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707100

Carroll L. Wilson, General Manager, Washington

February 20, 1948

J. C. Franklin, Manager, Oak Ridge

AUTHORITY FOR DISTRIBUTION OF RADIOISOTOPE-LABELED COMPOUNDS SYNTHESIZED IN COMMISSION LABORATORIES

REFER TO SYMBOL: AECK-6

Herein is suggested the necessary action to complete the arrangements developed by the Isotopes Division, Oak Ridge Operations, and your office for a coordinated program between Commission and commercial laboratories for the production and distribution of compounds labeled with radioisotopes, particularly C 14. The action suggested is based upon the latest discussion of this subject between you and Dr. Aebersold in Washington, January 19, 1948.

For your reference, copies of pertinent documents are attached (see list of enclosures).

As may be noted in Enclosure 3, dated October 2, 1947, Tracerlab, Inc., presented a proposal whereby this concern would produce and distribute C 14-labeled compounds. Following the Assistant General Counsel's opinion that no special contract was necessary for the resale of allocated radiomaterials and in line with the agreement reached in the October 30, 1947, meeting (Enclosure 4), 100 millicuries of C 14 were allocated to Tracerlab on December 29, 1947. This was an approval of their request, dated December 12, 1947. These documents are on file in the Isotopes Division.

On February 5, 1948, a meeting was held between members of Clinton Laboratory Division, Clinton National Laboratory, the Isotopes Division and Tracerlab, Inc. Details of Tracerlab's production plans were presented at this meeting. These plans are given in Enclosure 6. After review of the production facilities and other commitments of Tracerlab, it appears that this production schedule is reasonable.

At present, the organic synthesis program at Clinton National Laboratory has marketed only C 14-labeled methanol. Although work on other syntheses is about completed, no new compounds are expected to arise from Clinton National Laboratory within the next two months. In view of this outlook on the production of C 14-labeled compounds, the Isotopes Division wishes to recommend that authority be given to the Berkeley Area for the pursuance of Dr. Calvin's program with the necessary modifications to conform with agreement reached in the October 30, 1947, meeting. Dr. Calvin has recently submitted through the Berkeley Area

REPOSITORY Oak Ridge Operations
COLLECTION RHTG Class. Docs. 1944-1994
Records Holding Area, Bldg 2714-H Vault
BOX No. RHA H248-7 2 of 3
FOLDER Isotopes

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Carroll L. Wilson February 20, 1948

J. C. Franklin

AUTHORITY FOR DISTRIBUTION OF RADIOISOTOPE -LABELED COMPOUNDS SYNTHESIZED IN COMMISSION LABORATORIES

REFER TO
SYMBOL: ALCK-6

Office to the Isotopes Division more up-to-date information on production cost of certain C 14-labeled compounds which he is prepared to make. Please note Enclosure 5. Enclosure 7 is draft of a suggested memorandum to authorize this arrangement with the Berkeley Area. This office recommends that these modifications be accomplished by the Isotopes Division and the Berkeley Area with the assistance of Dr. Calvin.

Other AEC installations and sponsored laboratories have synthesized, or may synthesize, radioactive labeled compounds of varying complexity for use in research in the Commission's behalf. Once developmental work on the syntheses has been completed and apparatus assembled for the syntheses, little additional expenditure other than for C 14 would be involved to make larger batches of the compounds than are required to meet Commission needs. These extra quantities could be distributed through Clinton National Laboratory in the manner recommended for those produced by the Bio-Organic Division (Dr. Calvin's group) at Berkeley. For example, Dr. Wright Langham at Los Alamos Scientific Laboratories has synthesized C 14-labeled para-amino-benzoic acid and nicotinic acid. He has indicated to the Isotopes Division his willingness to make additional quantities of these useful compounds for other interested investigators both in and outside the Commission, provided suitable mechanism of distribution was established and authority granted. Since similar situations have arisen at Argonne National Laboratory and Brookhaven National Laboratory, it is recommended that a directive establishing this procedure be given the various Area Managers and that the coordination activities be delegated to the Isotopes Division, Oak Ridge Operations. Draft of suggested memoranda to authorize these arrangements is Enclosure 8.

All arrangements will be made in accordance with the understanding reached in the meeting of October 30, 1947.

J. C. Franklin

Encls.:
1. Cy. Memo fr WJW to CLF, 9/3/47 w/atts, Synthesis Program, Berkeley
2. Cy. Memo fr CLW to JCF, 9/29/47, Synthesis Program, Berkeley

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Carroll L. Wilson February 20, 1948

J. C. Franklin

AUTHORITY FOR DISTRIBUTION OF RADIOISOTOPE-LABELED COMPOUNDS SYNTHESIZED IN COMMISSION LABORATORIES

REFER TO SYMBOL: AEC-6

3. Cy. Proposal fr Tracerlab, Inc., to Isotopes Div., 10/2/47
4. Cy. Memo fr JCF to CLW, 11/21/47, w/Minutes of Oct. 30, 1947 Meeting
5. Cy. Memo fr RHB to FCA, 1/29/48 w/atts., Synthesis Program, Berkeley
6. Resume of Meeting Feb. 5, 1948
7. Draft of Memo fr CLW Authorizing Synthesis Program, Berkeley
8. Draft of Memo fr CLW Authorizing Production of Limited Quantities of C 14-Labeled Compounds for Isotope Distribution Program

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ENCLOSURE 1

1019428

COPY

rCA/jhm

Carroll L. Wilson, General Manager,
Washington, D.C.
Walter J. Williams, Manager, Field Operations,
Oak Ridge

September 3, 1947

PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM

SYMBOL: AECX-G

It is herein proposed that C 14-labeled compounds synthesized by the Bio-Organic Division, Radiation Laboratory, Berkeley, California, be included in the normal off-Commission radioisotope distribution program. The Berkeley synthesis program would be performed in close collaboration with the Isotopes Branch and Clinton Laboratories, and actual distribution would be made through Clinton Laboratories.

General availability of widely useful types of C 14-labeled compounds is essential to the progress of tracer research programs in many scientific and medical investigations. In fact, an active program for provision of isotope labeled compounds is exceeded only by the general isotope distribution program itself and the advisory isotope field service in its importance to such investigations.

Details of the proposed Berkeley program for synthesis of C 14-labeled compounds for off-Commission distribution, and further analysis of the proposal by representatives of Clinton Laboratories and by the Isotopes Branch, are contained in the following documents, copies of which are appended:

Appendix I - Memorandum "Synthesis and Distribution of C 14-Labeled Compounds", from A. P. Pollman, Area Manager, Berkeley, to W. J. Williams, Manager, Field Operations, dated July 24, and its attachments.

Appendix II - Memorandum, "Cost Estimate for Synthesis of C 14-Labeled Compounds", from A. P. Pollman to W. J. Williams, dated August 14, 1947, and its attachments.

Appendix III - Summary of Meeting on C 14-Labeled Compounds, Clinton Laboratories, July 30, 1947. (prepared by the Isotopes Branch).

Appendix IV - Cost Estimates of Proposed Berkeley C 14 Synthesis Program Based on Estimated Demand of Resulting Compounds (prepared by the Isotopes Branch).

