutus" Halverson	09/11/89	240	Yes	Pituitary adenocarcinoma	50	Yes	Yes	Yes	Yes	Yes	Yes
35447-88	"Scamper" Brewster	10/10/89	420	Yes	Pituitary adenocarcinoma	55	Yes	Yes	N/P	N/P	Yes	Yes
35447-97	"Kolsa" Joy	12/07/89	420	Yes	No tumor	55	Yes*	Yes	Yes	Yes	Yes	Yes
35447-101	"Ginger" Mott	12/12/89	180	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-104	"Killer" Divine	01/19/90	180	Yes	Choroid plexus papilloma	55	Yes	Yes	Yes	Yes	Yes	Yes
35447-117	"Toby" Page	04/27/90	180	No	Meningioma	50	Yes	P	Yes	Yes	No	No
35447-116	"Taffy" Gruel ^{2,3}	05/05/90	300	No	Pending	55	Yes*	P	Yes	Yes	Yes	Yes
35447-1846	N/A	05/23/90 ⁴	N/A	No	Normal laboratory dog	100	Yes	N/A	No	No	No	No
35447-2173	N/A	05/24/90 ⁴	N/A	No	Normal laboratory dog	100	Yes	N/A	No	No	No	No
35447-2174	N/A	05/24/90 ⁴	N/A	No	Normal laboratory dog	100	Yes	N/A	No	No	No	No

¹ Euthanasia time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.

² Boron pharmacokinetic data obtained on these animals using MRS.

³ Three-dimensional chemical shift imaging (CSI).

⁴ Normal laboratory dogs - treated, not euthanized

(P) Partial results

N/A Not applicable

N/P Not Performed

* Serum only (no urine)

INEL BNCT CANINE PHARMACOKINETIC STUDY

SUMMARY OF PATIENT DATA

BSH INTRAVENOUS INJECTIONS STUDY

ANIMAL	NAME OF DOG	EUTHANASIA		CASE SUMMARY	PATHOLOGY DIAGNOSIS	DOSE (mg/kg)	BLOOD SERUM AND URINE ANALYSIS		TISSUE ANALYSIS	CT		MRI	
		DATE	MIN ¹							UNENH.	E.JH	UNENH.	ENH
35447-121	"Shorty" Morgan	07/02/90	180	Yes	Pituitary adenoma	55	Yes*	Yes	Yes	Yes	Yes	Yes	Yes
35447-126	"Beau" Smith	07/26/90	180	Yes	Meningioma	55	Yes*	Yes	Yes	Yes	Yes	Yes	Yes
35447-127	"Sam" Warner	07/31/90	180	Yes	Reticulosis	55	Yes*	Yes	Yes	Yes	Yes	Yes	Yes
35447-128	"Niki" Fox ^{2,3}	08/05/90	297	Yes	Choroid plexus papilloma	55	Yes*	Yes	Yes	Yes	Yes	Yes	Yes
35447-136	"Penny" Bird	12/08/90	170	Yes	Fibrillar/piloeytic astrocytoma	55	Yes*	Yes	Yes	Yes	Yes	No	No
35447-149	"Shandy" McKeever	02/05/91	180	Yes	Reticulosis	55	No	Pending	Pending	Yes	Yes	No	No
35447-153	"Dingo" Martin	03/19/91	170	Yes	Diffuse astrocytoma	110	No	Pending	Pending	Yes	Yes	No	No
35447-1846	N/A	03/25/91 ⁵	180	Yes	Normal laboratory dog	100	Yes	Yes	Yes	No	No	No	No
35447-2174	N/A	03/27/91 ⁵	180	Yes	Normal laboratory dog	100	Yes	Yes	Yes	No	No	No	No
35447-363	N/A	04/05/91	120	Yes	Normal laboratory dog	100	Yes	Pending	Pending	No	No	No	No

¹ Euthanasia or irradiation time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.

² Boron pharmacokinetic data obtained on these animals using MRS.

³ Three-dimensional chemical shift imaging (CSI).

