June 14, 2011

"Thorenco LLC's Converter and Target for Actinium-225 Production"

DE FOA 0000517

Pre-Application Cover Sheet

This document is the pre application for Charles S. Holden's and Thorenco LLC's Submission Entitled:

"Thorenco LLC's Converter and Target for Actinium-225 Production"

Thorenco LLC's manager is Charles S. Holden and the Inventor of the Target, Principal Investigator. Richard Wittman Ph. D of Pacific Northwest National Laboratory is an investigator as is Robert E. Schenter who is in the private sector. Further, Darrell Fisher Ph. D of Pacific Northwest National Laboratory and Douglas Well of Idaho Accelerator Center will be providing technical assistance for the construction of the new target.

Contact Information for the PI is: rusthold@mindspring.com 415 398 7878.

Charles S. Holden and Thorenco LLC's Address is

333 Pine Street Suite 400 San Francisco California 94104.

Confidential Submittal

The methods and materials set out in this pre application to produce actinium-225 and other isotopes are business confidential and are protected as trade secrets or under US patent filings. Intellectual Property Owners Reserve all rights. No license to use the technology is granted for any use to any third party.

Thorenco LLC's Converter and Target for Actinium-225 Production

Project Description

1. Introduction.

Charles S. Holden (individually and as manager of Thorenco LLC) intends to build a new target that produces copious Bremsstrahlung gammas by high energy electron interactions with high-Z nuclei. The new target enables production of actinium-225 by gamma, n reactions from radium-226. Thorenco's process uses energetic gamma radiation generated from electrons to transmute radium-226 to radium-225 that soon decays to actinium-225. The process appears to be more productive and less costly than other methods of making actinium-225.

Actinium-225 is needed for medical research as it is the essential material from which bismuth-213 is generated. Using the gamma, n production process, actinium-225 can be produced at lower cost than methods that start with fissile uranium-233. Thorenco's gamma, n process will increase the availability of bismuth-213 to the medical research community for therapeutic treatments for many types of single cell cancers and potentially for selected intractable or antibiotic resistant infectious diseases.

In contrast to the difficult and expensive methods of producing actinium-225 starting with separation of thorium-229 from fissile uranium-223, Thorenco's gamma, n process starts with radium-226. No longer is there a requirement to separate fissile uranium-233 from its first decay product, thorium-229, by expensive and tedious chemical separations and then to milk the thorium-229 to isolate actinium-225. The defining difference is that Thorenco's gamma, n process increases availability of actinium-225 to the medical research community because there is no need to separate thorium-229 from weapons grade uranium-223. Because gammas are used production exceeds methods using protons. Further, in reactor irradiation using energetic neutrons is not needed for this process.

In contrast to other methods of making actinium-225, Thorenco's new production method can be operated to produce actinium-225 as it is needed. The production can be started and ended by energizing and de-energizing the electron beam. Production can be intermittent at first to meet limited demand for this promising isotope. Using the gamma, n approach, far less capital is expended to develop an appropriate inventory of actinium-225 for the medical research community to conduct clinical trials. Once, however, market demand increases, the production method allows for a quick ramp-up of production to meet growing market demand. Provisioning clinicians with an adequate supply of actinium-225 can be accomplished by increasing the number of gamma, n targets in service. Capital can be more efficiently deployed using the production method. Actinium-225 is very promising for many treatments, and now that infectious micro organisms are becoming increasingly resistant to antibiotics, alternate treatments using targeted alpha therapies must be developed to deal with intractable or drug

415 398 7878 rusthold@mindspring.com Pre-application DEFOA0000517

resistant infections. Bismuth-213 is well suited for these potential applications. Use of actinium-225 to generate bismuth-213 to treat patients with single cell blood cancers has been successfully demonstrated. .

Electron accelerators able to produce actinium-225 exist and are in service at Idaho Accelerator Center. Appropriate separations facilities exist at Pacific Northwest National Laboratory. Importantly target fabrication expertise exists at both PNNL and IAC. The purpose of the grant is to provide the funds to get actinium-225 production targets constructed. Here, Thorenco provides its general business plan, its technical details and its compliance with the underlying purposes of the grant in DEFOA0000517 which is to place a new target in service that reliably produces actinium-225 and other isotopes.

