COVER SHEET FOR GRANT PROPOSALS

State Board of Education

SBOE PROPOSAL NUMBER: (to be assigned by SBOE)	AMOUNT REQUESTED: **$74,100**

TITLE OF PROPOSED PROJECT: Development of a Commercial Process to Produce ^{123}I Using an Electron LINAC

SPECIFIC PROJECT FOCUS:

Executive Summary:

This request provides support to develop a novel process for producing iodine-123 (^{123}I) using an accelerator at the IAC. The project involves building and testing a target, developing an extraction process, and verifying yields and purity. An outcome of this project is a commercial process for production to be utilized by our industry partner, International Isotopes Inc. (INIS) to eventually produce and ship ^{123}I through its customer network.

^{123}I is a widely used SPECT diagnostic imaging isotope with a short, 13 hour half-life that is replacing the more commonly used ^{131}I . ^{123}I has many advantages over ^{131}I due to improved image quality and lower patient radiation dose. The disadvantages include a much higher cost and less supply. International Isotopes is an FDA approved supplier of ^{131}I and is interested in supplying ^{123}I. The IAC and INIS are jointly investigating a new method of production using a photo-nuclear reaction instead of a high power cyclotron. The potential advantage would be high purity at an equivalent or lower cost of production.

North American radiopharmaceutical demand in 2012 was approximately $1.9B with SPECT imaging products the bulk of those sales. ^{123}I is the fourth largest usage SPECT isotope with estimated NA sales of approximately $30M.

If the process development is successful, meets business goals, and achieves FDA approval, this project could lead to an Idaho production facility dedicated to ^{123}I production, operating 5 days/week with several employees. In addition, ^{123}I would be available to intermountain area hospitals and imaging centers, improving growth of their businesses.

PROJECT START DATE: 07/2015	PROJECT END DATE: 06/2016
NAME OF INSTITUTION: **Idaho State University**	DEPARTMENT: **IAC**
ADDRESS: : **921 S. 8th Avenue, Pocatello, Idaho 83209**	
E-MAIL ADDRESS:	PHONE NUMBER:

	NAME:	TITLE:	SIGNATURE:
PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR	Jon Stoner	Director of Technical Operations, IAC	Jon Stoner
CO-PRINCIPAL INVESTIGATOR	Dr. Frank Harmon	Professor Emeritus, Dept. of Physics, ISU	Fk Harmon

NAME OF PARTNERING COMPANY: International Isotopes, PMC, INL	COMPANY REPRESENTATIVE NAME: Steve Laflin

	NAME:	SIGNATURE:
Authorized Organizational Representative	Dr. Cornelius Van Der Schyf	[signature] for CVdS.

SUMMARY PROPOSAL BUDGET

Name of Institution: Idaho State University

Name of Project Director: Jon Stoner

A. PERSONNEL COST (Faculty, Staff, Visiting Professors, Post-Doctoral Associates, Graduate/Undergraduate Students, Other)

Name/ Title	Salary/Rate of Pay	Fringe	Dollar Amount Requested
Dr. Frank Harmon	$16,200	$1,458	$17,658
Tim Gardner Radio Chemist	$9,264	$4,380	$13,644
Kevin Folkman	$8,846	$4,014	$12,860
Undergraduate	$3,120	$278	$3,398
% OF TOTAL BUDGET: 64%			$47,560

B. EQUIPMENT: (List each item with a cost in excess of $1000.00.)

Item/Description	Dollar Amount Requested
Target/End station raw materials (aluminum piping, pumping system) Components may or may not cost over $1000 each. We are investigating used equipment and requesting bids, but, since the used market is volatile, we are unsure final costs. We estimate final value of the equipment will be $14,000	$14,000
SUBTOTAL:	$14,000

G. TRAVEL:

Dates of Travel (from/to)	No. of Persons	Total Days	Transportation	Lodging	Per Diem	Dollar Amount Requested
					SUBTOTAL:	0