⁴ Normal laboratory dogs - treated, not euthanized

⁵ Normal laboratory dogs - treated previously, now euthanized

(P) Partial results

N/A Not applicable

N/P Not Performed

* Serum only (no urine)

INEL BNCT CANINE PHARMACOKINETIC STUDY SUMMARY OF PATIENT DATA BSH INTRA-ARTERIAL INJECTIONS STUDY

<u>ANIMAL</u>	<u>SEX</u>	<u>DATE</u>	<u>EUTHANASIA (MIN)¹</u>	<u>BLOOD SERUM AND URINE ANALYSIS</u>	<u>TISSUE ANALYSIS</u>
2181	M	10/19/89	420	Yes	Yes
2067	F	10/26/89	420	Yes	Yes
2148	F	11/16/89	420	Yes	Yes

¹ Euthanasia or irradiation time in minutes following start-of-boron administration. Boron administration requires approximately 50 minutes.

INEL BNCT CANINE TUMOR TREATMENT STUDY
PHASE II - SURGERY/IRRADIATION

<u>ANIMAL</u>	<u>SEX/AGE</u>	<u>NAME OF DOG</u>	<u>BIOPSY DIAGNOSIS</u>	<u>SURGERY DATE</u>	<u>IRRAD DATE</u>	<u>BORON DOSE</u>		<u>START DURATION TIME¹</u>	<u>MINUTES²</u>	<u>CALCULATED DOSE (cGy)</u>	<u>¹⁰B ESTIMATED AVG (ppm)</u>	<u>SURV. DAYS</u>	<u>DEATH DATE/CAUSE</u>
						(mg ¹⁰ B/ kg/bw)							
35447-154	F/12	"Mokie" Elkin	Meningioma	05/29/91	--	---	---	---	---	---	---	No	05/30/91 Necrotizing encephalitis secondary to surgery complications

¹ Time from start of boron injection to start of irradiation.

² Irradiation time in minutes.

INEL BNCT CANINE PLASMAPHERESIS STUDY

GROUP	ANIMAL	SEX	DATE	PLASMA EXCHANGE			EUTHANASIA (MIN.)	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
				FIRST MIN ²	SECOND MIN ²	THIRD MIN ²			
1	2095 ¹	M	06/08/88	360	---	---	430	Yes	Yes
1	2084 ¹	M	06/09/88	360	---	---	446	Yes	Yes
1	2109 ¹	F	06/10/88	360	---	---	410	Yes	Yes
1A	2114 ¹	F	08/18/89	360	---	---	445	Yes	Yes
1A	2140 ¹	F	08/10/89	365	---	---	455	Yes	Yes
1A	2117 ¹	M	08/11/89	360	---	---	417	Yes	Yes
1B	2139 ¹	F	07/31/89	362	---	---	750	Yes	Yes
1B	2169 ^{1,3}	M	08/02/89	363	---	---	770	Yes	Yes
1B	2127 ¹	F	08/01/89	383	---	---	800	Yes	Yes
2	2097	M	06/14/88	360	---	---	413	Yes	Yes
2	2074	M	06/15/88	360	---	---	410	Yes	Yes
2	2092	F	06/16/88	360	---	---	400	Yes	Yes
2A	2066	F	08/17/89	360	---	---	390	Yes	Yes
2A	2145 ³	F	08/14/89	422	---	---	440	Yes	Yes
2A	2155	M	08/15/89	360	---	---	395	Yes	Yes
2A	1902	F	09/07/90	360	---	---	401	No	No
3	2103	M	06/20/88	360	---	---	755	Yes	Yes
3	2081	M	06/22/88	360	---	---	755	Yes	Yes
3	2089	F	06/24/88	360	---	---	790	Yes	Yes

¹ Control Animal (reinfused same boronated plasma that had just been extracted).

² Time from start of boron injection.

³ Dog went into respiratory arrest at 412 minutes, but was revived.