COPY

1019429

C O P Y

Carroll L. Wilson September 3, 1947

Walter J. Williams

PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM

SYMBOL: ABCK-6

Appendix V- Suggested Sale Prices of Compounds and Resulting Income (prepared by the Isotopes Branch).

In brief, these appendices contain the following information:

Appendix I. Berkeley Proposal

The Bio-Organic Division, headed by Dr. Melvin Calvin, has made extensive progress in the synthesis of C 14-labeled compounds. The progress of this Division exceeds by far that made by any other Commission or off-Commission laboratory, making its experience and facilities unique at this time.

Although Dr. Calvin's progress is one of research and development and in the long run does not propose to be otherwise, Dr. Calvin is willing as an expedient interim measure to use the unique experience and facilities of his group to synthesize quantities would be forwarded to Clinton Laboratories and made available for both Commission and off-Commission uses.

The proposal has the enthusiastic endorsement of the Laboratory Director, Professor E. O. Lawrence, and the provisions are approved by the Berkeley Area Manager. Dr. Calvin's proposal and the compounds his group is prepared to synthesize are detailed in the attachment to the covering memorandum.

Appendix II. Berkeley Cost Estimates

From information furnished by the Isotopes Branch on the types and quantities of compounds that would most likely be in immediate need, Dr. Calvin prepared an outline of a C 14 synthesis program that would meet these needs. The Berkeley Area Office and Dr. Calvin then prepared the table of estimated costs of the compounds, which is attached to the supporting memorandum.

C O P Y

1019430

Carroll L. Wilson September 3, 1947

Walter J. Williams

PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM

SYMBOL: ABCE-6

It is to be noted that the formula used for estimating costs is the same as that used by Clinton Laboratories in the pricing of all radioisotopes and isotope compounds. This is desirable for uniformity in pricing. As pointed out by Mr. Pollman's memorandum, care was taken in the preparation of these estimates to insure that they will not be exceeded in actual practice; further, several factors would tend to reduce the cost of these items should they be put into routine, large-batch production, namely: techniques and apparatus are rather new and hence can be improved in time; increased efficiency may be obtained as the batch size is increased; and it may be economical to recover C 14 from residues and waste solutions. It is accordingly believed that these cost estimates are quite reasonable, and that they are in the range that may later prove commercially feasible.

Appendix III. Meeting on Berkeley Proposal.

A meeting was held with interested members of Clinton Laboratories and the Clinton Laboratories Division to discuss the Berkeley proposal. The proposal met with hearty approval as being a highly desirable and most worthwhile addition to the isotope distribution program. It was generally agreed that Commission laboratories in the long run should not engage in production of labeled items which develop into a commercially attractive demand, but that for the useful compounds as byproducts of their legitimate programs of research and development on labeled compounds. This arises because of their presently unique experience, facilities and handling of health safety measures.

General agreement was also obtained on amounts and types of compounds to be synthesized, method of packaging, mode of distribution, reasonableness of the cost estimates, and manner of accountability of C 14 used and costs incurred.

Appendix IV. Cost of Berkeley Program

The Isotopes Branch has compiled an estimate of the total cost incurred by the Berkeley Area program should the program be approved. This is based on the Berkeley estimated costs per synthesis and a reasonable guess as to the quantities and types of compounds that will need to be synthesized by the end of the fiscal year.

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Carroll L. Wilson

September 3, 1947

Walter J. Williams

PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM

SYMBOL: ABCW-6

The total figure is $48,770. This includes, however, $30,600 for the cost of the 612 mc of C 14 required by the program. The latter amount would not actually be paid out by Berkeley but would be transferred on a cost voucher from Clinton Laboratories. Hence, the estimated maximum possible financial outlay by Berkeley is $18,170.

This estimate is based on the Clinton Laboratories' schedule of salary per man-day and overhead, which probably exceeds that of Berkeley. Actually most of the required equipment has been already set up in the research and development program. Dr. Calvin states that his main expense will be the hiring of two graduate students at around $300-$400 per month, for a total of less than $10,000 for the year. The actual Berkeley financial outlay incurred by the addition of the proposed "production" synthesis to the existing synthesis program should therefore be considerably less than the formally calculated value of $18,170.

Appendix V. Selling Prices and Income

The Isotopes Branch has prepared a table of suggested selling prices together with the resulting total income based on reasonably expected yields and sales. Comparison with Appendix IV indicates that there is a reasonably good chance that the proposed program would not result in loss to the government. If yields are better than expected, the C 14 in residues is economically recoverable, and the off-Commission sales are sufficiently great, the program would be indicated as possible of making profit. The cost and sales data obtained from the program could then be used in an endeavor to attract a satisfactory commercial synthesis program.

It is to be noted that the minimum suggested selling price of any labeled compound is $100 per mc of C 14 content. The reason for this is to achieve uniform selling price for some of the simpler compounds, as well as to leave some margin for recovery of losses that may result on more complex compounds. Prices suggested for the more complex compounds are the nearest round number within $10 of the estimated synthesis costs.

1019432

Carroll L. Wilson September 3, 1947

Walter J. Williams

PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM

SYMBOL: AECK-6

Substantiation of Proposal

1. Numerous users of C 14 and several major research committees, including the Committee on Growth, have indicated to the Isotopes Branch the great value to scientific and medical research of labeled compounds of the type which would become available under the proposed synthesis program.

2. Many cases are known to the Isotopes Branch where programs have been, and will continue to be, delayed for 3 to 6 months due to lack of a suitable labeled starting compound (other than the $BaCO_3$ now available) for undertaking the synthesis of more complex labeled organic molecules. This has been particularly true of the program of the Memorial Hospital, New York City, Western Reserve Medical School and others active in medical and cancer research.

3. Although several commercial organizations have shown interest in the commercial provision of labeled compounds, there is considerable doubt that any off-Commission group could immediately undertake a synthesis program on the desired scale. This doubt is shared by a number of experienced radiochemists and organic chemists, such as Drs. M. Calvin and W. G. Brown. It is based on the difficulties that experienced groups within Commission laboratories have had in obtaining satisfactory quality of products and efficient yields and on the knowledge of the facilities and personnel experience of the interested concerns. Also a very important fact is that the handling of hundreds of millicuries of C 14 by any single outside firm at present would be quite hazardous.

4. Commission laboratories, such as that of Drs. Calvin (Berkeley) and Brown (Oak Ridge) now have facilities and experienced personnel to perform some of the generally desired syntheses in a safe and efficient manner. It would take approximately a year for an outside group to set up adequate facilities and train sufficient personnel, even with Commission assistance, to undertake the proposed program which can be immediately initiated within the Commission. This will result in a highly desirable gain in expediting off-Commission programs of C 14 users.

1019433

C O P Y

Carroll L. Wilson September 5, 1947

Walter J. Williams

PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM

SYMBOL: ABCK-6

5. The Commission's program of supplying labeled compounds will not interfere with the small amount of synthesis now being performed by commercial firms for isotope users. There are thousands of kinds of labeled compounds that research groups will want eventually to synthesize or have synthesized. The compounds which would be sold by the Commission would in general be only first steps toward the desired compounds. Availability of useful intermediates should greatly enhance the business of specialized small scale syntheses.