H. Participant Support Costs:

	Dollar Amount Requested
1. Stipends	
4. Other	
SUBTOTAL:	0

I. Other Direct Costs:	Dollar Amount Requested
1. Materials and Supplies (Chemicals and Target materials)	**$2500**
2. Publication Costs/Page Charges	
3. Consultant Services (Include Travel Expenses)	
4. Computer Services	
5. Subcontracts	
6. Other (specify nature & breakdown if over $1000) Accelerator Beam Time	$10,000
SUBTOTAL:	
J. Total Costs: (Add subtotals, sections A through I) **TOTAL:**	**$74,060**
K. Amount Requested: **TOTAL:**	**$74,060**
Project Director's Signature:	Date:

INSTITUTIONAL AND OTHER SECTOR SUPPORT
(add additional pages as necessary)

A. INSTITUTIONAL / OTHER SECTOR DOLLARS

Source / Description	Amount
Idaho Accelerator Facility	
Consulting from International Isotopes (estimate value of hours of support = 200 @ $50/hour)	$10,000

B. FACULTY / STAFF POSITIONS

Description
Jon Stoner – Director of Technical Operations, IAC - supported by other funds

C. CAPITAL EQUIPMENT

Description
Idaho Accelerator Center Isotope Accelerator

D. FACILITIES & INSTRUMENTATION (Description)

Idaho Accelerator Center Chemistry Laboratory, ICP-MS, Multi-channel analyzer and assorted instrumentation.

Project Narrative

HERC 2016 Incubation Fund Request: : Development of a Commercial Process to Produce ^{123}I Using an Electron LINAC

Institution: Idaho State University – Office for Research

PI: Jon L. Stoner – Director of Technical Operations, Office of Research

Previous requests: The original research into medical isotopes for commercialization received HERC funding in FY 2012 and a HERC/IGEMs grant in FY-13- FY 15. This Incubation fund request has not been previously made.

Background:

Over the last 4 years, the IAC developed a method of producing ^{67}Cu isotope from ^{68}Zn using an electron LINAC and a proprietary separation procedure (work support by HERC and reported previously). The IAC is currently shipping ^{67}Cu to multiple customers. We are working to leverage our expertise into new isotopes and new markets. Our long term goal is to create an isotope supply and research hub for Idaho at the IAC to drive commercial and research growth in the intermountain region.

We have been researching the production of ^{123}I as a new isotope for our portfolio. ^{123}I is a relatively short half-life (13 hour) medical isotope used as a SPECT diagnostic tool for imaging organs in the body, especially the thyroid, and detecting various cancers. ^{123}I is replacing what has been the traditional isotope for this purpose, ^{131}I. ^{123}I is now the isotope of choice for diagnostic pharmaceuticals containing radio-iodine because it has a shorter half-life and does not decay with beta radiation which significantly reduces the radiation dose delivered to the patient compared to ^{131}I. The production and distribution of these two iodine isotopes is significantly different. ^{131}I is produced in nuclear reactors and with its half-life of 6 days is convenient to transport from source to user. Currently ^{123}I is produced by using large cyclotron accelerators whose energy is about twice that of the more usual medical cyclotron. Only a few large cyclotrons capable of producing ^{123}I exist in North America and the isotope must be shipped regionally to be used in approximately 30 hours.

We believe it is possible to produce ^{123}I using a photonuclear process and an electron LINAC, similar to the activation process we developed for producing ^{67}Cu. The potential advantages would be high purity of production, lower cost of manufacturing, and a regional supply. Demand exists for ^{123}I. Our distribution partner International Isotopes has received requests from a major medical supplier for a new source of the isotope. International Isotopes has supplied a strong letter of support for this project (attached).

Market

^{123}I is the fourth largest produced SPECT isotope world-wide. The total North American market for SPECT isotopes was estimated at ~$1.9 B in 2012 with an annual growth of 7.2% [Markets and Markets report]. While we don't have explicit data for the market size for ^{123}I, a review of annual revenues from the largest producers, Malinkrodt, Nordion, very conservatively suggests the market size is in the range of $13-30M with a 5-10% annual growth. Based on reviews of current pricing, remuneration values from Medicare and customer feedback, we believe our addressable market is approximately $2-5M with future expansion. The appropriate price point for ^{123}I is approximately $100/mCi for substantial profit margin. This, incidentally, is the same price point we set for our ^{67}Cu project.