INEL BNCT CANINE PLASMAPHERESIS STUDY

GROUP	ANIMAL	SEX	DATE	PLASMA EXCHANGE			EUTHANASIA (MIN.)	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
				FIRST MIN ²	SECOND MIN ²	THIRD MIN ²			
3A	2076	F	08/04/89	365	---	---	760	Yes	Yes
	2112	M	08/03/89	374	---	---	775	Yes	Yes
3A	2149	M	09/27/89	---	---	---	420	Yes	Yes
	2131	F	09/28/89	---	---	---	420	Yes	Yes
	2165	F	09/27/89	---	---	---	420	Yes	Yes
	2143	M	09/28/89	---	---	---	420	Yes	Yes
	2179	M	09/29/89	---	---	---	420	Yes	Yes
	2182	F	09/29/89	---	---	---	420	Yes	Yes
	2148	M	11/16/89	---	---	---	420	Yes	Yes
	2181	M	10/19/89	---	---	---	420	Yes	Yes
	2067	F	10/26/89	---	---	---	420	Yes	Yes
4	2096	M	06/27/88	360	470	600	640	Yes	Yes
4	2104	M	06/28/88	360	480	600	660	Yes	Yes
4	2098	F	06/29/88	385	545	640	785	Yes	Yes
5	2091	M	08/18/88	120	---	---	163	Yes	Yes
	2073	F	09/08/88	130	---	---	160	Yes	Yes
5	2090	M	09/09/88	129	---	---	180	Yes	Yes
5	2078 ¹	F	09/15/88	120	---	---	180	Yes	Yes
6	2093	M	10/07/88	360	400	---	455	Yes	Yes
	2086	F	10/13/88	360	401	---	480	Yes	Yes
6	2068	M	09/23/88	405	505	---	560	Yes	Yes
6	2082 ¹	M	10/28/88	365	400	---	440	Yes	Yes

¹ Control Animal (reinfused same boronated plasma that had just been extracted).

² Time from start of boron injection.

INEL BNCT CANINE PLASMAPHERESIS STUDY

Page 3 of 3

GROUP	ANIMAL	SEX	PLASMA EXCHANGE			EUTHANASIA (MIN.)	BLOOD SERUM & URINE ANALYSIS	TISSUE ANALYSIS
			DATE	FIRST MIN ²	SECOND MIN ²	THIRD MIN ²		
A	I179	F	07/20/90	120	---	---	No	No
A	EG79	M	07/23/90	120	---	---	Yes	No
A	ACK79	M	08/08/90	120	---	---	Yes	No
B	G-1	F	03/16/90	145	---	---	Yes	Yes
B	G-8	F	03/22/90	120	---	---	Yes	Yes
B	G-10	F	05/04/90	120	---	---	Yes	Yes
B	G-11	F	06/06/90	120	---	---	Yes	Yes
B	2146	F	09/01/90	155	---	---	Yes**	Yes
C	G-2	F	03/23/90	360	---	---	Yes	Yes
C	G-6	F	03/23/90	370	---	---	Yes	Yes
C	G-7	F	04/06/90	360	---	---	Yes	Yes

¹ Control Animal (reinfused same boronated plasma that had just been extracted).

² Time from start of boron injection.

* Dosage was 100 mg boron/kg body weight.

