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David Ehst

Initiatives for Proliferation Prevention
Nuclear Engineering Division
Argonne National Laboratory
9700 South Cass Avenue, Bldg. 315
Argonne, IL 60439

1-630-252-4829 phone
1-630-252-7308 fax
EHST@ANL.GOV

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Dr. Eduard Smetanin
FSUE "State Scientific Center of the Russian Federation—
Institute for Physics and Power Engineering" (IPPE)
Obninsk, Russia

Dear Eduard,

The IPP/DOE program office has finished its evaluation of our alpha-emitting isotope work with Kurchatov Institute and IPPE, and they have made an important decision about the future of this work. IPP/DOE has directed us to re-program the work and add more funds, so the emphasis will be on production of Th228.

By making this re-direction of the isotope work, IPPE will see several important benefits: (a) the payments will be made faster to IPPE by using the ISTC Agreement; (b) a larger amount of money will be paid to IPPE; and (c) a profitable future business opportunity for IPPE is more probable.

Let me mention several important points to consider.

1. The history of the US-Russian relationships to supply Ac225 has been very difficult and disappointing. Several attempts were made since 1998 to provide Ac225 to US medical researchers, and one particular Russian representative offered to ship 1500 mCi/month of Ac225 to the US, after one year of cooperative funding. However, after eight years working with several Russian laboratories, I have become very discouraged; it does not seem possible that more than ~40 mCi/month of Ac225 can be provided. If you would like, I can provide a description of the bad experience the US has had: many promises were made but the results were not satisfactory.

2. Both the US and Russia want to accelerate the progress on developing alpha-emitting isotopes for cancer therapy. We propose to do this in two ways: we will change from the former DOE Master Contract to the ISTC Agreement for payments; and we will change the leadership of the project from Kurchatov Inst. to the IPPE.

The former Master Contract had difficulties with both the US and the Russian government. In the US the DOE procurement and payment procedures do not work properly. This results in many months of delays in issuing the contract task order and also in making the payments (which go through CRDF). In Russia, it seems that every report on the work performed must be reviewed by institute or government authorities; this results in very slow delivery of the reports to us and long delays in making the payments.

The new work will be issued as an ISTC Agreement, which will be much better for payments. When the ISTC proposal paperwork is finished, then the Agreement will be signed by IPPE, ISTC, and by IPP/DOE. Then, payments will be made to the Russians every quarter, like clockwork.

3. IPP/DOE has agreed to provide additional funds to make this happen.

The former Master Contract was planned to pay $315,000.00 to the Russian scientists to produce Ra225/Ac225 for AlphaMed Inc. (AMI). When this project is stopped at the end of Phase 2, a total of $160,000.00 will have been paid to the Russians.

The new ISTC Agreement will pay another $337,000.00 to IPPE to provide Th228 to AMI.

This will bring the total paid, for U/Th radiochemical separations and research, to $497,000.00, a large increase over the former budget for Russia.

4. The new Th228 project can start quickly (as soon as the ISTC Agreement is signed).

From the former Master Contract project, we have already paid enough funds for the Russian groups to remove all the Th from at least ~ 0.5 kg of U233/U232; and it is possible that IPPE has actually cleaned more of the uranium (~ 1 kg). From this clean batch of U233/U232, I expect that around 80 to 150 mCi of Th228 will grow in by the fall of 2007. From this batch of uranium, IPPE must separate the Th228, using the radiochemical methods developed previously, and ship the Th isotope to AMI.

5. Commercial companies which provide radio-isotopes to customers are in a business full of risk. Starting new sales (new products) is difficult and very competitive. [See Attachment A for some examples of isotope companies which have experienced business failures.]

The Ac225/Bi213 business has no future because there is no reliable source of large amounts of Ac225 (in the range of tens of Curies).
- Human doses are estimated to be in the area of 300 mCi. Due to short half-life, this means that we must start with more than one Curie of Bi213, to allow time for preparation, delivery, and administering the radio-labeled compound. This would require access to hundreds of kilograms of U233 (plus the ability to ship the isotope reliably and routinely). From our experience it is not likely that such large amounts of the isotope will be made available, or that the isotope can be shipped in a timely way on a routine basis.
- Medical research customers are not willing to invest their resources on an isotope that has no chance of being available to support the clinic. (Leukemia trials at Memorial Sloan Kettering, which have been in process for a number of years, still have not finished, due to a lack of isotope availability.)
- Isonics is having a difficult time selling Ac225 to its customers.
- In the eight years that AMI and Argonne National Laboratory (ANL) have worked with Russian researchers, the value of Ac225 has dropped from ~ $1000/mCi to nearly zero. The medical researchers can not afford to pay the high price, and they need large quantities (~ 1000 mCi) for human trials.

Isotope production via Th228/Ra224/Pb212 has a very positive potential:
- AMI is already doing pre-clinical tests with Pb212 from its own U232 supply, and it has ready customers.
- The supply of U233/U232 already available to IPPE will allow shipments of ≥ 150 mCi of Th228 each year to AMI. The IPP program will pay the $337,000.00 to the Russians for multiple years of these shipments, and for processing additional amounts of U233/U232 for more Th228.
- After the two years of this project, IPPE and AMI would negotiate additional deliveries of Th228 as a private contract, under terms arranged during this IPP project.

[See Attachment B for a comparison of the Russian material inventory for Ac225/Bi213 vs. Th228.]

(Any Th229 obtained by further processing of U233 can be added to the current stock of Th229 in Russia, which would allow IPPE to produce additional amounts of Ac225. Sale of Ra225/Ac225 from this source, to support on-going medical trials in the US, can be discussed separately between IPPE and AMI.)

6. I suggest we arrange the following steps to make this work a success:
(a) Let us prepare for the meeting at Argonne National Laboratory to discuss the new project. (Travel by the Russian participants will be paid with the $13,000.00 of funds provided as Task 9 under the Master Contract with Kurchatov Inst.) This should be soon, in April or May.
[See Attachment C for an agenda of topics for the meeting discussions.]
(b) You should provide an English draft of your ISTC proposal to me; you can do this now.
(c) When the IPP/DOE program office knows that we have the draft ISTC proposal, they will issue the Partner Commitment Letter (PCL) to ISTC, which promises to pay the $337,000.00 for the new work.
(d) After the PCL is sent to the ISTC, your institute should be able to get the Host Government Concurrence (HGC), which is the final permission by Rosatom for the ISTC project work.
(e) Soon after HGC is received, the ISTC Partner Agreement should be ready for signature by all parties. If we work promptly, I predict we can start the new ISTC work around July.

Eduard, please give careful thought to the items in this letter. US government funding for this type of work is very difficult to find. The IPP/DOE program office must carefully consider how to use its funds for the best results. The decision was made that the former Ra225/Ac225 project (ANL-T2-0213-RU) with Kurchatov Inst. and IPPE must be stopped after Phase 2; and the new Th228/Ra224 project (ANL-T2-0213A-RU) with IPPE should be started now.

I would like to quickly start on items 6 (a), the meeting preparation, and 6 (b), the draft ISTC proposal. Please send me your response as soon as you are able to answer.

Kind regards,

Dave Ehst