2. Technical Overview.

The new target generates energetic and penetrating gammas for actinium-225 production via gamma, n reactions on radium-226. Penetrating and energetic gammas are generated from high energy electron interactions in a novel converter assembly in the target. Produced gammas expel neutrons from radium-226, making radium-225 that decays to actinium-225 with a 14.9 day half life. Past computational studies done for Thorenco by PNNL have shown that the production peak for actinium-225 is 400 or so millibarns when the incident gamma energy peaks at 11 MeV.

Energetic electrons from the beam slow down promptly in the new converter assembly producing gammas. Lead, bismuth and a thin uranium disk present in the converter assembly produce gammas in sufficient quantity and with enough energy to drive gamma, n reactions in radium-226.

Thorenco's pre application follows up on computational modeling work done at Pacific Northwest National Laboratory in 2007. In the 2007 PNNL study, production rates for actinium-225, and other isotopes were quantified using an earlier and less efficient converter assembly tuned to the 11 MeV production peak. The earlier converter used virtual tungsten cooled by circulating liquid lead bismuth eutectic. The present and proposed converter assembly uses uranium cooled by liquid lead bismuth eutectic. Uranium being denser than tungsten provides for more efficient gamma production. Further, the radium target is closer to the uranium converter in the present design, closer than the radium was to the tungsten in the earlier design.

Produced gammas tend to travel in the direction of the electron beam. The produced gammas interact with the nuclei of radium-226 located in sealed silver disks clad with stainless steel. The radium containing disks are placed immediately down beam from the uranium disk. The two disk types one made from uranium and the other, silver, containing radium chloride are enclosed or clad with stainless steel that is compatible with lead bismuth eutectic.

Using the target's new geometry and materials, electron to gamma conversion is now appreciably more efficient enabling production of clinically relevant amounts of actinium-225.

The funds applied for will be used to build a new target that uses the gamma, n method to make actinium-225. The electron beam interacts with a thin sheet of liquid lead bismuth eutectic and with a thin

415 398 7878 rusthold@mindspring.com

uranium disk to make the gammas. The electron beam will sweep over a "large" surface area to avoid a heat failure of the up beam side of the target. To control heat on the up beam side, liquid eutectic is circulated, as well, over the surface of the up beam side of the thin uranium disk. The eutectic and the uranium slow the electrons down and copious numbers of high energy gammas are generated. The gamma spectrum emerging from the uranium disk depends on the energy of the incident electron beam; the more energetic the electrons, the greater the population of more energetic the gammas. In the recently updated configuration of the target, the electron beam interacts with lead bismuth eutectic and thin uranium disk(s) and thin silver disk(s) containing radium chloride both types of disks being enclosed in stainless steel cladding. The clad disks are placed in slots in a stainless steel frame or enclosure. The radium containing target disk array is placed almost in contact with the down beam side of the uranium disk array. The radium chloride containing disk is a hollow sealed stainless steel clad silver disk containing radium chloride.

The earlier version of the device, discussed in the provided 2007 PNNL report, used tungsten instead of uranium as the second converter material and the radium was electro-plated on copper beads. In both versions lead bismuth eutectic is present to export beam deposited heat to an exterior heat sink.

When the incident electrons are energized to 20-30 MeV, the resultant gamma flux includes photons from 5 MeV to 15 MeV as is charted below in Figure 3 page 8 below. The more energetic gammas interact with radium target nuclei causing neutrons from the radium-226 nuclei to be ejected. For the best production rate, the energy of the electron beam is tuned to produce the most gammas between the gamma, n threshold and just below the gamma, 2n threshold of radium-226 at 11 MeV. The irradiation proceeds continuously as heat is exported to the eutectic and then to heat exchangers in the eutectic bath.

Thorenco has access to radium chloride in the possession of the Pacific Northwest National Laboratory under the control and custody of PNNL. PNNL will grant Thorenco access to the radium-226 for use in the targets. PNNL's separations facilities are also available to manufacture the isotope for use in existing bismuth-213 generators to provide bismuth-213 in satisfactory form to the US community of medical researchers. The radium will be returned to PNNL after irradiation.