** Serum only (no urine)

INEL BNCT CANINE DOSE-TOLERANCE STUDY

ANIMAL	SEX	IRRADIATION			ppm ¹⁰ B EST AVG	BLOOD SERUM URINE ANAL.	SURVIVING	DAYS	EUTHANASIA/DEATH		TISSUE ANALYSIS	
		START TIME ³	DURATION (MINS)	CALCULATED DOSE (cGy)					DATE	CAUSE		
1592 ¹	M	01/11/89	345	58.0	1,273	31.1	Yes	No	0	01/11/89	Euthanasia	Yes
1587 ¹	M	01/12/89	21	36.0	1275	57.8	Yes	No	0	01/12/89	Euthanasia	Yes
966	M	02/08/89	235	48.0	1453	47.6	Yes	No	365	02/08/90	Euthanasia	N/A
1588	M	02/09/89	220	49.0	1258	38.5	Yes	No	368	02/12/90	Euthanasia	N/A
995	M	02/09/89	238	42.0	1275	47.8	Yes	No	365	02/09/90	Euthanasia	N/A
1591	M	02/10/89	194	90.0	2629	45.5	Yes	No	368	02/13/90	Euthanasia	N/A
1564	M	02/28/89	204	87.0	2545	45.6	Yes	No	379	03/14/90	Euthanasia	N/A
997	M	03/02/89	190	74.0	2687	59.6	Yes	No	375	03/12/90	Euthanasia	N/A
983	M	03/02/89	160	149.0	3834	38.6	Yes	No	128	07/08/89	SeizuresN/A	N/A
1590	M	03/01/89	176	140.0	3800	41.4	Yes	No	155	08/05/89	Seizures	N/A
946	M	04/11/89	195	109.0	3821	57.1	Yes	No	137	08/26/89	Neurologic disease	N/A
985	M	04/13/89	170.0	168.0	6363	62.7	Yes	No	153	09/13/89	Neurologic disease	N/A
1700	M	04/12/89	182.0	166.5	6374	63.5	Yes	No	158	09/17/89	Neurologic disease	N/A
980 ²	M	04/11/89	155.0	120.0	Sham	4.0	Yes	No	372	04/18/90	Euthanasia	N/A
1589 ²	M	04/15/89	125.0	120.0	Sham	4.0	Yes	No	370	04/20/90	Euthanasia	N/A
2255	M	01/31/90	N/A	157.0	1000	0	No	No	369	02/04/91	Euthanasia	n/a
2256	M	01/30/90	N/A	236.0	1500	0	No	No	90	04/30/90	Euthanasia	Yes
2257	M	02/01/90	N/A	157.0	1000	0	No	No	369	02/05/91	Euthanasia	n/a
2258	M	01/31/90	N/A	236.0	1500	0	No	No	91	05/02/90	Euthanasia	Yes
2259	M	02/01/90	N/A	157.0	1000	0	No	No	365	02/01/91	Euthanasia	n/a
2260	M	02/02/90	N/A	236.0	1500	0	No	No	101	05/14/90	Euthanasia	Yes
2261 ²	M	02/05/90	N/A	N/A	N/A	N/A	No	No	N/A	08/08/90	Euthanasia	n/a
2262	M	02/01/90	N/A	157.0	1000	0	No	No	361	01/28/91	Euthanasia	n/a
2263	M	02/05/90	N/A	236.0	1500	0	No	No	98	05/14/90	Euthanasia	Yes
2264	M	02/02/90	N/A	236.0	1500	0	No	No	88	05/01/90	Euthanasia	Yes
2265	M	02/05/90	N/A	157.0	1000	0	No	No	360	01/31/91	Euthanasia	n/a
2266 ²	M	02/05/90	N/A	N/A	N/A	N/A	No	No	N/A	08/13/90	Euthanasia	No

¹ Dosimeter animals euthanized after irradiation.

² Control dogs given sham irradiations (0 cGy)

³ Time from start of boron administration

N/A Not applicable

INEL BNCT BMRR CALCULATED DOSE CONTRIBUTIONS AT LOCATION OF THE PEAK BLOOD-VOLUME DOSE (Dose rate components at peak dose location)

DATE	SUBJECT	Beam Size (cm)	D _b	D _f	D _g	D _n	D _r
12/16/88	Dog head phantom						
01/10/89	Dog head phantom						
01/11/89	Dog 1592	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
01/12/89	Dog 1587	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/08/89	Dog 966	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/09/89	Dog 1588	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/09/89	Dog 995	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/10/89	Dog 1591	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
02/28/89	Dog 1564	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
03/01/89	Dog 1590	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
03/02/89	Dog 983	5 x 10	0.1680	0.1600	1.6700	0.2600	2.0920
03/02/89	Dog 997	5 x 10	0.1680	0.1680	1.6700	0.2620	2.0920
04/11/89	Dog 946	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
04/12/89	Dog 1700	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
04/13/89	Dog 985	5 x 10	0.1680	0.1600	1.6700	0.2620	2.0920
07/07/89	Dog 35447-079, "Pugee"	10 x 10	0.2750	0.3000	2.4200	0.4300	3.1500
08/07/89	Dog head phantom						
08/07/89	Dog 35447-080, "Mugsy"	10 x 10	0.3480	0.3580	3.1200	0.6070	4.0850
08/25/89	Dog 35447-083, "Rusty"	10 x 10	0.2310	0.3000	1.9210	0.4030	2.6240
09/28/89	Dog 35447-087, "Benji"	10 x 10	0.2660	0.3000	2.4800	0.4280	3.2080
10/24/89	Dog 35447-095, "Godfrey"	10 x 10	0.2160	0.3000	1.735	0.3770	2.4120
10/25/89	Dog 35447-094, "Brandy"	10 x 10	0.2580	0.3000	2.1500	0.4505	2.9005
10/31/89	Dog 35447-093, "Brandy"	10 x 10	0.2920	0.3000	2.3300	0.5090	3.1390
11/30/89	Dog 35447-100, "Juno"	10 x 10	0.2521	0.3000	2.3000	0.4396	3.0396
02/16/90	Dog 35447-108, "Trixie"	10 x 10	0.2430	0.3000	2.2300	0.4250	2.9550
			0.2630	0.3000	2.092	0.4580	2.8500

D_r = Dose rate (Cgy/(minMW-ppm)) from the ¹⁰B(n,α)⁷Li reaction.
D_n = Dose rate (Cgy/(minMW)) from above-thermal neutron (primarily hydrogen recoil).
D_f = Gamma dose rate (cGy/minMW).
D_b = Dose rate (cGy/minMW) from the ¹⁴N(n,p)¹⁴C reaction, assuming 1.87 weight percent nitrogen in brain tissue (also a peak location).
D = D_r + D_g + D_n.