6. The proposed program will not interfere with later entrance of private enterprise into the larger scale supplying of basic types of labeled compounds. The program will actually improve the opportunity for such entrance by immediately helping to build up a market and by accumulating data on synthesis procedures and costs as well as on degree of demand. This should enable the Commission within 12 to 18 months to offer private concerns a definite industry and market. It will save private firms a considerable initial investment in C 14, in facilities and in development costs without their having even an approximate knowledge of the market. It will allow the Commission time to perfect the techniques employed in the syntheses and to aid in the training or dissemination of information that will be required for larger scale off-Commission operations with C 14.

7. The Commission has sufficient stocks of extracted C 14, as well as many curies produced but unextracted, to permit a considerable inventory in labeled compounds even though the rate of demand for the items is unknown.

Recommendation

It is recommended that:

1. The Bio-Organic Division, Radiation Laboratory, be authorized to synthesize C 14-labeled compounds for off-Commission distribution.

2. The allocation and distribution of these compounds be handled in the customary manner of other radioisotope materials, shipment and charges being made by Clinton Laboratories but proper acknowledgement of the source of production being noted on compound containers.

C O P Y

1019434

C O P Y

Carroll L. Wilson September 3, 1947

Walter J. Williams

PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM

SYMBOL: ANCE-6

3. Budget allowance for the program at Berkeley be provided not to exceed $50,000 to the end of the fiscal year June 30, 1948, this cost to include charges for C 14, man-days, expendable materials and overhead on the same schedule as used in estimating costs, but not to include charges for research and development, capital equipment and rental of facilities.

4. Within the budget allowance, the choice of quantity and quality of synthesized compounds be flexible (although approximately as listed in the proposal), the final decision on such production being made by the Isotopes Branch after weighing advice from interested Commission and off-Commission sources.

5. Records of costs and C 14 accountability for the program be maintained independently of other programs of the Bio-Organic Division, such records being suitable for future determinations of production costs of each compound.

6. Selling prices be determined according to the approved cost estimate schedule as used by Clinton Laboratories, the minimum price being $100 per mc of C 14 content and other prices being uniformized to some extent by rounding off estimates to the nearest even figure within $10.

7. Prices for items which may be added to or modified from those listed herein may be determined by the Isotopes Branch without further reference to the Washington Office on the basis of cost data furnished by the Berkeley Area and the pricing schedule of 6 above.

Walter J. Williams

1 Inclosure:
5 Appendices

CC: Area Manager, Berkeley Area (A.P. Pollman)
Clinton Laboratories Division (J.C. Stewart)

C O P Y

1019435

APPENDIX I

1019436

C O P Y

Walter J. Williams, Manager, Field Operations
Oak Ridge
A. P. Pollman, Area Manager, Berkeley

July 24, 1947

SYNTHESIS AND DISTRIBUTION OF C-14 LABELED COMPOUNDS

SYMBOL: AECBY4

Forwarded herewith are 1) three copies of a report by Dr. M. Calvin entitled "Status of the Synthetic Activities of the Bio-Organic Division of the Radiation Laboratory, University of California as of 10 July 1947", 2) three copies of an accompanying proposal by Dr. Calvin for the distribution of C-14 labeled compounds by the Atomic Energy Commission, and 3) a letter from Professor Ernest O. Lawrence dated July 14, 1947 in which he approves for the Radiation Laboratory the proposals submitted by Dr. Calvin.

This office considers Dr. Calvin's bio-organic group to be well qualified from the standpoint of experience, personnel and equipment to undertake such a program as has been proposed by Dr. Calvin.

The basis of establishing a price schedule for C-14 labeled compounds as suggested by Dr. Calvin (i.e., $50.00 per millicurie, per step removed from CO_2) is considered a fair estimate of actual production costs.

It is to be noted that Dr. Calvin's present budget was established without consideration of such a production program as is now proposed, and made no allowance for a production staff. It is therefore suggested that the moneys resulting from the sale of these C-14 labeled compounds be credited to Dr. Calvin's budget in order that the research activities of the bio-organic group be not curtailed by expenditure of effort on the proposed production program.

Accordingly, the inclosed proposals are recommended for consideration and approval.

/s/ A. P. Pollman
A. P. Pollman

3 Incls.:
1. Rpt dtd 10 July '47 (in trip.)
2. Proposal by Dr. Calvin (in trip.)
3. Ltr dtd July 14, 1947 from E. O. L.

1019437

C O P Y C O P Y

UNIVERSITY OF CALIFORNIA

Radiation Laboratory
Berkeley 4, California

July 14, 1947

The Area Manager
U.S. Atomic Energy Commission
Berkeley, California

Attention: A. P. Pollman

This is just a note to say that I approve with enthusiasm the proposal of Dr. Calvin to collaborate with Oak Ridge in making available labeled synthetic organic compounds from our Bio-Organic Laboratory.

/s/ Ernest O. Lawrence
Ernest O. Lawrence

EOL:EI

C O P Y

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C O P Y

DISTRIBUTION OF C 14 LABELED COMPOUNDS BY THE ATOMIC ENERGY COMMISSION

The following constitutes a proposal for making available the products of the synthetic activities of the Bio-Organic Division, Radiation Laboratory, University of California, Berkeley, to the Atomic Energy Commission (Isotopes Branch) for distribution to qualified researchers through out the nation.

It is proposed that:

1) A list be prepared of compounds which are now available on a routine basis, and further, that this list be kept up to date as more compounds are gradually reduced to routine synthesis.

2) This list be put into the hands of the Isotope Branch for publication.

3) The Isotopes Branch supply the C 14 in the form of barium carbonate and receive in return various amounts of compounds in the above list, the relative amounts determined by the demand.

4) A price scale be established for these routinely available compounds as follows: Not more that $50 per millicurie, per step removed from carbon dioxide, be added to the initial price of $50 per millicurie of carbon. For those compounds made by biosynthetic methods (glucose by photosynthesis), the prices will have to be set in each individual case, determined by the complexity of the isolation process.

5) The Isotopes Branch receive applications for these compounds upon much the same basis as it now receives applications for the simple isotope (barium carbonate).

6) The compounds bear the name of the laboratory of their origin in our case "Bio-Organic Division, Radiation Laboratory, University of California, Berkeley," as one of the laboratories of the Atomic Energy Commission.

7) Additional lists be prepared of compounds which would be available only for limited periods of time, until a given batch is run out. Prices on these would be set individually, on much the same basis, however, as the routinely available compounds. This list would be changed from time to time as repeat batches are made or new compounds synthesized.

8) The activities of the various laboratories engaged in this program be so coordinated as to avoid excessive duplication of compounds of different laboratories in the Commission.

C O P Y

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APPENDIX II

1019440

COPY

Walter J. Williams, Manager, Field Operations
Oak Ridge
L. F. Pollman, Area Manager, Berkeley

August 14, 1947

COST ESTIMATE FOR SYNTHESIS OF C-14 LABELED COMPOUNDS

AECBY4

Reference is made to letter from this office dated July 24, 1947, subject: Synthesis and Distribution of C-14 Labeled Compounds. In response to a verbal request from Dr. Aebersold to Mr. Ball, there is forwarded herewith a tabulation of the cost data presently available on the synthesis of C-14 labeled compounds.