Further, the design specifications of the new radium containing target will be approved by both PNNL and the Idaho Accelerator Center where the irradiations will take place. The radium will be encased in silver disks and clad by stainless steel. The new target will be irradiated by electron accelerators available at the Idaho Accelerator Center. The candidate electron beam is located in the Main Accelerator Hall. It is a Linac with output of 4-30 MeV and a maximum beam current pulse of 100 milliamps in short pulses. Dr. Douglas Wells of the Idaho Accelerator Center must be satisfied that the radium confinement measures function without risk of leakage of radium outside of the target. Presently the design contemplates that radium chloride will be enclosed in a hollow metal containers that will transport heat from the target disks to the eutectic. The radium container and the uranium container will be enclosed in a stainless steel enclosure that is the housing for the target.

415 398 7878 rusthold@mindspring.com Pre-application DEFOA0000517

The electron beam interacts with the new converter target/assembly that converts electrons to gammas. The new converter is a composite of three metals: lead, bismuth and (natural or depleted) uranium, the three being enclosed in stainless steel along with the radium containing target disks. The converter/target uses circulating liquid lead bismuth eutectic to export the heat deposited in the converter by the electron beam and to provide some gamma shielding. The circulating eutectic cools the up beam side of a thin disk of uranium (mounted within the stainless steel enclosure). The entire target assembly sits in a stainless steel "enclosure tank" that contains and confines the cooling lead bismuth eutectic. The eutectic transports heat away from the uranium disk and the metal disks containing radium. The eutectic bath is cooled by a heat exchanger that transports the heat to an external heat sink.

The liquid lead bismuth eutectic coolant slows the accelerated electrons, produces gammas but most importantly exports heat deposited by the electron beam on the thin computationally optimized uranium disk that generates gammas. The advantage of using lead bismuth eutectic is that it cools the target, slows the electrons down generating gammas and provides gamma shielding. Gammas are produced copiously in the uranium disk and these interact with the isotope precursor disk located immediately down beam of the uranium disk.

The natural uranium disk and the precursor disks containing radium chloride are mounted together and placed inside a stainless steel "can" that is immersed in the eutectic. An exterior stainless steel "tank" encloses the eutectic. The target for production of actinium-225 and radium-225 is radium-226 chloride, the intermediate radium-225 having a 14.9 day half life.

The development team includes Charles S. Holden, Richard Wittman PhD employed by PNNL and Robert E. Schenter Ph.D. in the private sector. The development team also includes Darrell Fisher Ph. D. of PNNL and Douglas Wells Ph. D. of IAC and their respective teams.

There is patent protection for the gamma, n process on radium-226. See, "Method of Producing Actinium-225 and Daughters" US patent number 6680993 Stanley Satz and Scott Schenter, inventors, issued 1-20-2004. The concepts relating to the new target are trade secrets of Charles S. Holden and Robert E. Schenter.

3. Discussion

The computational studies undertaken in 2011 have focused on ways to increase production of penetrating and energetic gammas to expel neutrons from radium-226 nuclei. The gammas produced must be numerous and be near the 11 MeV peak to cause neutrons to be efficiently expelled from the nuclei of radium-226.

The new converter assembly generates gammas at the rate 3 times 10 ^17 per second with the gammas per square centimeter displayed in Figure 3 below for a high power case. The gamma spectrum has high energy tail energy above the threshold needed for production of actinium-225. See, Figure 3 page 8 below.

415 398 7878 rusthold@mindspring.com

Because copious gammas are produced from electron irradiation of natural or depleted uranium and lead bismuth, gamma driven reactions enjoy competitive advantage. There is no longer any need to chemically separate thorium-229 from uranium-233. There is no longer any need to separate actinium-225 from thorium-229. PNNL is able and ready to provide separations and to put the produced actinium-225 in proper form for use in bismuth-213 generators. Because the new form of doubly sealed target is comparatively inexpensive to assemble, irradiate and to maintain production costs are anticipated to be significantly less than the present methods used to make actinium-225. No more uranium-233 needs to be milked for thorium-229 to increase use of the isotope. There is no further need for proton or neutron irradiation of radium-226 to make actinium-225.

Energetic electrons slow down inside of the high z materials in the converter: depleted or natural uranium metal and circulating liquid lead bismuth eutectic. The electrons slowing down in the converter are energetic, having been accelerated to an energy that generates a gamma peak at 11 MeV. The electrons in the beam "feel" the electric fields surrounding the densely packed uranium nuclei and are deflected by these fields. When deflected, the electrons emit gammas. The greater the deflection and change in direction and velocity of the electrons, the higher the frequency of the outgoing gammas.