INEL BNCT BMRR CALCULATED DOSE CONTRIBUTIONS AT LOCATION OF THE PEAK BLOOD-VOLUME DOSE (Dose rate components at peak dose location)

DATE	SUBJECT	Beam Size (cm)	Db	Df	Dg	Dn	Dr
10/19/90	Dog 35447-118 "Scuzzy"	10 x 10	0.331	0.398	2.450	0.555	3.734
10/18/90	Dog 35447-129 "Too Wide"	10 x 10	0.325	0.352	2.797	0.546	4.020
10/19/90	Dog 35447-132 "Sarge"	10 x 10	0.289	0.387	2.406	0.484	3.566
10/29/90	Dog 35447-134 "Peggy"	10 x 10	0.279	0.342	2.258	0.468	3.347
01/22/91	Dog 35447-139 "Hobart"	10 x 10	0.316	0.405	2.692	0.530	3.943
01/22/91	Dog 35447-140 "Muffy"	10 x 10	0.233	0.340	1.761	0.391	2.726
01/23/91	Dog 35447-142 "Sugar"	10 x 10	0.310	0.340	2.715	0.520	3.885
02/07/91	Dog 35447-147 "Bomber"	10 x 10	0.288	0.352	2.456	0.263	3.5480
02/28/91	Dog 35447-151 "Dudley"	10 x 10	0.336	0.418	2.560	0.563	3.877
03/19/91	Dog 35447-152 "Zar"	10 x 10	0.311	0.362	2.802	0.522	3.997

D_b = Dose rate (cGy/(min·MW·ppm)) from the $^{10}\text{B}(n,\alpha)^4\text{Li}$ reaction.
 D_t = Dose rate (cGy/(min·MW)) from above-thermal neutron (primarily hydrogen recoil).
 D_g = Gamma dose rate (cGy/min·MW).
 D_n = Dose rate (cGy/min·MW) from the $^{14}\text{N}(n,p)^{14}\text{C}$ reaction, assuming 1.87 weight percent nitrogen in brain tissue (also a peak location).
 $D_r = D_t + D_g + D_n$

* Beginning with dog 35447-118, "Scuzzy," a D_{olhw} has been included in D_r .
 This dose rate has been included to account for all components not treated explicitly, most Cl, O, and C. It has been defined to be equivalent to D_b at 1ppm ^{10}B .