Process

As mentioned, our approach to this market is to develop a photonuclear process. In this process, an isotopically enriched target of ^{124}Xe will be irradiated with gamma rays produced by an electron LINAC. The precise process is: $^{124}Xe(\gamma,n)^{123}Xe$ followed by ^{123}Xe decaying to ^{123}I , a 2 hour half-life. The current cyclotron process produces approximately 800mCi to 1000mCi per day of production using $^{124}Xe(p,pn)Xe^{!23}$. Our initial estimates place our yield at approximately 500mCi/day of production. While cyclotron yields look substantially higher based on published data, the e-LINAC should have lower operating costs compared to the cyclotron. In addition, our process has potential advantages over the existing cyclotron process in that a larger enriched target can be used (increasing total yield) and an energy can be selected that minimizes production of other contaminating iodine isotopes. In this project we will be developing a target system to contain the enriched ^{124}Xe , developing an extraction process for the final material, sodium iodide, and testing the process with natural Xe. This work allows us to test our theory of production and provide solid data for a business analysis and commercialization.

FDA approval

Certainly a major concern with any product destined for the medical market is approval by the FDA. International Isotopes addresses this concern in their letter, but, essentially, since the drug is in production today, the starting material for its production is the same in our process, and International Isotopes is a GMP approved producer of isotopes, FDA approval should be substantially smoothed, presenting a much shorter timeline for drug acceptance, as short as 18 months from application.

Initial Business Case

Based on our initial estimates of yields including de-rating factors for decay and production losses, our target estimates for daily salable production would be 220 mCi, at our estimated price point $2200. Five day/week operation and 45 weeks/year gives approximately $500k of annual revenue per operating system. Based on our knowledge of operation costs, this will achieve at least a 40% GPM with significant future potential for improvements. We believe the business case will be very attractive with a prove-out of the technology.

Intellectual Property

The process we are proposing has been somewhat studied by others [1981, 1987, 1996]. However, the market is significantly larger now and a stronger impetus for development exists. A review of existing patents suggests that, if successful, our technology could have patentable and valuable intellectual property. In the long term, this process could be licensed to a number of producers.

Project/Timeline/Budget

The personnel involved in this project are: Dr. Frank Harmon, Jon Stoner, Tim Gardner, Kevin Folkman, and an undergraduate student. Total project budget request is $74,060. The project will be done in these stages (elapsed time):

A. Target System

1). Paper design and monte carlo simulation of target: Jon Stoner/Kevin Folkman (2 months)

2). Procurement of materials and construction of target system (cryopumping apparatus, sweep magnets, target chamber, piping, valves, etc.) Folkman/Stoner/Frank Harmon (5 months)

3). Beam testing, counting, yield analysis: Harmon/Stoner/Engineer (2 months)

4). Quality analysis

B. Separation and purity analysis

1). Review and cold testing of separation and purification techniques: Tim Gardner (1 month)

2). Development of system for hot isotope testing: Gardner (3 months)

3). Product analysis: Gardner/Stoner (1 month)

Facilities & Other Resources

Introduction

The Idaho Accelerator Center (IAC) was created by the Idaho State Board of Education in 1994. The IAC is charged with undergraduate and graduate education, conducting applied physics research, creating new applications of accelerator physics and supporting the economic development of Idaho. Current IAC research emphases include (i) fissile material detection for nuclear non-proliferation, safeguards and homeland security, (ii) photon activation and nuclear forensics for environmental, archaeological and national defense applications, (iii) radiation effects in biological and solid-state systems, (iv) basic nuclear physics, (v) accelerator physics and, most recently, (vi) isotope production.

The IAC has 6 operating accelerators in 3 research facilities with over 40,000 sq. ft. of laboratory space. This is one of the most extensive university accelerator laboratories in North America. The operational and user personnel at these facilities consist of scientists, engineers, safety personnel and administrative assistants. In addition, undergraduate and graduate students have ongoing research projects at the IAC.

Main IAC "Campus"-Accelerator Laboratory #1

The main IAC campus, was constructed in 1999 and initially consisted of office space and Accelerator Laboratory #1. This accelerator lab was built into the hills that surround Pocatello Idaho and the 2,010 sq. ft. hall is 20 feet underground providing ample radiation shielding. This accelerator hall houses a 44 MeV Short Pulsed LINAC and one of the 25 MeV LINACs. In addition, this accelerator hall has a well shielded experimental cell that is separated by a six foot wall from the accelerator hall. This wall has four penetrations allowing collimated bremsstrahlung beams to be delivered to a "low" radiation environment, which is critical for precise photonuclear measurements. This accelerator laboratory and its two accelerators may perform supplemental irradiations for this project. A picture of the facility is shown below.