Heat and gammas are generated in the depleted uranium converter disk. Heat is managed by exporting heat to external heat exchangers by circulating the liquid metal coolant.

The gammas produced from the deflected electrons tend to travel in the same direction as the electrons in the beam. These gammas leave the converter assembly and interact with target nuclei to generate atoms of product isotopes by gamma, n reactions.

Thorenco's proposal demonstrates that the new converter assembly and target is commercially relevant. The device uses an existing electron beam to produce gammas in a thin uranium disk that expels neutrons from the radium or radium chloride target disks. The 2007 PNNL Letter Report was prepared by Dr. Wittman of PNNL is furnished with this pre-application. The Letter Report is titled: "Electron Beam Production of Isotopes Ac-225, In-111, Cu-64" The letter report is provides background information which reveals production rates of these three isotopes and the underlying anticipated profitability.

The recent calculations for production of actinium-225 have been performed by Bob Schenter. The modeling results are displayed in Table 1, Figure 2 and Figure 3. The method will produce 400 millicuries of actinium-225 in a thirty day irradiation in which the target contains one gram of radium 226 and the Electron Power is set at 35 kW. When the target has a mass of ten grams of radium-226, thirty days irradiation at 35 kW Electron Power generates 4 curies of actinium-226. A mass of one gram of radium exposed to 350 kW for thirty days also generates 4 curies of actinium-226. As a practical matter, beam power must be kept reasonably low and the target mass must be kept reasonably low. In the low power production mode, produced heat will be less of an adversary and production can be improved by increasing the mass of the radium in the target. Perhaps, the optimum power is 40 kW irradiating 2 grams of radium for 30 days which makes one curie of actinium-225 and about one half a curie in 8 days or so.

415 398 7878 rusthold@mindspring.com Pre-application DEFOA0000517

Table 1. Ac-225 Production for 30MeV Electrons, 30 Day Irradiation

Ra226 Mass (Grams)	Electron Power (KW)	Ac225 Activity (MCi)
1.0	17.5	200
1.0	35	400
2.5	35	1000
2.0	40	1000
1.0	350	4000
10.0	350	40000

The irradiated product when separated from radium-225 and radium-226 will be almost pure, with the harvest occurring at intervals to optimize actinium-225 recovery. The optimal irradiation period will not exceed 30 days. Irradiation will be conducted at Idaho Accelerator Center and Post Irradiation Services will be conducted at Pacific Northwest National Laboratory.

The following Figure 2 depicts production curves of actinium-225 using electron beams of varying energy, 20 MeV and 30 MeV. Production of one curie per month using a power setting of 40 kW on two grams of radium-226 appears to be a promising production specification for the new target. But production of one half of a curie in approximately eight days of irradiation at 40 kW appears to be the most efficient and the starting point for evaluation.

