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TO : Files

DATE: December 31, 1959

THRU : C. L. Dunham, M.D., Director, DBM
C. W. Shilling, M.D., Deputy Director, ~~DBM~~

FROM : H. D. Bruner, M.D., Chief, Medical Research Branch, Division of Biology and Medicine

SUBJECT: NOTES ON THE CA-47 CONFERENCE AT THE IAEA VIENNA, DECEMBER 14-17, 1959

SYMBOL: BMM:HDB

The trip over was uneventful except that we went through weather that would ground planes in the USA. I got in just before the weather closed down; Will Siri, due to get in on Saturday night, got in very late Sunday because his plane had to land at Frankfurt and he had to come by train to Munich and then to Vienna taking what he could get. I was able to talk with most of the people in our Mission to the IAEA before going into the conference.

I would suggest that all persons going to Vienna prepare a generous time schedule so as to permit adjustments against the very bad flying weather of Europe in winter and also to allow their metabolism to adjust to the six-hour differential. It took me two days to re-establish--more or less--my physiological rhythms.

The first part of the following deals in some detail with the discussions of the conference; Dr. Vetter (IAEA) will shortly send the summarized data and recommendation agreed to. The second part reports information of possible interest to us and my contacts in Geneva and Paris.

Those present at the Conference on Ca-47 were: Phil S. Baker; Stable Isotopes Division, ORNL, USA; Will Siri; Physicist, Donner Laboratory, LRL-UC, Berkeley, USA; Louis C. Stang, Jr.; Isotopes Development, BNL, USA; J. C. Charlton; Isotopes Production, Amersham, AERE; J. F. Fowler; Hospital Physicist, Hammersmith Hospital, London; A. H. W. Aten, Jr.; Physicist, Institut Voor Kernphysik, Onderzoek, Netherlands; I. Dostrovsky; Chemist, Weizmann Institute, Israel; J. Halberstadt; Physicist, Division of Research, IAEA; H. Vetter; Medicine, Division of Isotopes, IAEA; H. D. Bruner; Medicine, Division of Biology and Medicine, USAEC.

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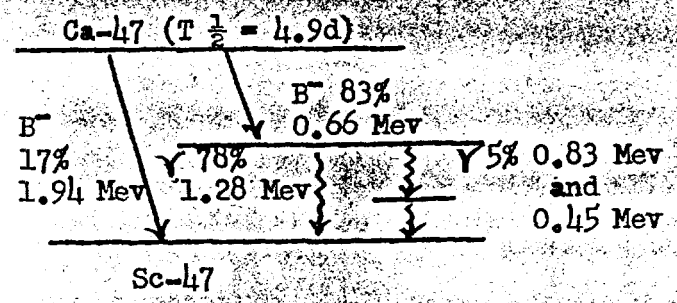
On each day there were three-hour morning and afternoon discussions and these were usually continued by most of the group at lunch or dinner.

The best decay scheme for Ca-47 presently is:

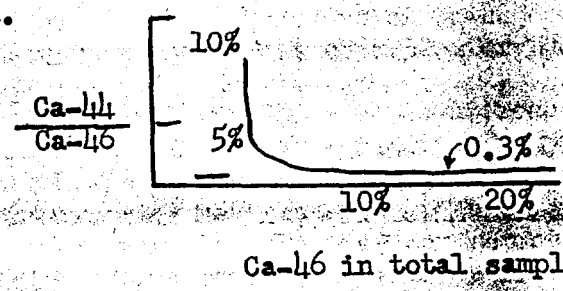


Part I: Technical Discussions

It was agreed to discuss first the methods of production of Ca-47 and then go on to economics, feasibility, plans, etc.

Phil Baker (ORNL-Stable Isotopes) described the electromagnetic separation methods using the calutrons at the Y-12 area. Since last year he has assigned two calutrons on-and-off to the separation of Ca-46 with the idea of learning what can be produced and how much it would cost.

