IGEMs/HERC Project Status Report
Idaho Incubation Fund Program
Quarterly Progress Report
January 1, 2013

Proposal No.	**AHRC03**
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Name of Institution:	**Idaho State University/ Idaho Accelerator Center**
Project Title:	**Development of Commercially viable accelerator produced Isotopes**

1 PROJECT STATUS REPORT MILESTONES

This is a quarterly status report beginning FY 2013 for the IGEMs funded project, **Development of commercially viable accelerator produced isotopes**. The project proposal listed the following major project outcomes:

a. Have we established a commercially viable method of producing an isotope that is of economic potential and/or heretofore unavailable?
b. Have we created a technology, method or material that allows the creation of an isotope at a significant improvement in cost (either in direct material expense or capital requirements i.e. "fixed" costs)?
c. Are either a. or b. above proprietary, protectable and licensable to others with the objective of generating a positive return?
d. Have we trained a work force capable of advancing this industry and advancing our technology?

Our milestones are:

1). Simplify and improve the product separation processes suitable for operation in a commercial hot cell 2). Complete all equipment for high power accelerator tests 3). Complete multiple full process tests 4). Transfer separation and purification process to our commercial partner's hot cell, 5). Delivery of approved quantities to researchers for human trials.

In addition to these milestones, we are employing full time or part-time 6 researchers and engineers and 2 students.

Each of these key milestones will be detailed below with progress.

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2 PROJECT STATUS REPORT – Milestone review

For the three months ending December 31th, 2012, (Q2 FY 2013), the following items were completed against the project plan:

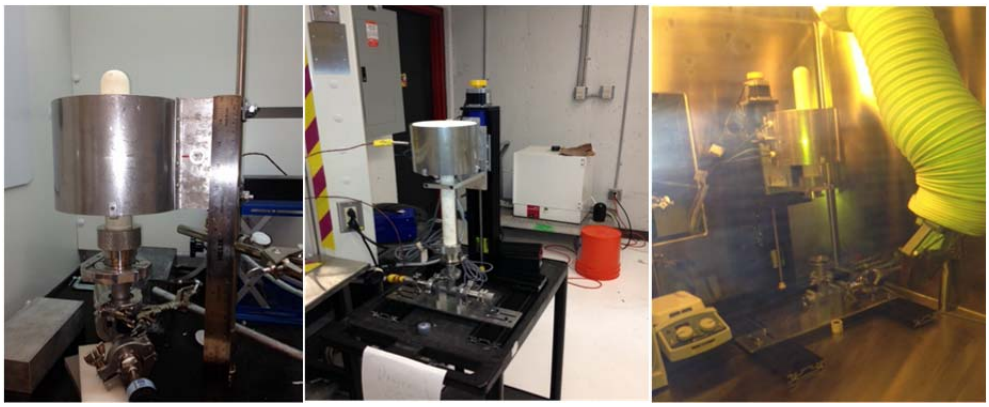
1). Simplify and improve the product separation processes suitable for operation in a commercial hot cell.

Summary: Excellent progress was made in improving the separation processes for the hot cell environment. Equipment was purchased and development completed on an automated sublimation furnace for use in the hot cell. Automation methods were begun for the peristaltic pump transfer system. The research team met with the commercial distribution partner to test-fit the equipment in the hot cell and review the process. As a result, several additional equipment modifications were started.

a). **Sublimation:**

The sublimation furnace that was completed in Q1 and tested successfully was retrofitted with equipment to automate the process. Picture 1a, below, shows the furnace as originally configured and tested and 1b, shows the furnace as retrofitted with a programmable linear

actuator to raise and lower the tube and heating element. These modifications are crucial for operation within the hot cell because of the limited access of the manipulator arms (see picture 1c).

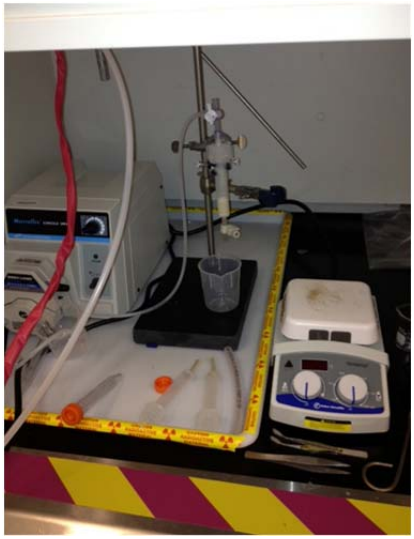


Picture 1a (left) shows the prototype furnace as originally constructed and tested. Picture 1b (center) shows the automated furnace using a linear actuator to raise and lower the heating element and sublimation tube. Picture 1c shows the furnace as installed in the hot cell for initial configuration testing.