415 398 7878 rusthold@mindspring.com

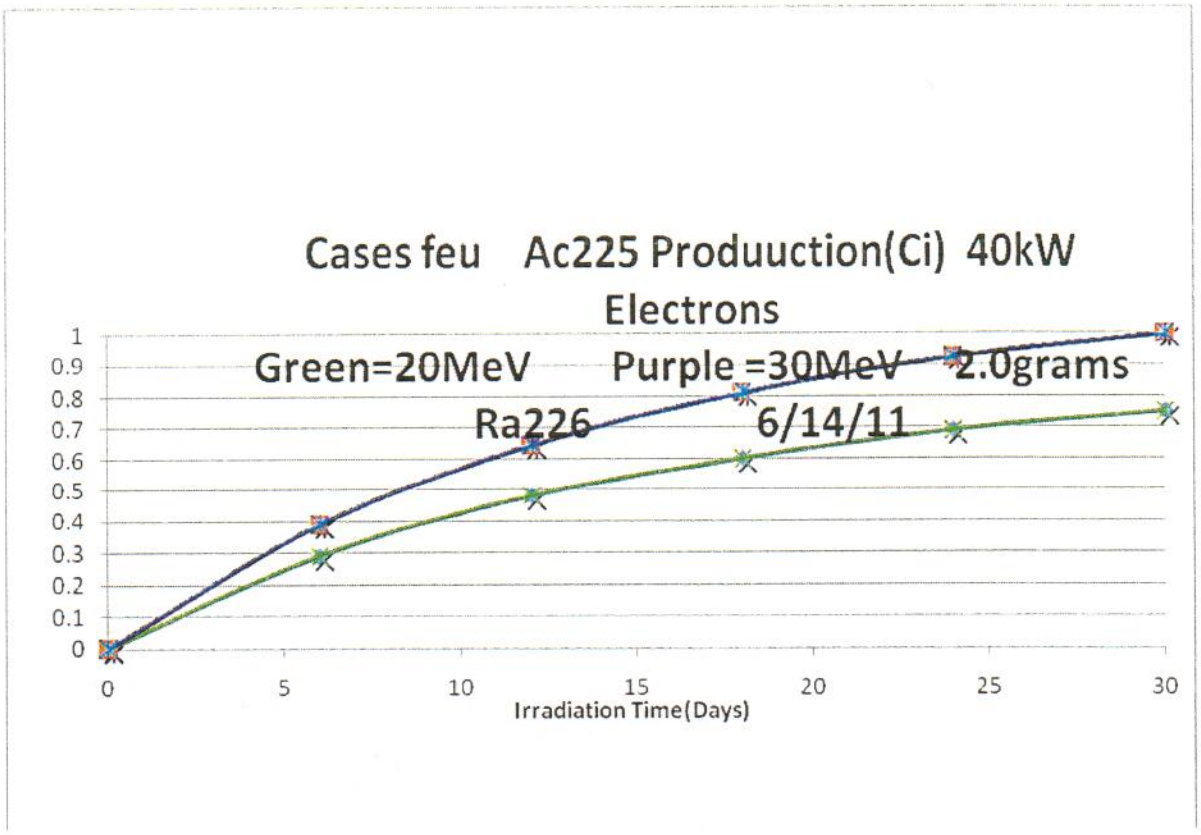

Figure 2 above suggests that irradiation for a period of approximately eight days produces one half of a curie of actinium-225. Almost 600 millicuries are produced in a ten day irradiation. Thorenco anticipates that greater production efficiencies can be obtained by tuning the electron beam power to maximize production of 11 MeV gamma photons.

Figure 3 below depicts the production of gammas from two incident electron beams one having energy of 20 MeV and the other 30 MeV.