Unfortunately, the purity does not improve greatly beyond a certain degree of separation as shown. This appears to be due to molecular wandering out of the beam and the difficulty of fine control.



When some of the better samples, such as 18% enriched Ca-46, is irradiated for three weeks at a 2×10^{14} flux, with about a 1:1 fast to thermal neutron distribution, he secured a 24 Ca-47/ 1 Ca-45 ratio giving 11 curies per gram of material—actually it was 22 mc in a 2 mg sample.

Charlton (Amersham, AERE) reported that he had produced an 8% enriched sample of Ca-46 with 10% Ca-44 which gave 2 mc per mg after 10 days at a 1.2×10^{14} flux and secured a 15 Ca-47/1 Ca-45 ratio. Both agreed that the capture cross-section was about 1.5 barns for Ca-46.

1149365

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but this remained to be determined. The duration of activation is importance since:

Days	Ca-45	Ca-47
5	x	y
10	2x	1.5 y
15	3x	1.75y
20	4x	1.87y

In other words, the maximum Ca-45 contamination for a normal person taking the practicalities into consideration, would be about 5%; this would be about 2.5% at time of pile-out. Hence for a 20 uc dose of Ca-47 there would be carried over about 1 uc of Ca-45 at time of use.

Any reasonably low specific activity would be satisfactory due to the large amount of Ca present normally. Probably 20 uc of Ca-47 would be enough for whole body counting.

Baker said there are relatively large amounts of low enrichment (Ca-46/Ca-44 = 1) Ca-46 presently available which would be useful for much biological work. Also, he said that he could commit his group to producing 4 mg of 18% enriched Ca-46 per month which would result in 20 mc/month.

I-B Dr. Charlton (Amersham) said that their facilities limit him to 1 mg of Ca-46 per year by electromagnetic separation at 10% abundance, or 1 mg of Ca-46 in 10 mg of Ca-44,46. This would equal about 10 mc/year at a cost of $1500 for the 10 mg sample.

II-A Siri reported that the Ti-50(d,α+ p) Ca-47 reaction using the 60" Berkeley cyclotron is a useful reaction. By starting with about 300 mg of Ti-50-O_2 costing $1000 they can get a yield of 4/3 uc/u amp/hr using 23 mev deuterons. The yield on chemical extraction is only about 75%, so they can get about 1 uc/u amp/hr. The cost is $40/hour approximately, with a maximum production (based on available time) of 4 mc/month. The cost, including processing might equal about $500/mc.

The threshold for this reaction is about 17 mev, but the curve of yield with energy is not known. It is calculated to rise steeply to peak reaction at 28 mev.

1149366

DOE ARCHIVES

The sample of Ti-50 used had the indicated composition. The presence of the other Ti isotopes perturbes the reactions with Ti-50 and it would be desirable to have purer starting material.

Ti-50	84.7%
Ti-49	2.7%
Ti-48	10.6%
Ti-47	1.2%
Ti-46	1.4%

Berkeley, however, does not propose to go into production. The 23 mev deuterons are just marginal for this reaction. There are not many, maybe only two, cyclotrons which have the mev and the currents to be economical producers assuming that the reaction curve is known.

The cost here should be about $1000/mc for the finished product.

II-B The reaction with fast neutrons on Ti-50, Ti-50 (n, α) Ca-47, is possible but needs a large mass of Ti-50, maybe 100 grams, to make the reaction efficient, perhaps $300,000 worth; the Ti-50 would have to be continuously milked of its Ca-47 and this is a formidable, and probably expensive, job.

II-B-1 The production of fast neutrons by cyclotrons using Be (d,n$\rightarrow$) is excellent, but this reaction is not too well known as to yields, procedure, extraction and control. The optimal yield comes from deuterons in the neighborhood of 7 to 15 mev; other targets for production of neutrons are possible, such as Li B, or Li D.

The (n,α) cross section for Ti-48 may be 10 times that for Ti-50, but this is not known with any certainty.