It is to be noted that the cost of synthesis is given per batch of material handled. This has been done since the cost of synthesis of a given compound is essentially independent of batch size except for the cost of packaging the final product.

With the present equipment the batch sizes of all but the first two compounds may be increased to use 5 grams of $BaCO_3$. This amount of Ba^*CO_3 normally contains about 40 mc of C-14. By rebuilding certain portions of the equipment it would be feasible to increase batch sizes to utilize a maximum of approximately 100 mc of C-14. This is considered the upper limit of active material which can be handled consistent with the hazard to personnel in the event of breakage of equipment. In the case of glucose, the product of a number of photosynthesis may be accumulated and purified as a single batch, the size of the accumulated batch being as large as desired. Also in the case of each compound listed in the inclosure, approximately one of the man days for each batch is devoted to packaging of the product.

In an attempt to anticipate questions as to the cost of synthesis of these compounds as a function of output, this office has calculated and tabulated below the approximate cost data for each compound for three batch sizes. These sizes are estimated to be the minimum, intermediate and maximum amounts feasible to handle with the present or improved apparatus.

It is to be remembered that the figures given by Dr. Calvin in the inclosure, and consequently the calculations tabulated below, are approximations based upon the results of a relatively small number of laboratory syntheses. The extent to which these figures will be modified by future improvements in techniques, methods and apparatus must of necessity be determined by the passage of time.

There are two further items which will tend further to reduce the cost of these compounds but upon which specific information is not yet available.

1019441

W. J. Williams, Manager, Field Operations, Oak Ridge
A. P. Pollman, Area Manager, Berkeley

August 14, 1947

COST ESTIMATE FOR SYNTHESIS OF C-14 LABELED COMPOUNDS

ARCHY4

These are the increased efficiency of the syntheses as the batch size is increased and the recovery of C-14 from residues and waste solutions. As data on these items is accumulated, corresponding adjustments in unit prices can be made.

Care has been taken in the preparation of these estimates to insure that they will not be exceeded in actual practice. Should this program be undertaken, cost data will be frequently reviewed and reported in order that the above costs may be kept currently accurate.

/s/ A. P. Pollman
A. P. POLLMAN

2 Incls.:
1. C-14 Synthesis Program
2. Estimated Cost of Synthesis w/attach

1019442

C O P Y

UNIVERSITY OF CALIFORNIA
RADIATION LABORATORY

C O P Y

C 14 Synthesis Program

8 August 1947

I Compounds. Cost and time analysis not including cost of the radiocarbon.

		Mo. C 14 per Mo.	Yield	Man days per batch	Cost* per batch
1)	$C^{14}H_3I$	50 used 40 yield	80%	5	$ 225
2)	$C^{14}H_3CO_2Na$	42 used 25 yield	60%	6	316
3)	$NH_2C^{14}H_2CO_2H$	33 used 10 yield	30%	10	509
4)	$NH_2CH_2C^{14}O_2H$	23 used 10 yield	45%	6	307
5)	$CH_3C^{14}OCO_2Na$	20 used 10 yield	50%	5	256
6)	Glucose	60 used 20 yield	30%	15	525

Equipment maintenance, preparation of catalysts, clean ups, analyses, etc. 20 man days/month

*Cost formula = time cost plus chemical cost

$$= \{[(\text{man days} \times 20)\ 1.33]\ 1.85\} + [(\text{mo.}C^{14})\ 50 \times 0.01]$$

This is figured using the Clinton figures of:

a) Man days at $20 per day for the man x 1.33 (direct cost to keep the man in laboratory, smocks, etc.)

b) Direct laboratory cost x 1.85 (total overhead of running the laboratory, such as fire department, guards, safety, and other service groups.

c) Cost of chemicals and chemical supplies is estimated as 1% of cost of C 14 used. Liquid nitrogen is the most expensive single item.

II Properties and analysis of compounds. (Tentative)

1) $C^{14}H_3I$

a) Analysis = BP 42-43° C

$$n^{22}_D = 1.5280$$

b) Preparation. See: Tolbert, J. Am. Chem. Soc. 69, 1529 (1947)

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c) Water content - dried over P_2O_5 in vacuo

d) Possible contamination -PH_3, HI

2) $C^{14}H_3CO_2Na$

a) Analysis - Molecular weight 82

b) Preparation - from $C^{14}H_3MgI+CO_2$

c) Water content - anhydrous, dried in High vacuum

d) Possible contaminants - traces of NaI, NaCl

3) $NH_2C^{14}H_2CO_2H$

a) Analysis - m.p. 225° C Dec

b) Preparation - See: Ostwald, BC-56

c) Water content

d) Possible contaminants - traces of NH_4Cl

4) $NH_2CH_2C^{14}O_2H$

a) Analysis m.p. 252° C

b) Preparation - see: Ostwald, BC-56

c) Water content -

d) Possible contaminants - traces of NH_4Cl

5) $CH_3C^{14}OCO_2Na$

a) Analysis -

b) Preparation - see: Calvin & Lemmon, J.Am.Chem.Soc. 69, 1232 (1947)

c) Water content - dried in vacuo

d) Possible contaminants - traces of $CH_3C^{14}O_2Na$

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6) Glucose

a) Analysis - crystalline glucose

b) Preparation - See: Arnoff, Benson, Hassid, and Calvin, Science, 105, 664 (1947)

c) Water content - anhydrous

d) Possible contamination - traces of fructose and other sugars.

III Notes

1) An expensive and time consuming item is the aliquoting and bottling of samples. Thus, the cost of break off seals for methyl iodide will be fairly large (guess estimate: cost per tube - $1), vacuum line to be used for filling tubes $200-300 five man days to set and calibrate system, two man days per batch of 40 mc. thereafter for filling, sealing, etc.).

Similarly, if it takes ten minutes to make two weighings, cost of bottling 25 mc. of sodium acetate (20 - one mc. samples and 10 - one-half mc. samples) including labeling and redrying of acetate as it picks up water, would be not less than one man day. Of course, such estimates as these are tentative, and only when the program get underway can we get reliable information.

2) These figures are for a given rate of out put and can be used to estimate maximum costs at higher rates. Estimates on new compounds cannot be made until further data is available, probably about the end of the year.