415 398 7878 rusthold@mindspring.com

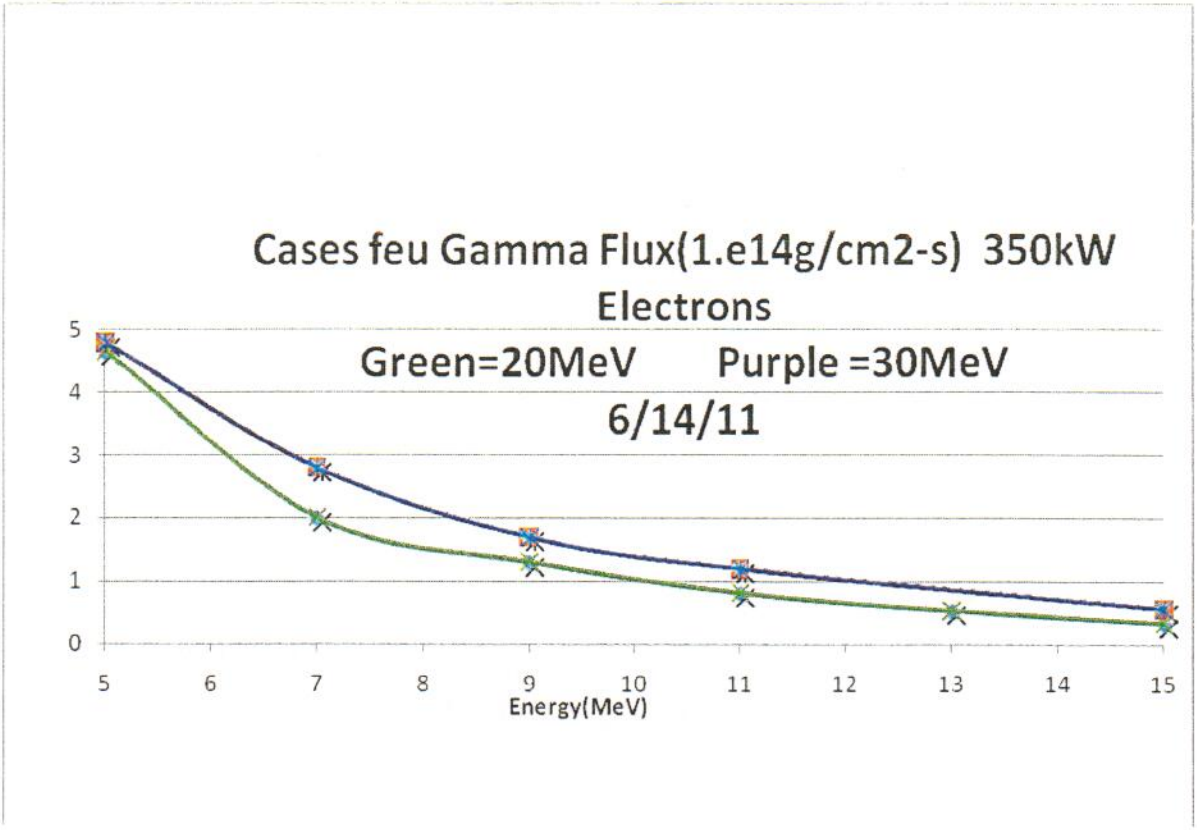

Figure 3 shows photon production at 20 MeV and 30 MeV. The important gammas produced are those between 10 MwV and 12 MeV. Additional "tuning" of the incident beam and the converter will yield increased production of the important gammas.

4. Scope of the Work Required For Establishing the New Target for Production of Actinium-225

(Method and Materials)

The new target is a compact nuclear appliance designed to produce actinium-225, (and other important isotopes including zirconium-89, copper-64, indium-111 and protactinium-231. The other isotopes can be formed in other clad disks when the beam is set at different energies. Different clad disks would be placed in the target to make the other isotopes.)

The set up has four components for actinium-225 production:

1. Electron accelerator with operating crew and target fabrication expertise (Contracted services, Idaho Accelerator Center at standard rates)

2. Proprietary electrons to gammas converter assembly; proprietary stainless steel housings for inner and outer portions of target, uranium disk, in stainless steel cladding (production start up costs) for cooling in lead bismuth eutectic bath.

415 398 7878 rusthold@mindspring.com Pre-application DEFOA0000517

3. Proprietary Radium-226 Disk Targets will be fabricated. Suitably clad and sealed disks containing radium chloride will be manufactured as production start up costs.

4. Lead Bismuth Shielding and Cooling System in Stainless Steel Exterior Enclosures. (To be constructed as production start-up costs.)

The electron beam and irradiation services will be furnished by Idaho Accelerator Center.

IAC's beam interacts with a natural or depleted uranium converter disk that is cooled by liquid lead bismuth eutectic. The electrons are slowed down in the converter assembly by uranium, lead and bismuth nuclei. Heat and gammas are generated. The heat from the electron beam is transported from uranium disk region by the liquid metal working fluid. A heat exchanger sits in the eutectic bath to export heat from the eutectic bath to an external heat sink using a different working fluid.

The electron beam enters the top of the converter assembly passing out of the beam window, slowing down first in the eutectic and second in the uranium. The uranium disk is thin as are the radium containing disks. The cover metal (over the converter and target disks) is stainless steel that is chemically compatible with the eutectic. Under the stainless steel cover metal cladding, the radium chloride is enclosed in a silver disk. Presently, the depleted uranium disk is 1.5 mm thick and its radius is 4 centimeters. The lead bismuth eutectic circulates over the stainless steel enclosing the two disks. The flowing eutectic is 3 mm thick. The virtual radium disk is 1 cm. in radius.

Startup costs include all needed to complete the design and to fabricate the new target(s) and shielding. Fabrication costs for the initial converter are estimated to be in the range of $160,000. "Break- in" and target qualification beam time of 720 hours is estimated to cost $180,000 at the Idaho Accelerator Center. Some instrumentation and product design will be included in the beam time rental fee which also includes the beam operators. Upon confirmation of the computations and approval of the design, a radium chloride containing silver disk clad with stainless steel will be irradiated for production of actinium-225.

The separations and assay of the produced isotopes and specific activity measurements will be performed at PNNL at an estimated cost of $50,000. Hourly fees to the developer will cost $125.00 per hour for 600 hours. The PI's transportation and hotel costs among San Francisco, California Pocatello, Idaho and Richland Washington are estimated at $5,000.