Conceivably the reaction could be competitive, maybe $10/mc, but there are so very many unknowns. Many techniques would have to be vastly improved and there would be a very large capital investment.

II-B-2 Stang (BNL) reported that he got production of Ca-47 by the Ti-50 (n,α) Ca-47 reaction using the fast neutrons of the BNL graphite reactor. Scaled up this would give about 0.8 uc of Ca-45 and 44 uc of Ca-47 at 10^{12} neutron flux for 85% enriched Ti-50; 5 grams of 85% enriched Ti-50 at $\sim 2 \times 10^{14}$ neutrons would give 4 mc of Ca-47.

The main problem in this reaction seems to be the chemistry of separating the Ti-50 from the Ca-47 without losing any of the expensive separated target.

Use of Li-6-D in bulk form close to their target to get 15 mev neutrons would improve the probability of the reaction by a

1149367

DOE ARCHIVES

factor of 4, but the reaction is still rather poor. Stang has studied a number of ways to get 100% separation, including the potentially useful volatilization of the halide of Ti, chelation, ion exchange, solubility, etc., but is not satisfied that he won't lose too much of one or the other with present methods; his best separation gave 100% of the Ca-47 but only 94-98% of the Ti-50 using Dowex-50.

Charlton (Amersham) has also looked at this fast neutron procedure but is not very optimistic because a 5 or 6 gram inventory of Ti-50 would be a very expensive capital investment for him and losses would make it still less economical. In any case, it is necessary first to get the excitation functions of Ti-50 for fast neutrons.

Baker (ORNL), on the other hand, using 10 mg of 85% Ti-50 in a 2×10^{14} flux for one week got 60 uc of Ca-47, and feels that this would be a good reaction if the chemistry were improved. The cyclotron-produced neutrons would not be competitive unless a 100 gram Ti-50 target could be used, but at present there are too many unknowns.

Calculations to equate the data by Stang, Baker and Charlton gave agreement within a factor of two and the more this reaction was discussed, the more enthusiastic these men became. They agreed that there must be a resonance peak to this reaction and that the curve should be studied by means of cyclotron-produced neutrons. If any sort of peak is found this would at once become the method of choice, although much ancillary work would be needed.

III A Szillard-Chalmers reaction was discussed by Stang in connection with the possibility of conserving the expensive, separated Ca-46 target. Ca-46 phthallocyanine dissolved in fuming H_2SO_4 is exposed to thermal neutrons from any sort of source; the captured neutron produces Ca-47 by the (n,γ) reaction and at the same time the Ca-47 recoils into the solution where it is readily separated. There is some decomposition of the chelate and release of some Ca-46; if the metal is not free of Ca-44, Ca-45 would come through. There are other chelates and holder compounds which could be looked into, but this seems to be far and away the best.

Cost figures are not clear because of the extra handling but it would greatly extend the Ca-46.

IV Ca-48 is a very promising starting material; also, being in higher material abundance and at the end of the Ca list, it can be more easily and cheaply separated by calutron.

1149368

DOE ARCHIVES

IV-A Charlton has found by experiment that the (n, 2n) reaction does not go well in a pile; the threshold is above 10 mev. With an 84.6% Ca-48 target the yield was low, about 4 uc/mg. Baker's yield was not as good. This contradicts Goren Bauer's claim of having secured Ca-47 by this reaction from the MTR. Also, Baker got 10 times as much Ca-45, in spite of having wrapped the enriched Ca-46 in cadmium to eliminate the (thermal n, γ) reaction on Ca-44.

IV-B The 1.3 mev γ-rays from Co-60 give no (γ, n) reaction; x-rays of 22 mev peak yielded 0.1 uc of Ca-47 per gram of Ca-48 at saturation according to Fowler (Hammersmith).

IV-C The (p, pn) reaction has been found to be trifling. Theoretically, the reaction should be a good one, but the target Ca-48 is lost. More data are needed on resonance peaks above 10 mev.