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C O P Y

ESTIMATED COST OF SYNTHESIS

Compound	Amount C-14 Used	Batch Yield	Approximate Cost per Batch: Synthesis Only	Approximate Cost per Batch: Including C-14 at $50 per millicurie	Approximate Cost per mc: Synthesis Only	Approximate Cost per mc: Including C-14 at $50 per millicurie
1) CH_3I*	50 mc	40 mc	$225	$2,725	$5.50	$ 68.00
	---	---	---	---	---	---
	---	---	---	---	---	---
2) CH_3COONa*	42 mc	25 mc-	316	2,416	12.50	97.00
	---	---	---	---	---	---
	---	---	---	---	---	---
3) H_2NCH_2COOH*	33 mc	10 mc	509	2,159	51.00	216.00
	40 mc	12 mc	520	2,520	43.00	210.00
	100 mc	30 mc	610	5,610	20.00	187.00
4) H_2NCH_2COOH*	23 mc	10 mc	307	1,457	31.00	146.00
	40 mc	17.5 mc	344	2,344	20.00	134.00
	100 mc	43.5 mc	480	5,480	11.00	126.00
5) $CH_3COCOONa$*	20 mc	10 mc	256	1,256	25.00	126.00
	40 mc	20 mc	307	2,307	15.50	115.00
	100 mc	50 mc	460	5,460	9.25	109.00
6) Glucose	60 mc	20 mc	525	3,525	26.00	176.00
	120 mc	40 mc	787	6,787	19.60	170.00
	240 mc	80 mc	1180	13,180	14.75	165.00

* Radioactive Carbon

Notes:

1) CH_3I* It would not be possible to enlarge the batch size of this compound without encountering severe technical difficulties.

2) CH_3COONa* Same as for (1)

3) H_2NCH_2COOH* The first batch size given is that now normally produced. The second batch size given is estimated to be the maximum possible with existing equipment. The third batch size given is estimated as the maximum which could be handled safely after modification of equipment.

1019446

APPENDIX III

Summary of Meeting on C 14-Labeled Compounds, Clinton Laboratories, July 30, 1947.

Attending: E.J. Murphy, J.A. Cox, Waldo Cohn, Logan B. Emlet, Weldon Brown, M. Kuna, H. Stringfield, Jr., of Clinton Laboratories, John Martens, Clinton Laboratories Division, X-10; P.C. Aebersold, S. Allan Lough and Nathan Woodruff, of Isotopes Branch.

Dr. Calvin's proposal was given a hearty indorsement as being most worthwhile and fulfilling a definite scientific need.

The group recommended that the production of C-14 labeled compounds follow essentially the information presented in "Cost Estimates of Berkeley Proposed C 14 Synthesis Based on Estimated Demand of Resulting Compound."

The group also suggested that:

a. The resulting compounds be packaged in breakoffski ampoules whose over-all lengths are not greater than eleven inches and whose diameters do not exceed one inch.

b. The resulting compounds be packaged by the synthesizer in lots containing 0.5 mc and 1 mc activity of the compounds (perhaps 80% of a given compound should be packaged in 1 mc quantity while the remaining 20% be packaged as 0.5 mc lots).

c. Labels on all such lots arising from Dr. Calvin's group should not only show their origin but should give (1) labeled compound, (2) net weight, (3) activity present, (4) water content and (5) all other data which would be pertinent for further synthetic and biological work. In regard to the last item, the group felt that Dr. Calvin should be free to exercise his own judgment on the extent of the included data.

A discussion was held regarding the selling price for labeled compounds arising at Clinton Laboratories, the Bio-Organic Division (Berkeley) and/or other project installations. It was suggested that the pricing system follow that in practice at Clinton Laboratories at the present time. However, it was felt that the cost of any synthesized compounds should not be, at this stage of the program, below $100 per millicurie. (The prices recommended under "Suggested Sales Prices of Compounds and Resulting Income" are based primarily upon the cost indicated in A. P. Pollman's memorandum, dated August 14, 1947)

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APPENDIX III

It was suggested that C 14 allotted to the Bio-Organic Division (Berkeley) and other institutions for the synthesis of C 14-labeled compound is subject to accountability. Therefore, records should be kept on C 14 received, C 14 sent to Clinton Laboratories along with the chemical form of moved materials, and C 14 in residues from organic synthesis. It is hoped that feasible methods will be found to recover the C 14 from such residues. All recoverable residues should be saved. This arrangement does not prevent the useful application of residues in the synthesizing or other applications. However, these applications should be listed in the accountability report.

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APPENDIX IV

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APPENDIX IV

COST ESTIMATES OF BERKELEY PROPOSED C 14 SYNTHESIS PROGRAM BASED ON ESTIMATED DEMANDS OF SYNTHESIZED COMPOUNDS[a]

	SYNTHESES BATCHES			Approximate Cost per mc per Batch	Estimated Requirements to 6/30/48	Total Cost
	No. of Batches	C 14 to be used	Batch Yield			
1. Methyl Iodide C^*H_3I	2	50	40	68.00	80	$ 5440
2. Methyl labeled Sodium Acetate $C^*H_3.COONa$	2	42	25	97.00	50	4850
3. Methyl labeled Glycine $NH_2.C^*H_2.COOH$	2	40	12	210.00	20	5040
4. Carboxyl labeled Glycine $NH_2.CH_2.C^*OOH$	1	40	17.5	134.00	20	2345
5. Carbonyl-labeled Sodium Pyruvate $CH_3.C^*O.COONa$	1	40	20	115.00	20	2300
6. Glucose	1	120	40	170.00	40	6800
7. Fructose	-	120[c]		200.00	40	8000
8. Other Synthesis to be determined	-	80[c]		175.00	40	7000
9. Other Synthesis to be determined	-	80[c]		175.00	40	7000
		612			350 mc	$48,775[b]

a. Reference is made to data and information given in "Estimated Cost of Synthesis of C 14 Labeled Compounds."

b. Includes $30,600 for cost voucher transfer of 612 mc of C 14 from Clinton Laboratories.

c. Estimations only.

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APPENDIX V

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C O P Y

APPENDIX V

SUGGESTED SALE PRICES OF COMPOUNDS AND RESULTING INCOME

	Suggested Sale Price	Anticipated Millicuries of Compounds	Anticipated Income
1. Methyl Iodide - C^*H_3I	100	80	$ 8000
2. Methyl-Labeled Sodium Acetate $C^*H_3.COONa$	100	50	5000
3. Methyl-Labeled Glycine $NH_2-C^*H_2.COOH$	210	24	5040
4. Carboxyl-Labeled Glycine $NH_2.CH_2.C^*OOH$	140	17.5	2450
5. Carbonyl-Labeled Sodium Pyruvate: $CH_3.C^*OONa$	120	20	2400
6. Glucose	170	40	6800
7. Fructose	200	40	8000
8. Compound from other Synthesis to be determined later	175	40	7000
9. Same as 8	175	40	7000
		TOTAL	$ 51,690

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ENCLOSURE 2

1019453

OFFICE MEMORANDUM

TO: Mr. J. C. Franklin, Manager, Oak Ridge Directed Operations September 29, 1947

FROM: Carroll L. Wilson, General Manager

SUBJECT: PROPOSAL FOR DISTRIBUTION OF C 14-LABELED COMPOUNDS SYNTHESIZED UNDER BERKELEY AREA PROGRAM.

This proposed program which has been comprehensively covered in the memo submitted to me by Mr. Williams dated September 3 bearing symbol ABCR-6 has been studied carefully by members of my staff here and I discussed it both with you and with Dr. Aebersold. The program proposed is a rather natural extension of the present program for distribution of radioisotopes. The reasons advanced for taking this additional step seems very persuasive.