INEL BNCT CANINE MELANOMA PHARMACOKINETIC STUDY

SUMMARY OF PATIENT DATA

D, L-BPA STUDY

ANIMAL	NAME OF DOG	DATE	BORON DOSE	FORM OF BPA**	ADMINISTRATION		SURGERY OR EUTHANASIA	DATE
					ROUTE*	LENGTH		
39412-001	"Cindy" Coyne	01/11/89	50 mg/kg	D,L HC1	Orally	6 hrs	Euthanasia	01/11/89
39412-002	"Smokey" Griffith	01/18/89	50 mg/kg	D,L HC1	Orally	6 hrs	Euthanasia	01/18/89
39412-003	"Minnie" Martin	02/10/89	50 mg/kg	D,L HC1	Orally	6 hrs	Euthanasia	02/10/89
39412-004	"Tracker" Gill	04/25/89	183 mg/kg	D,L Nat	SQ,QID	36 hrs	Euthanasia	04/26/89
39412-005	"Percie" Nissley	06/07/89	200 mg/kg	D,L Nat	SQ,QID	48 hrs	Surgery	06/09/89
39412-006	"Heidi" Meshishnek	08/16/89	200 mg/kg	D,L Nat	SQ,QID	44 hrs	Surgery	08/18/89
39412-007	"Corky" Treadway	08/21/89	478 mg/kg	D,L Nat	SQ,QID	48 hrs	Surgery	08/23/89
39412-008	"Lucy" Dowling	10/27/89	500 mg/kg	D,L Nat	Orally	6 hrs	Euthanasia	10/27/89
39412-009	"Peanuts" Wetterayer	08/23/89	203 mg/kg	D,L Nat	SQ,QID	47 hrs	Surgery	08/24/89
39412-010	"Mindy" Sachjen	09/05/89	250 mg/kg	D,L Nat	SQ,QID	12 hrs	Euthanasia	09/06/89
39412-011	"Benji" Gebhard	09/14/89	750 mg/kg	D,L Nat	SQ,QID	48 hrs	Euthanasia	09/16/89
39412-012	"Muff" Hoglund	10/02/89	400 mg/kg	D,L Nat	SQ,QID	48 hrs	Surgery	10/04/89
39412-013	"Corky" Newby	10/11/89	491 mg/kg	D,L Nat	Oral,QID	48 hrs	Euthanasia	10/13/89
39412-015	"Missy" Freeman	11/14/89	750 mg/kg	D,L Nat	Orally	6 hrs	Euthanasia	11/14/89
39412-016	"Lucky" Nisonger	03/29/90	250 mg/kg	D,L Nat	Orally	6.5 hrs	Surgery	03/29/90
39412-017	"Winston" Sisteck-Lane	04/10/90	250 mg/kg	D,L Nat	Orally	5.5 hrs	Surgery	06/06/90
39412-017	"Winston" Sisteck-Lane	04/26/90	250 mg/kg	D,L Nat	Orally	6.5 hrs	Surgery	04/26/90
39412-017	"Winston" Sisteck-Lane	09/28/90	48 mg/kg	D,L in M	IV	7.0 hrs	Euthanasia	09/28/90

* SQ = subcutaneously
 QID = four times per day
 BID = two times per day
 ** 3-p-Boronophenylalanine

IV = intravenously
 M = molécusol

APPENDIX B

ACRONYMS

Acronyms

AAPM	American Association of Physicists in Medicine
ACS	American Chemical Society
ADM	Action Description Memorandum
ANS	American Nuclear Society
ASN	American Society of Neuroradiology
ATR	Advanced Test Reactor
AWU	Associated Western Universities
B/C	Boron-to-carbon
BMRR	Brookhaven Medical Research Reactor
BNL	Brookhaven National Laboratory
BNCT	Boron Neutron Capture Therapy
BPA	Boronophenylalanine
BSA	Bovine serum albumin
BSH	Borocaptate Sodium ($\text{Na}_2\text{B}_{12}\text{H}_{11}\text{SH}$)
BSS(B)	$\text{B}_{24}\text{H}_{22}\text{SS}^{4-}$
BSSO(B)	$\text{B}_{24}\text{H}_{22}\text{S}_2\text{O}^{4-}$
CAT	Corrective Action Team
CCF	Change control form
CD	Contrast diaphragm
CHNS	Carbon-hydrogen-nitrogen-sulfur
COCA	Consent Order Compliance Agency
CR-39	Allyl diglycol carbonate
CRADA	Cooperative Research and Development Agreement
CRF	Corticotropin releasing factor
CRH	Corticotropin releasing hormone
CSF	Cerebrospinal Fluid
CSI	Chemical shift imaging
CT	Computed tomography
DEA	Diethanolamine
DMAP	Dimethylaminopyridine
DMS	Data Management System
DOE	Department of Energy
DOE-ER	Department of Energy-Energy Research
DOE-HERAC	Department of Energy-Health and Environmental Research Advisory Committee
DOE-HQ	Department of Energy-Headquarters
DOE-ID	Department of Energy-Idaho Operations Office
DOE-NE	Department of Energy-Nuclear Energy
DOE-OHER	Department of Energy-Office of Health and Environmental Research
DOP	Detailed operating procedure
DORT	Two-dimensional S_n computer code
DSPC	Distearoyl phosphatidyl choline
EA	Environmental Assessment
ECAG	European Concerted Action Group
ECC	Elaidyl carborane carboxylate
EDF	Engineering Design File
EE	Environmental Evaluation
EGS	Engineering Graphics Systems
EGTA	ethylene glycol-dis(β -aminoethyl ether) MN,N,N',N'-Tetraacetic acid
EIRMC	Eastern Idaho Regional Medical Center
EKG	Electrocardiogram