IV-D Using the (d, dn) reaction, Aten (Onderzoek) made some identifiable Ca-47 but he doesn't think it as good as the (p, pn) above.

IV-E An (He-3, α) reaction is possible by use of He-3 accelerated to 30 mev in the Birmingham accelerator. It is an unknown reaction and the cost of the He-3 must be added. An (He^3, 2n) reaction giving Ca-45 is possible also.

IV-F Spallation reactions were passed over as being negligible and not warranting consideration.

Following completion of the nuclear considerations the discussion turned to ways and means of getting Ca-47 into the hands of investigators. It seems that the best immediate method is the (n, γ) reaction on Ca-46 which has been enriched to some 10 to 20% in the calutron. This would give at pile-out some 10 mc/mg of 15% enriched Ca-46 at a cost of $200/mc before shipping and excluding decay; production is to be at both Amersham and Oak Ridge.

Since the solution is to be sterilized it should be put in 0.1N HCl or isotonic NaCl.

Oak Ridge would have to have a group of orders totalling at least 10 mc before irradiating a Ca-46 sample; O.R. could produce two batches per month and Amersham one. It was understood that no research group would be permitted to put in a standing order that would gobble-up the total Ca-46 separated and so corner the research on Ca-47.

To that end, I proposed an announcement of the availability of Ca-47 production be made in Science. I shall undertake to see

1149369

DOE ARCHIVES

that this is done and to coordinate O.R., Amersham and IAEA. Dr. Vetter was curiously hesitant on this point, but I feel we should give everyone equal notice.

The difference in attitude between the panel members of last year and this was very noticeable. This year's panel was enthusiastic and research-minded, and presented a number of possible future courses of action centering around the production of Ca-47 by the foregoing, somewhat exotic reactions.

I personally feel (and have suggested to Dr. Brady and to Dr. Vetter) that IAEA now might cease its efforts to setup the electromigration contract with Harwell and use the remaining funds from our $20,000contract to purchase separated Ca-46, or Ti-50, or other isotopes which would be distributed or loaned by IAEA to research men studying these other possible reactions. Some of this money might also be used in defraying the cost of the present Ca-47 to men in places such as Tokyo, South Africa, etc., where transportation will result in decay losses.

In this connection, it may be noted that Dr. Vetter would like the IAEA to act as a central coordination point for all work on Ca-47, with minimal or no funding to people. And yet, he said that they need a new isotope to get to work on such as I-130 or I-132. He implied very strongly that there would be no more conferences on Ca-47.

The AEC could help this project very greatly by making more calutrons available for production of second-pass Ca-46 and/or Ti-50. This appears to depend on decisions by the Division of Production; this will cost more than DBM can afford, but possibly DIA may help by putting some of these special funds to use if IAEA does not find ways to use up those funds by the end of <u>our</u> fiscal year.

Part II - General Notes

I visited our mission before the conference began and again on Thursday to report the Conference. I saw Dr. Edward Brady, Dr. Clyde McClelland, Mr. John Trevethick and Mr. Dwight Cramer. In addition, we discussed the control of movement of IAEA research projects between IAEA and DBM/AEC as this may become a problem if the number increases; a lost or misplaced proposal would be most embarrassing. (Our own management must be checked.) I mentioned to these men that some of these contracts may become a source of concern and embarrassment to us if we had to consider them as contracts to be funded from DBM program budget funds. I did not discuss with them the scuttlebutt about the next

1149510

DOE ARCHIVES

year's allocations for IAEA research, suggesting merely that Admiral Foster would probably return with budget information and that it ought to come from a more reliable source than myself.

They also questioned me closely about the Jugoslav reactor project. Apparently the cost of it has sky-rocketed to $120,000 without the heavy water because the Jugoslavs have said, in effect: You can use this reactor for your experiment, if you insist on it, and we will lend you our reactor operator, but beyond that it's your baby and your responsibility-insurance, instruments, etc. The reason apparently is that the group plans to operate this zero-power reactor at a kilowatt in order to make the measurements. The Russians have said they would supply the heavy water, but beyond this IAEA can't get a word out of them. If they go back on their oral promise at the last minute, it will be embarrassing to IAEA and we will have to supply the heavy water at a total cost of maybe another $100,000. I think I'm correct on these figures, but they ought to be checked.