5. Outline of Business Plan

At least one half of the actinium-225 produced will be sold to Oak Ridge National Laboratory at a price equaling the average five year sales price of actinium-225, less a discount of 10% for a period of five years provided this is profitable to Thorenco and so long as Thorenco can "access" radium from PNNL and return the radium to PNNL for post irradiation recovery of product actinium-225 and radium-226. The other half of the actinium-225 production will be sold to the US market directly or to Oak Ridge. The precise economic terms will have to be worked out once production is regularized. Actinium-225 is available for $1450 per millicurie presently from Oak Ridge's isotope program. Supply

415 398 7878 rusthold@mindspring.com

is so limited that clinical trials are not supported by the inventory of thorium-229 that is milked at 6 week intervals. The Oak Ridge actinium-225 price is under review presently and may be adjusted upward. Thorenco's supply price on confirmation will be in the range of $1300 per millicurie if there is no upward adjustment in price by DOE Management. Sales to Oak Ridge would have to be firmed up after the new target demonstrates satisfactory performance and production of enough actinium-225 to supply bismuth-213 generators.

The calculations performed in June of 2011 reveal that ten grams of radium will produce 4 curies a month of actinium-225 at low power and that at 35 kW, on. 2.5 grams of radium or at 40 kW on 2 grams of radium will produce a curie per month. Ten day low power irradiations on two grams of radium-226 appear to produce approximately 600 millicuries of actinium-225. After the product introductions are made, and the clinicians are assured a supply of the material for their trials, ORNL could be supplied with approximately one half a curie per month. The range of potential production rates shown on Table 1 will provide an adequate supply of the isotope to the medical research community. Further, other isotopes can be made with the gammas that emerge from the converter assembly when the radium target is removed. These alternate isotopes include zirconium-89, copper 64, and protactinium-231.

Thorenco has no radium-226 chloride in inventory but has received assurances it will have access to radium chloride in the possession of PNNL as PNNL's expression of interest shows. The post irradiation production work will be completed at PNNL as well and the materials will be separated there as required. The bismuth-213 generators can be stocked with actinium-225 at PNNL or as is done presently by the researchers.

The isotope team at PNNL is competent to perform the separations and testing of the irradiated materials made in the new target. The Idaho team is likewise competent to perform and supervise all irradiations. Product will be transported from Idaho to PNNL in DOT certified containers as will its transport to Oak Ridge or to customers.

Respectfully Submitted,

-s-

Charles S. Holden

June 13 2011

Thorenco LLC

415 398 7878 rusthold@mindspring.com Pre-application DEFOA0000517

Pacific Northwest
NATIONAL LABORATORY

Proudly Operated by **Battelle** *Since 1965*

June 13, 2011

Charles S. Holden
333 Pine Street Suite 400
San Francisco California 94104

Dear Mr. Holden,

LETTER OF COLLABORATION AND SUPPORT: "THORENCO'S CONVERTER AND TARGET FOR ACTINIUM-225 PRODUCTION" (DOE ISOTOPE PRODUCTION)

The Isotope Sciences Program at Pacific Northwest Laboratory expresses interest in your plans to produce actinium-225 from radium-226 using gamma ray interactions by transmutation of radium-226. Our Laboratory would be pleased to cooperate with you and Thorenco by providing access to radium-226 source material and technical assistance needed for manufacturing new Ra-226 target capsules according to your specifications. We are also interested in helping perform the ultra-high-purity post-irradiation radiochemical separations needed to prepare actinium-225 for bismuth-213 generators. We have extensive experience and all facilities and infrastructure support needed to receive, handle, and process Ra-226 and associated reaction byproducts. We also have considerable experience designing and testing Bi-213 generators, including automated generator systems.

In our prior collaborations with Thorenco, we have studied the advantages of the (gamma,n) method for actinium-225 production from radium-226 targets, including methods for heat dissipation. This previous work demonstrated the basic economics of isotope production by the (gamma,n) irradiation method. We look forward to assisting you in your efforts to develop this method of Ac-225 production. The success of your work will make Ac-225 more available to the medical research community.

Sincerely,

Darrell R. Fisher

Darrell R. Fisher, Ph.D.
Senior Scientist
Isotope Sciences Program

902 Battelle Boulevard | P.O. Box 999 | Richland, WA 99352 | 1-888-375-PNNL (7665) | inquiry@pnl.gov | www.pnl.gov
Telephone (509) 375-5098 ■ Email dr.fisher@pnnl.gov ■ Fax (509) 375-5099