EPA	Environmental Protection Agency
EPRO	Experimental Power Reactor Operator
ERDP	Exploratory Research and Development Project
ES&H	Environmental Safety and Health
ESMS	Event Sequence and Monitoring System
FCF	Facility Change Form
FDA	Food and Drug Administration
FIA	Flow injection analysis
FMEA	Failure Mode and Effects Analysis
GA	General Atomics
GE	General Electric
GHRH	Growth hormone releasing hormone
GIT-NRC	Georgia Institute of Technology-Neeley Research Center
GTRR	Georgia Tech Research Reactor
HAT	Hypoxanthane aminopterin thymidine
HDW	High pressure demineralized water
HEPA	High-efficiency particulate air filter
HERAC	Health Environmental Research Advisory Committee
HFR	High flux reactor
HMPAO	Hexamethyl-Propylene-Amineoxime
HP	Hewlett-Packard
HPLC	High Performance Liquid Chromatography
HPLC-UV	High Performance Liquid Chromatography-UltraViolet
IACUC	Institutional Animal Care and Use Committee
ICP-AES	Inductively Coupled Plasma-Atomic Emission Spectroscopy
ICP-MS	Inductively Coupled Plasma-Mass Spectrometry
IM	Ion microscope
IND	Investigational New Drug exemption from FDA
INEL	Idaho National Engineering Laboratory
INPO	Institute of Nuclear Plant Operations
IP-RP-HPLC	Ion pair-reversed phase-high performance liquid chromatography
ISU	Idaho State University
IV	Intravenous
KURRI	Kyoto University Reactor Research Institute
LDL	Low density lipoprotein
LET	Linear energy transfer
LOCA	Loss-of-coolant accident
LOFT/OECD	Loss-of-Fluid Test/Organization of Economic Cooperation and Development
MCNP	Three-dimensional Monte Carlo computer code
MIT	Massachusetts Institute of Technology
MR	Magnetic resonance
MRI	Magnetic resonance imaging
MRS	Magnetic resonance spectroscopy
MSTI	Mountain States Tumor Institute
MSU	Montana State University
NAS	National Academy of Sciences
NCAR	National Center for Atmospheric Research
NCI	National Cancer Institute
NCS	Network computing system
NDE	New Device Exemption (FDA)
NEPA	National Environmental Policy Act
NESHAPS	National Emission Standards for Hazardous Air Pollutants
NIM	National Institute of Medicine
NIST	National Institute of Science and Technology

NMR	Nuclear magnetic resonance
NWI	Northwest Imaging
OCT	A low-temperature adhesive
OHSU	Oregon Health Sciences University
ORAU	Oak Ridge Associated Universities
ORNL	Oak Ridge National Laboratory
ORSU	Oregon State University
OSF	Open Software Foundation
OSHA	Occupational Safety Health Administration
OSU	Ohio State University
PBF	Power Burst Facility
PDARS	Patient Data Acquisition and Retrieval System
PET	Position Emission Tomography
PMT	Photo multiplier tube
PNL	Pacific Northwest Laboratory
POM	Plant operating manual
PRP	Power Reactor Programs
PTC	Permit to Construct
QC/QA	Quality control/quality assurance
RAP	Requirements Awareness Program
RBE	Relative Biological Effectiveness
RCRR	Reed College Research Reactor
RESL	Radiological and Environmental Sciences Laboratory
RF	Radiofrequency
RFP	Request for Proposal
RIS	Resonance ionization spectroscopy
RP-HPLC	Reversed phase-high performance liquid chromatography
RTT-MC	Monte Carlo Transport Module
SAR	Safety Analysis Report
SDD	System Design Description
SIMS	Secondary Ion Mass Spectrometry
SIRIS	Sputter-Initiated Resonance Ionization Spectroscopy
TLD	Thermoluminescent dosimeter
TRA	Test Reactor Area
TTAF	Test Train Assembly Area Facility
UC/Berkeley	University of California Berkeley
UC/Davis	University of California Davis
UCLA	University of California Los Angeles
UCSF	University of California San Francisco
UOR	Unusual occurrence report
UofR	University of Rochester
UofU	University of Utah
USDA	United States Department of Agriculture
WAS	Work Authorization Statement
WSU	Washington State University

END

**DATE
FILMED**

12/23/91