The mission seems to be of two minds about this project. They have been led to believe that we biologists would get some badly-needed data on the Jugoslav's radiation doses. On this, I expressed considerable doubt because at least 5 of the 6 were moving around the area during the time the reactor went above zero and, therefore, the best one could do would be to get a ± 50% estimate, if that much. Even if they could recall their sequences of movements it would still be necessary to relate this to the 5 or 10 minutes of a longer period when the reactor was at power. From the other standpoint, the project is politically touchy because: (a) Mr. Cole reported IAEA was going to do the review before the Jugoslavs had made up their minds about it; (b) although there will be men from several countries on the team, it is still regarded as "American" and regardless of how well it is handled we'll be in the position of analyzing an embarrassingly stupid mistake made by the Jugoslavs on an under-instrumented Russian reactor and, as noted above, I am not confident we can come up with a reliable biological dose; we won't know whether we can improve matters without trying, but a failure, or plus-minus data will make us look bad.

I felt Dr. Jammet's opinion on whether the Jugoslavs could retrace their movements would be very useful for he saw them on arrival in France. Due to weather, I missed my appointment with him but have asked Dr. Rouleau to get Jammet's views.

Dr. Vetter mentioned with considerable feeling that it was impossible to cooperate with Dr. Lowry Dobson (WHO-Radiobiology and Radiation Medicine) except on Dobson's terms. Supposedly,

1149371

DOE ARCHIVES

IAEA and WHO cooperate on even terms on matters such as this where there is a clear overlap of interest. Dobson apparently has pre-empted certain areas and subjects and has blocked Vetter from doing anything in these fields, e.g., whole body exposure conference, because IAEA has adopted an ultrasoft policy in all such inter-agency relationships. Meanwhile this important area may be slipping away from IAEA control. If WHO were to establish complete dominance of this field, this pattern could thereby be more easily developed in the USA.

I frankly suggested to Dr. Vetter, if he wished to undertake a project or Symposium such as this and Dobson proves intransigient, that he tell Dobson that he was going to do such-and-such, invite his cooperation, and push ahead regardless of what Dobson may think or claim. Actually, of course, this field is big enough to assimilate the efforts of many agencies, and there is no reason for anyone to try to exclude another.

While in Geneva, I tried to contact Dr. Dobson to learn whether he intended to remain with WHO and how matters stood between him and Vetter. Apparently he was enroute to Berkeley to discuss his appointment at the Donner Laboratory with John Lawrence, and Mrs. Dobson was at a relative's home.

I spent one evening with Dr. Jean Posternak, Professor of Physiology, Faculté de Médecine, University de Genéve. He has a grant from the Swiss Government to study electroencephalography and ganglionic transmission in animals relative to radiation. He had also just signed a contract with IAEA to expand this work; apparently the Swiss Government felt this did not compromise their neutrality. Dr. Posternak is one of the best neurophysiologists in Europe and we should watch for his data.

Dr. Lough (HASL) had arranged for me to visit Dr. Pierre Wenger, Director, Institut du Radium, Blvd. de l'Cluse et Rue Alcide-Jentzer (34-30-57). Dr. Wenger is interested in studying radium poisoning in Swiss watchmakers. This is of special interest to us because some dial painting is done as a cottage industry and very likely there are people currently being poisoned; this phase of radium poisoning is of special interest to us in calculating excretion and cumulative dose data. He was reluctant to talk about this phase of his program but was most interested in developing a whole body counter for studying radium patients. He is supported by the cantonal governments of Zurich, Lucern and Geneva, and by a grant from the IAEA; he is a visiting-type professor of the University. A new building with provisions for a whole body counter is being designed. It will be arranged for him to visit for two months or so at BNL, Argonne, HASL, and perhaps Los Alamos,

1149372

DOE ARCHIVES

so as to obtain a solid basis for his whole body counter work; presumably he will use IAEA grant funds for this trip (and for the counter), but if not we should find a way of supporting his studies here.