The automation of the furnace required extensive machining of parts to integrate the linear actuator with the custom furnace and tube. Remarkably tight tolerance must be kept for the equipment because the activated crucible has less than 1mm of clearance *in total* for the entire operation of the furnace and the tube must be able to seal tightly to maintain a vacuum of 10^{-3} torr. Our next phase of work with the furnace is to further simplify the programming and the multiple wires that must be inserted through "feed-throughs" into the hot cell. We will be testing these configuration changes in Q3 as well as reinstalling the furnace in the hot cell for manipulation testing.

b). **Column separation:**

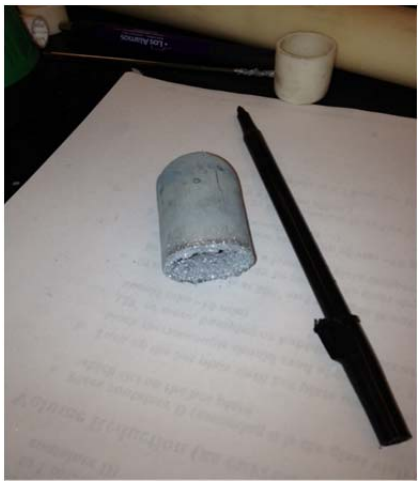
Last quarter we successfully improved the column separation process by simplifying to a single anion exchange process. We also eliminated the need for extensive pH adjustments prior to separation of the activated species. However, when we tested the equipment in the hot cell with our distribution partner, we found the equipment we selected for development in the lab was far too cumbersome for the manipulators. Picture 2 shows the pump system, column and hot plate configured from commercial sources. We brainstormed with our partner and designed a custom peristaltic pump system that can be operated external to the hot cell and will provide the ability to transfer acids and product between key steps. We have designed a two motor unit, constructed a PWM motor controller that will enable micro-liter volumes of material and procured the equipment for the system. We are currently waiting on the machining of the proprietary rotor and holding units for the system. We believe that this may become a critical component to the overall process and may be patentable. After the system is completed and tested in Q3 (both in the lab and in the hot cell) we will determine if we need to protect it with a patent application.



Picture 2 showing the peristaltic pump (left side of tray, column (center on ring stand) and hot plate (right side of picture). The new custom system will shrink all of the apparatus to approximately the size of the pump alone.

c). **Zinc recovery efforts**

As has been reported, a critical step to full commercialization is the use of a very expensive initial starting material, ^{68}Zn. ^{68}Zn is required to increase the yield of the product, ^{67}Cu and to decrease the unwanted radioactive impurities (such as ^{65}Zn). The initial amount of ^{68}Zn required is approximately 45 grams, or nearly $40,000. Only a very small amount (micro grams) of ^{68}Zn is converted to ^{67}Cu each run, therefore the starting material can be reused virtually forever if no other losses are occurring. One loss area that we have focused on is the ability to recover the Zn directly from the sublimation tube without additional processing. We found that significant losses can occur from melting the Zn for recovery, however, we have been able to limit those losses to 100-300 milligrams. This still represents from $100-$300 of loss each production run. This quarter we tried a technique of using liquid N_2 to dramatically cool the sublimed Zn and allow it to "slide" out of the sublimation tube. We were successful with this technique in a single trial (see picture 3) and intend to further test this method in Q3.



Picture 3, the Zn slug on the left represents approximately 30 grams of material that were removed directly from the sublimation tube using a liquid N_2 charge and light mechanical vibration.

d). **Analytical testing**

In Q2 we embarked on an ambitious effort to find a simplified analytical technique to determine the specific activity of the ^{67}Cu product we are manufacturing. The standard method used up to now to determine our purity levels has been an ICP-OES (inductively coupled plasma optical emission system). We cannot use this system when using radioactive samples because of potential contamination. Our commercial distribution partner has an ICP-MS system (mass spectrum) for final assay of material for shipment, however, we still require a simplified method that can be quickly used for sample preparation. Therefore, we selected a UV absorption method since we have that equipment in our lab and it will be similar to techniques used by our customers. After extensive literature review and discussion, we opted for a technique that combines our product with a chelating ligand. We tested two agents EDTA and PGTSC. The EDTA is readily available and provided an absorbance spectrum in the 240-260 nm region when combined with copper. The PGTSC had to be synthesized by us from two precursors using organic synthesis techniques. Remarkably, both techniques worked well with sensitivity in the hundreds of parts per billion, with the PGTSC being the preferred approach since the absorbance spectrum was approximately 400 nm and the binding characteristics with regard to zinc impurities in the samples is similar to the chelating agents our customers will use when combining our product with the Mab(s) (mono-clonal antibodies).

Next quarter actions:

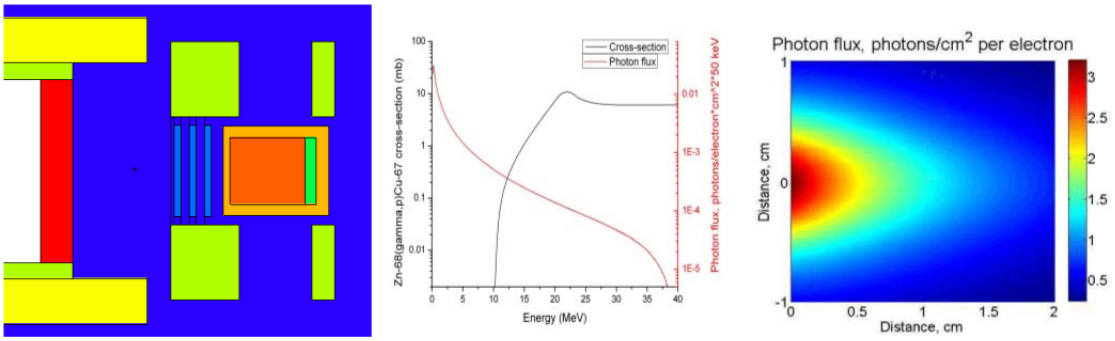
Complete construction of hot cell ready column separation system. Test all systems with full activations, retest all systems in the hot cell environment, verify analytical assays and zinc recovery.

