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**Fred Hutchinson Cancer Research
and Pacific Northwest Laboratory**

**Cooperative Study of Clinical Benefits from
Use of the Fully Portable Blood Irradiator**

F. P. Hungate

October 1994

**Prepared for the U.S. Department of Energy
under Contract DE-AC06-76RLO 1830**

**Pacific Northwest Laboratory
Operated for the U.S. Department of Energy
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Staff exchanges, such as the one described in this report, are intended to facilitate communication and collaboration among scientists and engineers at Department of Energy (DOE) laboratories, in U.S. industry, and academia. Funding support for these exchanges is provided by the DOE, Office of Energy Research, Laboratory Technology Transfer Program. Funding levels for each exchange typically range from \$20,000 to \$40,000. The exchanges offer the opportunity for the laboratories to transfer technology and expertise to industry, gain a perspective on industry's problems, and develop the basis for further cooperative efforts through Cooperative Research and Development Agreements (CRADAs) or other mechanisms.

Following a request from the Fred Hutchinson Cancer Research Center (FHCRC) to assist them in developing a new approach to treating leukemia, a Cooperative Research and Development Agreement (CRADA) was initiated to produce irradiator units and to complete the task associated with the cooperative work.

Purpose/Objective

The primary objective was to move the blood irradiator toward clinical applications. The associated objectives were

- to assist FHCRC staff in the performance of clinical research through application of blood irradiation technology developed by Pacific Northwest Laboratory (PNL)
- to restart the technology associated with producing, calibrating, and providing irradiators for potential clinical users
- to allocate tasks between FHCRC and PNL so that the clinical objectives could most effectively be met.

Summary of Activities Performed

Prior to initiating the project, we contacted Dr. Ed Thomas, the head of the bone marrow transplant group at FHCRC, to seek assurance that the request for cooperative research from FHCRC was appropriate and would lead to clinical uses if positive results were achieved. Having received assurance from Dr. Thomas that such was the case, we proceeded to collaborate with Dr. Jim Bianco who had made the initial request of PNL.

The task of producing irradiators was more formidable than we had anticipated. The neutron source previously used had been the N reactor at Hanford. With that source no longer available and with the Fast Flux Test Facility lacking means for short period access to its neutrons, we finally found that the only suitable facility in the U.S. is a reactor at the University of Missouri. However, even with this information and with good cooperation from personnel at that site, it took nearly a year to get the appropriate paperwork in place to initiate the irradiation activity.

Meanwhile equipment required for fabrication of the irradiators was assembled by PNL's Roy Bunnell who directed fabrication of preliminary units for activation in the University of Missouri reactor. An initial activation was necessary to permit us to put the appropriate amount of thulium oxide in each irradiator so that the proper dose to blood could be achieved.

During this same period PNL's Bill Ricmatti designed and had appropriate shielding fabricated. This included shielding associated with use of the irradiators as well as shielding needed for disposal of irradiators no longer needed.

Also during this time it was learned that Dr. Bianco was no longer involved in research or associated with FHCRC. Dr. Fred Appelbaum, with whom Dr. Bianco had worked took over the project. It was agreed that the animal surgeries would be done at FHCRC and that they would supply the animals and hardware associated with installing the shunts. A contract to this effect had been agreed to.

However, in 1993, when irradiators became available, we found that initial attempts to install the A-V shunts at FHCRC were not successful and that FHCRC had been unable to obtain the required hardware. In fact, Quinitron Instruments, from whom the shunt hardware had been obtained several years ago, had thrown away all of their stocks as well as the molds used in fabrication. No other supplier was located, so PNL's Ross Gordon fabricated alternative shunt hardware. Dr. Richard Weller of PNL installed the shunts and treated animals were available for use in FHCRC experiments.

We were much taken back when Dr. Appelbaum declined to perform the planned experiments. His position at FHCRC changed drastically when he was appointed to be the physician in charge of the bone marrow transplant program of FHCRC, and his interest and availability to participate in specific research projects declined significantly. Although he continued to voice support for selected aspects of the blood irradiation research, we were unable to get FHCRC to follow through with a firm schedule for experiments and research protocols. No other physician at FHCRC was located to carry on the program, so it is now discontinued.

Significant Accomplishments

During the project, the following significant accomplishments were realized:

- blood irradiators were successfully fabricated by PNL
- the irradiators were activated at the University of Missouri and quality tested at PNL

- A-V shunts for the irradiators were successfully fabricated in the PNL plastics shop
- all activities necessary for experimental work on animals using the blood irradiators were completed.

At the completion of the project, animals and blood irradiation equipment necessary for planned experiments at FHCRC were fully available.

Significant Problems

The time required to place a subcontract with the University of Missouri and have the irradiators activated for experimental use delayed the planned schedule for the project. During this period, Dr. Bianco (who had originally contacted PNL regarding a joint research project utilizing the blood irradiators) left FHCRC. In addition, Dr. Thomas (the head of the bone marrow transplant group at FHCRC at the time the project was conceived) retired. As a result of these changes, the primary advocate of the planned experiments using the blood irradiators (Dr. Bianco) was no longer with FHCRC, and his replacement on the project (Dr. Applebaum) had substantially increased responsibilities. Communication with FHCRC regarding project activities and milestones became difficult. Ultimately, the project was unable to achieve its planned objectives because of a lack of interest and commitment to its successful completion on the part of the FHCRC.

Other problems that were faced and overcome by PNL staff resulted from the age of the blood irradiation technology. Shunts and other hardware that were previously available for use with the blood irradiators were no longer available. The need to seek out this equipment from potential vendors and ultimately, to fabricate some of the needed hardware at PNL increased project costs.

Industry Benefits Realized

No direct industry benefits were realized from this project as a result of the inability to bring the activities planned for the project to completion. The hoped for demonstration of the efficacy of the blood irradiation technology in improving cancer therapy was never realized.

Recommended Follow-On Work

PNL scientists continue to believe that the blood irradiation technology has potential for application in the medical area. Industry partners to explore such applications continue to be sought. However, no specific proposals for follow-on work have been developed at the time this report was prepared.

Potential Benefits from Follow-On Work

The potential benefits from follow-on work are difficult to discern until industry partners for such work are identified.

Lessons Learned

Although this project did not achieve its intended objective, there are several lessons that can be learned from the project

- So far as is possible, it is important to obtain the commitment of a company or an institution to a Cooperative Research and Development Agreement (CRADA) project, rather than an individual within the company or institution. If a commitment is totally focused on an individual, problems will occur if that individual leaves the organization.
- The difficulty of redeveloping and applying a technology after a two or three-year period of dormancy should not be underestimated. Many of the supporting factors necessary to expedite the reuse of the technology (e.g., access to irradiation facilities, available shunt material, etc.) may have changed.
- On many CRADA projects, the goals and interests of the industry partners will change during the course of the project. This project provides an extreme example of a partner whose interests changed over the course of the project to the degree that the project could not be successfully completed. The partner's change in interests was particularly difficult to address in this project because most of the partner's contributions to the project were planned to occur after PNL's efforts were largely completed.

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