At the same time, this proposal raises very important questions of policy. The primary questions is how far the Commission should go beyond the production, distribution and servicing of radioisotopes in the form of elements. The reason for taking a very close look at the program is that the making of compounds may well represent the basis for a useful business in the manufacture of chemical intermediates or final products. Unless the Commission considers very carefully the various steps in this direction, it may seriously prejudice the possibility of building a small but useful industry in the production and sale of compounds containing radioisotopes. It may be that the steps proposed in this program are needed to (a) provide the basic building blocks for making complex organic chemicals and (b) explore the field of usefulness of certain more complex compounds . It may also be that the prices proposed for these compounds will not prejudice successful commercial production of these and other materials at a later date when various chemical firms have personnel trained in the handling of isotopes and when they are prepared to engage in this business.

However, it seems to me very important that before we approve this program there be consultation with some of the chemical firms, perhaps those which have expressed interest in this business thus far, both in order to ascertain their state of preparadness to enter this field and to get their general advice as to how we might proceed.

There are some interesting legal questions as well as those of policy involved in opening this field up to commercial exploitation.

I suggest that after reviewing this matter with Dr. Aebersold you arrange a conference of appropriate industrial representatives for full discussion of these matters and that you attempt in such a conference to elicit from interested firms any specific proposals they may have or comments they may be prepared to make in relation to this business. We believe that the distribution of some of these compounds now would serve a useful purpose. Therefore, if possible, we should endeavor to find some basis on which we could proceed but with the definite expectation that industry would pick up the load and that the actions we would take would facilitate rather than deter industrial interest.

Please let me have your reactions and a report as to the steps which you propose to take exploring industrial interest and reaction in regard to this matter.

/s/Carroll L. Wilson

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ENCLOSURE 3

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ENCLOSURE 3

FROM: Tracerlab, Inc., Boston, Massachusetts October 2, 1947

To: Isotopes Division, U. S. Atomic Energy Commission, Oak Ridge, Tennessee

Subject: Proposal to Atomic Energy Commission Requesting Permission for Tracerlab to Synthesize and Stock Organic Compounds Containing Carbon 14.

It is believed that wider use of radioisotopes can be stimulated by a change in the mechanism by which a primary user obtains organic compounds containing Carbon 14. The change which we suggest will result in a saving both in time and money for the customer, permitting more experimental work to be done within a given time and permitting research organizations with limited budgets to more fully participate in research utilizing radioactive materials.

At present, Tracerlab is synthesizing compounds containing Oak Ridge Carbon 14 for a number of research projects. Inasmuch as the ultimate user must obtain A.E.C. permission to purchase Carbon 14 and have it shipped to us before actual synthesis work can be started, there is naturally a considerable delay between the time a request is submitted to Oak Ridge for the radioisotope and the time at which we are in a position to deliver the synthesized material to the ultimate user. Sometimes several months may be required between the placing of a request with Oak Ridge and final delivery of the synthesized material to the customer.

With the present procedure we can seldom combine several orders for a synthesis to effect savings of large scale operation. Normally each synthesis ordered by a customer is handled individually. If it were possible for us to schedule larger production runs, considerable savings could be made and passed on to customers in the form of lower prices for synthesis services.

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To permit both lower prices and more rapid availability of synthesized Carbon 14 compounds, it is requested that the present procedure be modified as follows:

1. Tracerlab shall be permitted to obtain relatively large amounts of Carbon 14 from Oak Ridge in the form of barium carbonate or, preferably, in irradiation units.

2. Tracerlab shall then synthesize relatively large amounts of various key organic compounds and package them in convenient units.

3. A standard price per millicurie will be set, with AEC approval, upon each item. Before a primary user can have one of these Carbon 14 compounds delivered to him, it will be necessary for him to first obtain permission, as at present, from the Atomic Energy Commission, after which Tracerlab will forward the desired compound directly to him.

4. Primary users will pay the standard price for Carbon 14, including handling charges, directly to the AEC. Tracerlab will then bill these users for a standard synthesis charge not including the cost of the radioactive materials. Upon ordering radioactive materials for stock from Oak Ridge, Tracerlab will not be billed for such materials but will be bonded to cover liability for any losses of materials which may occur during synthesis or at any time while they are in Tracerlab's possession.

5. The materials held by Tracerlab will be available for an inventory check at any time and could be recalled by the Atomic Energy Commission in the event that they should desire to take such action. Since no further dilution of activity would be made in any synthesis, the AEC could have material of the same specific activity returned to them as would be received by Tracerlab.

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It should be pointed out that Tracerlab will not qualify as a primary user of Carbon 14 but as an agent of the AEC, in a position similar to that now held by the Stuart Oxygen Company in distributing deuterium. As far as the procedure required for the primary user is concerned, virtually no changes would be made.

The magnitude of the savings which could be effected is well illustrated by considering the cost to a primary user of one millicurie of malonic acid containing Carbon 14. Under present conditions it would be necessary for Tracerlab to charge $2000 for a one millicurie order of malonic acid. However, if authorization for the above outlined plan were given, Tracerlab could synthesize a ten millicurie lot of malonic acid at a cost no greater than for a one millicurie lot namely $2000. Thus, we would then be in a position to supply primary users with malonic acid at a price of $200/millicurie.

Similarly, we charge $600 for synthesis of a one millicurie order of ethyl iodide. If the proposed plan were in effect, we could charge $60/millicurie or even less if conditions warranted a production run of greater than ten millicuries at one time.

In considering these and other similar examples which could be cited, it is evident that many users of radioactive materials are being charged far in excess of prices which could be attained by larger scale syntheses. We do not believe that such a situation is fair to the ultimate user nor do we believe that it is conducive to stimulating the widest possible use of radioactive materials as medical, research, and industrial tools.

To overcome this situation, Tracerlab desires to obtain 100 millicuries of Carbon 14, under the provisions already outlined, for making ten key organic substances in ten millicurie lots. Examples of the types of compounds which

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we would make and stock are methyl iodide, ethyl iodide, phenyl bromide, diazomethane, malonic acid, and acetyl chloride.

In making this proposal we believe its principal merits to be speed, a minimum of duplication in handling, lower cost, and full control of end use by the Atomic Energy Commission.

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List of Compounds Containing C 14 which either have been synthesized here, or are in the process of being synthesized, or are to come up shortly.-

Compounds Synthesized. -

(a) Barium carbide

(b) Acetylene

(c) Potassium cyanide

Syntheses in Progress.-

(a) Benzene

(b) Methyl iodide

(c) Methylamine

(d) Ethyl alcohol

Syntheses Tentatively Scheduled.-

(a) Acetic acid

(b) Steric acid

(c) Diazomethane

(d) Testosterone

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Encl. 4

ENCLOSURE 4

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ENCLOSURE 4

COPY

Carroll L. Wilson, General Manager, Washington November 21, 1947

J. C. Franklin, Manager, Oak Ridge

COMMERCIAL DISTRIBUTION OF ISOTOPE-LABELED COMPOUNDS

SYMBOL: AECK-6

Reference is made to your memorandum dated November 17, 1947 regarding results of a meeting held in Oak Ridge on October 30 to discuss commercial distribution of isotope-labeled compounds.

The Isotopes Division has forwarded copies of the minutes of the meeting to participants for comment and correction. A copy of the minutes is inclosed.