The Idaho Accelerator Center.

The 44 MeV Short Pulsed LINAC is an L-band traveling wave radio frequency accelerator operating at ~1.3 GHz. It is capable of delivering electron pulses with operator selectable widths between 70 pico to 4 micro-seconds at a repetition rate up to 120 Hz. This accelerator is currently capable of approximately 4 kW of average electron beam-power. The electron energy can be varied from ~4 to 44 MeV with an energy resolution of 0.5% to 4%, controlled by a set of retractable slits.

The 25 MeV LINAC in Accelerator Laboratory #1 is an S-band standing wave radio frequency accelerator operating at ~2.8 GHz. This machine is capable of approximately 2.5 kW of average electron beam power. The electron energy can be varied from ~5 to 25 MeV with an energy resolution of 5%, which can be reduced using collimators or slits. This accelerator has a broad parameter space, is easy to operate and when precise beam parameters or short electron pulses are not required this is often the accelerator of choice.

Main IAC "Campus"-Accelerator Laboratory #2

Accelerator Laboratory #2 houses the 10 kW 40+ MeV accelerator. It is a 777 sq. ft. accelerator hall built into the hill and is approximately 10 feet underground for radiation shielding. Beam parameters are from 1 to 9 micro-seconds width at 50 to 100 mA per pulse. Besides the accelerator, the room incorporates additional target cooling, shielding and monitoring.

Main IAC "Campus"-ISIS Laboratory

The SLIA Laboratory is a 7,659 sq. ft. high-bay accelerator laboratory, which houses the Spiral Line Induction Accelerator System (SLIA). SLIA is a pulsed-power accelerator that provides an extraordinary high power accelerator capability at the IAC. It consists of a ~3 MeV injection accelerator that generates an electron beam for a ten cell induction accelerator. Due to the spiral lines, the electrons make two passes through each induction cell. At full power ISIS can deliver a 35 ns, 9.5 MeV electron pulse with 10 kA of current for ~0.1 TW of peak power. Due to the capacitor charging times, ISIS can fire about once every two minutes. This accelerator has been used for radiation effects research in electronic and biological systems. This accelerator may be used for high peak-power testing of targets.

In addition, the IAC is in the process of installing a 3 MeV high current (20 KA) pulse power machine next to SLIA. This machine will be known as Tri-MeV and should be operational by end of year, 2015.

Physical Sciences Building-HRRL Laboratory

The HRRL Laboratory is located in the basement of the physical sciences building and is a 400 sq. ft. accelerator hall with an adjoining 700 sq. ft. well shielded experimental cell. This laboratory houses the High-Repetition Rate LINAC (HRRL). The HRRL is a 20 MeV S-band standing wave radio frequency accelerator operating at ~2.8 GHz. It is capable of delivering electron pulses with a width 70 ns at a repetition rate up to 1,200 Hz. The maximum charge per pulse is 8.4 nC. The electron energy can be varied from ~12 to 20 MeV with an energy resolution of 8%. The role of this accelerator will be to serve as a backup irradiation source and target testing. There is also a 2 MV Van de Graff in this laboratory.

IAC – open environment testing facility at the Pocatello Airport (IAC-airport)

The IAC-airport is located near the Pocatello Regional Airport and has a 20,000 sq. ft. high-bay space for large scale systems testing and 15 acres of open area for field testing. Currently at the IAC-airport, is a 25 MeV accelerator similar to the ones located at the IAC Main "Campus", which is being used by for investigating the detection of fissionable materials at large distances. In addition, there is a 10 MeV LINAC, which is part of the cargo container scanning test bed. This 10 MeV LINAC is an S-band standing wave radio frequency accelerator operating at ~2.8 GHz. This facility also serves as a storage facility for many accelerator subsystems, including targets, kylstrons, accelerating cavities, etc. As such, it is an excellent test-bed for developing and testing new accelerator or target systems.