An amusing incident happened at my hotel. When the concierge saw by my passport that I was travelling on USAEC business, I had to spend almost an hour discussing Sr^{90} and the Rollex watch before I could go to my room. This is a serious business to the Swiss.

Through Dr. Posternak, I met Dr. David Klein, Professeur de Genetique Humaine in the Department of Clinique Ophthalmologique. His research grew out of a genetic study of retinitis pigmentosa into a national (Swiss) registry of diseases recognized to be of genetic origin. He has these data on color coded 4 x 6 cards. These will eventually be the most complete index to human genetic defects in the world. He seems to have all the support he wants, but I suspect he may have to go to IBM equipment before long. At the very least I suggest that we tie him into our circle of men working on human genetics. He, incidentally, was a member of a group which made the preliminary study of the Indian monazite area at the request of WHO. (Jim Neal, Michigan, was a member of this party. Did he send us a copy of their report?) Klein said that the group felt there was a reasonable possibility of detecting changed mutation rates in these people particularly an altered sex ratio. Switzerland's highly coordinated way of life is ideal for studying genetic anomalies in the past 6 or 7 generations. I gather he has all the financial support he can use, but he ought to be assisted in getting his data onto an IBM system. In that connection, would an international conference on a universal coding system for human genetic characteristics be in order?

I arrived in Paris in time to be invited to Dr. Rouleau's very impressive cocktail party in his lovely apartment overlooking the Bois de Boulogne. The top seven officials of the French CEN were present as well as all the Embassy people not involved in seeing Mr. Herter off; also there were several representatives of American firms doing business in the nuclear field and a number of people from Washington.

The next day I visited with Dr. R. Wegmann who had written us about supporting research at his Laboratoire d' Histochimie in the Faculte de Medecine de Paris. He is a recent appointee, having come from a post at the University of Hambourg, a small provincial school in the Alsace-Saar region. He has good space, fair equipment, but not much financial backing. The laboratory is organized around him in typical European Institute fashion. His particular forte is infrared spectral analysis of sectioned

1149373

DOE ARCHIVES

tissues and extracts and he plans to correlate this with all other histochemical methods including autoradiography, into an "exact science." He can have students and assistants in unlimited numbers, if he can find money to support them. I would judge him to be a hardworking, ambitious man; he is secretary of the next International Conference on Histochemistry which will be held in his laboratory in August 1960. I promised to put him in contact with NIH and discussed the possibility of support of certain phases of his work.

Back at Dr. Rouleau's office, I saw a member of the Embassy staff who had worn a Rollex watch during the time that his psoriasis had recurred; I believe I was able to reassure him that his skin condition was not radiation damage.

Dr. Rouleau has become involved in another of Elliott Earl's schemes; Earl has attempted to entice Dr. Roger Audran, a section chief of the Pasteur Institut, into responding to an invitation to join the Institute for Nuclear Serology and carry out a research program. Audran finally must have smelled a rat because he came to Dr. Rouleau. I reported our dealings with Zuccala and Earl for Dr. Rouleau's use in responding to Audran.

Dr. Rouleau's report os his visit to Greece contains an item of importance to DBM. Apparently, a fly of the Dacia family endemic in the Eastern Mediterranean including Crete and the Peloponnesian Islands, causes great commercial loss to olive growers and it is said to be a one-time breeder. Unless it has an extraordinary range, this fly, then, is like the screw worm fly and we could be of direct assistance at the working level. First, however, it would be necessary to confirm that it is a one-time breeder and that its range is short. Which agency would be most able to carry out this work; it seems like a rare opportunity to accomplish something that would be appreciated by the people themselves.

cc: A. A. Wells, DIA

1149374

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