The office of the Assistant General Counsel is working out the details of the contract with Tracerlab, Inc., for the processing and distribution of C 14 compounds. Not all the problems of patents and reports have been resolved.

Before a general public statement is prepared here for publication by the Commission, Dr. Aebersold recommends that the new Advisory Committee on Isotope Distribution Policy which is to be organized soon be given an opportunity to review the problem and to offer suggestions on the long range policy.

J. C. Franklin

1 Incl.:
Cy. of Minutes

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CONFERENCE ON COMMERCIAL DISTRIBUTION OF ISOTOPE-LABELED COMPOUNDS

Minutes of the Meeting
October 30, 1947
Oak Ridge, Tennessee

List of those attending the conference:

Representatives of Industrial Firms:

William E. Barbour, Jr., Tracerlab, Inc., Boston
John Bates, Sun Oil Company, Philadelphia
W. C. Beamer, Dow Chemical Company, Midland, Michigan
A. V. Grosse, Houdry Process Corporation, Marcus Hook, Pennsylvania
C. A. Hochwalt, Monsanto Chemical Company, St. Louis
L. A. Matheson, Dow Chemical Company, Midland, Michigan
R. G. Miller, Tracerlab, Inc., Boston
E. J. Putzell, Monsanto Chemical Company, St. Louis
Merle Randall, Stuart Oxygen Company, San Francisco
D. W. Stewart, Eastman Kodak Company, Rochester, New York
R. C. Swain, American Cyanamid Company, New York
D. L. Tabern, Abbott Laboratories, North Chicago

Representatives of Clinton Laboratories:

E. J. Murphy

Representatives of the Atomic Energy Commission

J. C. Franklin, Manager, Oak Ridge Operations
P. C. Aebersold, Chief, Isotopes Division
H. L. Price, Assistant General Counsel

The following firms were invited to send representatives but were unable to do so:

Organics, Inc., Chicago
National Cylinder Gas Company, Chicago
Eli Lilly & Co., Indianapolis

Members of the Industrial Advisory Group to the Atomic Energy Commission were also invited but could not attend because of previous arrangements for the first formal meeting of this group which had been scheduled for the same date.

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The purpose of the meeting was:

1. To explain the need for isotope-labeled compounds and why their production and distribution presents a special problem to the Commission.

2. To encourage interest of firms in a production and distribution program--both immediate and long range.

3. To find a basis for proceeding on an immediate program for supplying isotope-labeled compounds, the program to include:

   a. Various possible sources of synthesized compounds, such as:

      (1) Commercial synthesis (possible profit)

      (2) Synthesis without profit as a public service

      (3) Commission laboratories

   b. Arrangements suitable for

      (1) Isotope users, particularly for research and medicine

      (2) Commercial synthesis firms

      (3) Commission, and its advisory groups and laboratories

4. To ascertain the extent of commercial production that can be obtained (a) within the next six months, and (b) in twelve to eighteen months.

5. To receive advice on the policies of a longer-range program which would include the various possible sources of synthesized compounds and consideration of the interests of producer, user, and Commission.

(Stenographic reports of the meeting are available in the files of the Isotopes Division. The following report is a summary of the points discussed.)

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I. Opening Remarks

A. Mr. J. C. Franklin reviewed the purposes of the conference and the reasons for meeting in Oak Ridge. He made the following points:

The Office of Oak Ridge Directed Operations has been set up recently as a unit of the Commission and among the duties assigned to it is the Commission's isotope distribution program.

Mr. Franklin indicated that the Commission feels that the isotope distribution program is one of the more important and fascinating aspects of the Oak Ridge Operation and is laden with tremendous possibilities. He outlined the desirability of getting industrial participation in research and development of isotope uses and asked for a statement on the broad policy of how industry should participate.

The reasons for Government control and distribution of basic materials are: Ownership of the pile and the questions of national security and public health. Within these limits it is the purpose of the Commission, as stated by Mr. Lillienthal in an address at Detroit on October 6, "to move away from the present Government monopoly so that the people of the United States will realize the full benefits of the initiative, the technical skill and the managerial ability of American industry. We must find opportunities for industrial participation; that is, opportunities for profit."

The operation of Commission facilities involves many ramifications which are not normal business operations; for instance, running a town like Oak Ridge, the necessity for security, the problems of health and safety are not normal business operations. It is our wish to cooperate insofar as possible and as soon as possible in a program to encourage competitive effort characteristic of the normal, free enterprise which built the great automobile and aircraft industries.

Our particular problem today may be relatively small in the matter of dollars and cents. But it is of major significance in establishing a precedent for future relations of private industry and the AEC.

B. As a basis for discussing an enlarged program which would include industrial participation, Dr. P. C. Aebersold presented the experience of the Isotopes Division in its first year of operation. The importance and need for the synthesis and distribution of isotope-labeled compounds were developed as follows:

The expected demand was projected from shipments already made and from a review of a C 14 survey which had been conducted by the Isotopes Division.

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The facilities available for synthesis include (1) AEC laboratories, (2) nonprofit laboratory operations undertaken by private and industrial institutions, and (3) commercial laboratories. Although Commission laboratories in their research and development program are prepared to furnish limited quantities of C 14-labeled compounds immediately, these compounds would not serve all the needs of isotope users and, in the long run, Commission research groups would not wish to function as production units.

The Commission has certain obligations under the Atomic Energy Act to

1. Insure adequate health protection to the public as well as the users of atomic energy (radioisotopes).

2. Encourage proper, safe and worthwhile uses of radioactive by-products of atomic energy (radioisotopes).

3. Strengthen free competition in private enterprise.

The ultimate user of isotopes, the customer, must be considered. He is concerned with the factors of

1. Price

2. Quality of product

3. Time

4. Priority of use (research and medical uses have precedence by law).

The production techniques of radioisotope-labeled compounds were briefly stated. Primary materials must of course be produced in Commission facilities (the pile). The scale of operation will be small, involving micro-techniques (1 millicurie to 20 millicurie batches involve 0.1 to 2 grams of radiocarbonate). Efficient processes are important for incurring high yields because of the value and scarcity of primary materials. It is also important that the dilution with ordinary carbon be a minimum and the position of labeling be definite. Radiochemical techniques become increasingly important as quantitites of materials become larger because of the greater health hazard.

Allocations, of course, must be controlled by the Commission. The Atomic Energy Act calls for close observance of health-safety standards (including recall of improperly used materials)and provides that fundamental research and medical research or therapy have prior use of materials available.

The Commission desires to adopt policies and make arrangements for supplying isotope-labeled compounds which will satisfy immediate as well as long range needs of isotope users and at the same time develop through

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private enterprise whatever business possibilities may exist. The participants in the conference were asked to give their advice on formulating desirable supply arrangements for isotope-labeled compounds.

C. Mr. H. L. Price, Assistant General Counsel, had no prepared statement. He wished, however, to assure those present that, although provisions of the Act must be observed he could see no great obstacle in the way of achieving the aim of the meeting; that is, the development of methods to obtain industry-wide participation in this program. Mr. Price stated that it was safe to assume that there were no legal aspects of this program which could not be met satisfactorily.