IAC – Chemistry Laboratory

The IAC main campus houses a 500 sq ft radiation chemistry laboratory with two hoods (one for radiation work). Analytical equipment includes a PE ELAN DRC II ICP-MS, NaI detector multi-channel analyzer, Hewlet Packard HPLC, UV spectrometer, and various analytical chemistry supplies.

Detectors and Data Acquisition

Detector, target, accelerator and data acquisition equipment to support this project is abundant. The IAC currently possesses over five HPGe detectors that can be utilize for post-irradiation analysis. There is also a large array of photomultiplier tubes, scintillators, ^{3}He detectors and a Detector Science Laboratory to support this research. The data from these detectors can be acquired, by three different multi-parameter data acquisition systems that can handle up to 16 channels of data each. There are also two VME systems that are very flexible. Modules for these systems include a 16 channel multi-hit time to digital converter, 16 charge to digital converters, a 16 channel pulse height analog to digital converter and 16 channel scalars. Finally, the IAC has over 100 nuclear instrument modules that can be employed for various pulse shaping functions and logic control.

New detector and data acquisition development, if any is required for real-time target monitoring, place in the Detector Science Laboratory, which is a 1,100 sq. ft. lab specifically for the construction and testing of new detectors. This lab includes a dark room for photomultiplier work, chemical hoods for potential hazardous vent gasses and optical tables for precision wire placement. One of the two VME data acquisition system in normally located in the DSL for development work.

Radiation Effects Simulation and Radiation Transport Simulation Capabilities

The Idaho Accelerator Center has excellent computational capabilities. The MCNPX radiation transport simulation program incorporates MPI technique to perform simulations in parallel. Thus, to reduce calculation time all MCNPX calculations can be done on several high computing network clusters. The first cluster, BREMS, has 12 nodes, 52 cores, 64 GB of aggregate memory, and 108 GHz of aggregate CPU power. This cluster is dedicated to the Idaho Accelerator Center research activities. The second one is MINERVE, which has 12 nodes, 192 cores, 384 GB of memory, and 384 GHz of aggregate CPU power. This cluster is shared among all researchers at the College of Science and Engineering at Idaho State University.

Engineering and Technical Support at the IAC

The IAC has 5 personnel on its engineering and technical staff. Staff are responsible for construction of the various accelerator systems, accelerator operations, care of the overall facilities and all aspects of safety with an emphasis on radiation safety. Support facilities heavily used by the technical staff include, the IAC machine shop, the IAC electronics shop and the IAC radiation dosimetry laboratory.

C.V.
Jon L. Stoner
209 Stanford Ave.
Pocatello, ID
208-760-0692

EXPERIENCE

Director of Technical Operations — **Date: March 2014 - present**
Office of Research and Economic Development
Idaho State University

CJ Tech Consulting LLC — **Date: April 2008 - present**
CEO/ Founder

Chief Technology Officer, Sr. Vice President, — **Date: 2001- March 2008**
General Manager of Image Sensor Products
Sr. Vice President, Acquisitions, Strategy
AMI Semiconductor

Director Business Development, Director Standard Product BU — **Date: 1988-2000**
Director R&D, Project Manager, Fab 10
Director R&D, Director Operations Engineering, Director Foundry Engineering
AMI Semiconductor

Various roles in engineering in Operations, R&D, Product Engineering and Development — **Date: 1980-1985**

EDUCATION & TRAINING

- MS Physics – Idaho State University
- Graduate School University of Montana, Utah State University (Chemistry, Engineering)
- University of Minnesota School of Dentistry
- BA Chemistry – University of Montana with Honors
- Additional coursework in management, product development, and marketing

OTHER

- Member of Advisory Committee to Idaho State Board of Education on Engineering education – 6 years
- Member Advisory Board for BSU school of Engineering
- Governor appointed member EPSCORE (Experimental Program for Competitive Research) committee for State of Idaho 6 years

RELEVANT PUBLICATIONS

Optimization of Commercial Scale Photonuclear Production of Radioisotopes, Bindu KC, Frank Harmon, Valeriia Starovoitova, Jon Stoner, Douglas P Wells, 22nd International Conference on the Application of Accelerators in Research and Industry, August 2012, Fort Worth, TX