2). Complete all equipment for high power accelerator tests

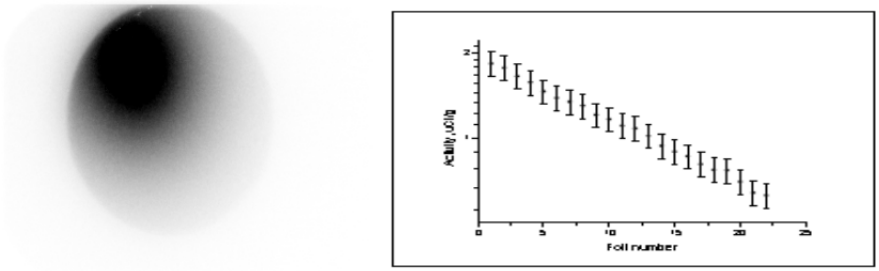
Summary: Equipment breakdown and repair prevented completion of more testing in Q2, however, a critical temperature vs power test was completed, a test for distribution of activation in the target with a new target system.

Accelerator:

Unfortunately, during high power testing of the accelerator early in Q2, a ceramic window failed allowing SF_6 from the microwave wave guide to enter the accelerator guide and gun. As a result, the accelerator was out of commission for nearly 8 weeks as a new window was constructed, a new gun purchased and installed and multiple tests completed of the accelerator to verify system integrity. However, we were able to complete some work for our next stage of production including implementing a new target system with an integrated converter (important to improve overall yield) and testing the heating of our target under low power to verify our heating models. An important part of the testing was comprehensive simulations using MCNPX (Monte-Carlo simulation program for nuclear reactions). Pictures 3a, 3b, and 3c show the configuration of the new converter/target system and the simulations of expected activity. The simulation predicted uniform and symmetrical activity, unfortunately, our actual experiment shows that the activity was not centered as we expected. Picture 4a and 4b show the activity as measured by a radio graph to be offset from the center of our target, however, the overall activity (4b) is in line with simulations. As a result of these results we are purchasing equipment for a laser alignment system that will allow precise location of the electron beam and the target. We expect to install this equipment and test it in Q3.



Picture 3a (left) shows the schematic illustration of our new target converter system that was simulated and tested. Picture 3b (center) shows the expected convolution of the bremsstrahlung spectrum with the target cross section. Picture 3c shows the simulated activity within the target as a function of position from the converter.



Picture 4a (left) is a radiograph showing activity within the target is offset from center. Picture 4b (right) shows the activity as measured down the target, in line with expectations.

Next quarter actions:

Complete all shielding of the target area including concrete and door. Complete new end-station. Run multiple 10 kW tests to evaluate stability and reliability. Complete new beam centering and monitoring systems.

3). Complete multiple full process tests

Summary: Because of configuration changes to separation equipment and loss of the accelerator for a significant portion of the quarter, we delayed additional full process testing until Q3.

4). Transfer separation and purification process to our commercial partner's hot cell

Summary: A very successful review was held with our commercial partner at their site. The results of this were noted in milestone 1. Our partner continues to be very involved with the development efforts and highly supported of efforts to fully commercialize the process.

5). Delivery of approved quantities to researchers for human trials.

Summary: We anticipate the ability to provide 10 mCi samples to researchers by the end of Q3 or the beginning of Q4, FY 2013. The gating items are the installation of critical alignment and monitoring systems on the accelerator and target and the procurement of sufficient ^{68}Zn. We believe we will have the technical details of these items worked out in Q3.

3 FINANCIAL

4 Intellectual Property and Commercial activity

Project Budget/Financial Status as of Q1, FY 2012

Budget Item	Planned Budget	Actual spend to date	Variance/Explanation
Salary + Tuition	290,000	83,082	Below spend plan
Consulting	56,500	36,990	Remaining on spend plan
Travel expenses	10,800	0	Below budgeted spend
Materials and Equipment	213,400	35,853	Below budgeted spend
Beam time	100,000	14,000	Below budgeted spend

Summary: We are committed to cautious use of funds while retaining top quality researchers and engineers on this project. We expect higher spend rates in Q3 and Q4 as we begin our push for sample delivery. No filings for patents have been made to date, however, we are considering several innovations for possible applications. We are engaged with International Isotopes Incorporated as our commercial partner.

We are highly indebted to the work of Dr. F. Harmon, Dr. V. Starovoitova, Kevin Folkman, Chad O'Neil, Mark Balzar, and Tim Gardner

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