Cu-67 photonuclear production, Valeriia Starovoitova, Bindu KC, Frank Harmon, Jon Stoner, Douglas P Wells, 7th ICI, September 2011, Moscow, Russia

PATENTS (applications in progress)

Methods for producing medical isotopes
Device for producing medical isotopes

SURNAME: Harmon **FIRST NAME(S): Frank**

Affiliation and official address:
Idaho Accelerator Center
Idaho State University
Pocatello, ID 83209

Telephone: (208)282-5877
email:harmon@physics.isu.edu

Date and place of birth:
02/23/39 Van Wert, Ohio

Nationality: American

Education (*degrees, dates, universities*)

Portland State University	Physics	B.S. 1963
University of Wyoming	Physics	M.S. 1965
University of Wyoming	Physics	Ph.D. 1968

Career/Employment (*employers, positions and dates*)

2006-present:	Senior Scientist, Idaho Accelerator Center
1997-2006:	Director Idaho Accelerator Center
1983 - 1997:	Chairman of Department of Physics
AY 91/92:	Acting Director of Particle Beam Laboratory
Spring 1990:	Sabbatical leave at University of Münster, Germany
1981 - 2006:	Idaho State University, Professor of Physics
1972 - 1977:	Idaho State University, Chairman of Department of Physics
1973 - 1980:	Idaho State University, Associate Professor of Physics
1969 - 1973:	Idaho State University, Assistant Professor of Physics
1968 - 1969:	Research Associate - Associate Instructor (Post-Doctoral appointment) Physics Dept., University of Utah, Salt Lake City, UT

Specialization
Applied Nuclear Physics
Instrumentation
Accelerator Applications

Honours, Awards, Fellowships, Membership of Professional Societies

Principle for more than 100 grants and contracts from various sources
Distinguished Researcher 1998 – 1999
The ISU Achievement Award 2000
Director of ISU Organization (Idaho Accelerator Center) which launched two new businesses.
Consultant to LANL, INEEL

Publications
-Number of papers in refereed journals: 38
-Number of communications to scientific meetings: 60

International Isotopes Inc.

June 17, 2015

To: Idaho State Board of Education Higher Education Research Council

Subject: International Isotopes Inc. Letter of Support for Developing a Commercial Process to Produce I-123 Using an Electron LINAC at Idaho State University

International Isotopes Inc. (INIS), is a commercial producer and distributor of isotopes, radiochemicals, sealed sources and various products required in nuclear medicine. INIS is partnering with the Idaho Accelerator Center to develop a novel process to produce the medical isotope I-123.

I-123 is used as an imaging agent distributed by some commercial companies in the U.S. and those products are approved by the U.S. Food and Drug Administration under several trade names. The I-123 isotope is made using cyclotrons of 25 MeV or greater and using enriched xenon isotope as the starting raw material. INIS intends to develop a generic drug product using I-123. Because of the very short (13.2 hour) half-life of the isotope there would be significant advantage to producing the I-123 product as close to the INIS facilities as possible. If this process can be developed, INIS would work to develop the abbreviated new drug application and eventually commercialize distribution of the I-123 product.

International Isotopes Inc. has been in business since 1996 and commercially shipping I-131 for about twelve years. INIS is in the process of submitting an abbreviated new drug application for its current I-131 product and can use most of these same processes to gain FDA approval of an I-123 product as well. INIS has the technical, market, and regulatory knowledge necessary to commercialize the I-123 product. INIS will be supporting the IAC with technical and commercial reviews of the process and guiding the development with its understanding of FDA and market requirements. INIS will be consulting with the IAC on infrastructure requirements for full commercialization. When commercial sales are realized Idaho State University will receive direct financial benefit from production of I-123 either through direct sales or as a royalty of the INIS drug product sales.

In addition, INIS would like to reserve the right to invest additional resources or capital into the project at the appropriate time if the technology is meeting our business requirements.

Sincerely,

Steve T. Laflin
President & CEO
International Isotopes, Inc.
STL-2015-52

4137 Commerce Circle, Idaho Falls, Idaho 83401
Phone: 208-524-5300, 800-699-3108 Fax: 208-524-1411
Website: www.intisoid.com