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II. Discussion

A. Fission Products. Dr. Grosse asked about the availability of fission products for industry. Mr. Hochwalt thought these products will be of great value in the future. Aebersold pointed out that because of the complexity of the mixture and large amounts of chemicals added, the isolation of fission product materials from waste sources remained largely an unsolved problem.

B. Patents. Mr. Hochwalt raised the question of patents--would industries have patent rights on processes and new production methods? Mr. Swain said that industry in general was very anxious to study the possibilities involved in this type of work, but could not continue indefinitely if they did not see opportunities for profit. Mr. Price said that a Commission advisory group was studying the whole problem of patents but that it was entirely reasonable to expect an independent statement of policy in this particular field--the use of unclassified radioactive and stable isotopes. The general opinion was that the AEC had no special interest in patents except those relating to the use of fissionable materials and the development of military weapons. It was admitted that by present allocation procedures, pressure could be brought on any one attempting undesirable exploitation of a discovery. Mr. Franklin pointed out that to spread this work in to industry it must be profitable industry. Industry must have an incentive to take a risk. He felt that the problem of patents could be worked out satisfactorily.

C. Reports. Mr. Putzell objected to that clause of the agreement form for radioisotope distribution which provides for reports on use of materials. He believes that there is a police power inherent in the requiring of reports. It was generally agreed that the question of patents and reports are closely related in the minds of industry. Aebersold explained that the agreement contained no clause requiring patent disclosures. He also showed that the Act requires an application be filed for materials and that materials be used only in the manner disclosed in the application. Rather than employ a large number of inspectors it was determined to select users carefully on the bases of safe uses and available facilities, and require written statements as to use. There has been no pressure brought on applicants to prepare more than a statement concerning the general use and such report does not have to be filed before patent applications are completed.

Mr. Franklin said that although the law provides for supervision in respect to health and safety practices, the actual production and health responsibility belongs to industry. Mr. Swain believed industry would not object, after a patent was obtained, to submitting to an investigation to see if unsafe use was being made of material. Maintenance of control by regulation and code rather than by policing or detailed reporting appeared to be the more acceptable solution to the industrial hygiene aspects.

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D. Pricing. Will the AEC attempt to control prices? The two means of control as visualized by Mr. Hochwalt could be (1) actual supervision and approval of prices, and (2) return of Commission laboratories into the business of producing compounds. The price system used by the AEC was explained by Aebersold as estimated "out-of-pocket" costs to the Government, excluding amortization of major plant facilities. Industry would have to realize a profit and meet competition. Even without competition, prices must be attractive to the user to develop a market. The general opinion was that proper price levels would be reached by industry through its normal practices.

Research done by AEC laboratories in developing a synthesis may constitute a subsidy for distribution of the particular item, but the information would be equally available to all firms.

The following suggestion was discussed but not accepted: That the AEC have each compound synthesized by the lowest bidder and returned to the AEC for distribution. Representatives of interested firms indicated they would prefer to distribute directly.

The Monsanto representatives presented estimated prices for methanol production which ranged from $250 per millicurie to $700 per millicurie, depending on the size of the batch (100 mc or 20 mc). The price included amortization of laboratory installation, equipment, labor, supplies, distribution costs and a net return of 15 percent on the investment. It was admitted that if a considerable number of compounds were being produced and sold by the same laboratory, the cost for a single item, such as the methanol, would be reduced.

E. Compounds of Particular Interest. The afternoon session of the meeting was directed toward obtaining specific recommendations on materials to be synthesized. Aebersold presented the following list of organic compounds of special interest. These are "intermediates" or compounds of most use as tracers or as the first step toward the preparation of more complex compounds.

1. Intermediates or General Products:

(1)	Barium carbide	(9)	Acetic acid	(17)	Diazomethane
(2)	Methyl iodide	(10)	Ethylene dichloride	(18)	Ethylene oxide
(3)	Methyl alcohol	(11)	Acetone	(19)	Phenyl bromide
(4)	Formaldehyde	(12)	Stearic acid	(20)	Acetoacetic ester
(5)	Formic Acid	(13)	Potassium cyanide		
(6)	Ethyl iodide	(14)	Malonic ester	(21)	Isoprene
(7)	Ethyl alcohol	(15)	Benzene	(22)	Urea
(8)	Acetaldehyde	(16)	Toluene	(23)	Pyridine

(24) Thiourea (25) Bromobenzene

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2. Special Products of Great Interest:

Sugars - fructose, glucose, etc.
Steroid hormones
Amino acids
Selected fatty acids

Tracerlab, Inc., has already presented to the AEC a proposal for production of isotope-labeled compounds. Mr. Barbour believes they can produce items above numbered 1, 2, 7, 9, 11, 12, 13, 14, 15, 17, and 19 and others not listed: glycine, acetyl chloride, phthalic acid, testosterone, and methylamine. Tracerlab was willing to undertake the production of about 10 millicuries of six to eight compounds on a month's notice.

Mr. Hochwalt said that if the basic principles are satisfactory, Monsanto would be interested. However, the company would not commit itself to a definite program until formal announcement of policy by the Commission.

Mr. Swain, speaking for Cyanamid, stated his company was not interested in commercial synthesis. However, Cyanamid would continue to make and use compounds for their own research.

The Dow Chemical Company, represented by Mr. Beamer and Mr. Matheson, would be glad to add to the availability list any compounds prepared in company laboratories in excess of needs. However, they were not interested in the enterprise on a commercial basis.

Mr. Tabern of Abbott Laboratories thought his firm would be interested only in a cooperative program with other users, preferably those in medical research. Abbott would be immediately concerned with urea, thiourea and possibly malonic ester.

Other firms represented were principally interested in stable isotope compounds. Mr. Randall of the Stuart Oxygen Company indicated his firm was considering re-entering the D_2 and D_2O production field (they now distribute these materials on contract with the AEC). Stuart is also considering production of deutero-compounds and setting up mass spectrometer analysis service.

Eastman Kodak makes N 15 and C 13. Mr. Stewart outlined their distribution procedure in some detail. Eastman will produce compounds of limited demand only after the total number of orders equals the minimum amount produced in a complete synthesis operation.

The Houdry Process Corporation and the Sun Oil Company, represented by Mr. Grosse and Mr. Bates, respectively, have a cooperative venture for constructing a plant for the production of C 13 and O 18. The plant is not in production as yet and plans for synthesis operations are incomplete.

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III. Summary

1. The Commission should make a general public announcement of policy in regard to the isotope distribution program on:

   a. Availability of materials for commercial uses.

   b. Patents in synthesis and use of materials.

   c. Reports on uses.

   d. Prices on isotope-labeled compounds.

2. A reasonable policy for the Commission to follow in the synthesis and distribution of isotope-labeled compounds would be as follows:

   a. The Commission distribute only those materials which commercial firms are not prepared to produce and distribute within the next six months.

   b. Quantities distributed by the Commission to each customer will be limited to immediate needs of the user (say, in general, not over one millicurie) to reduce the possibility of "stock piling" which would adversely effect future commercial prospects.

   c. The Commission would withdraw from production of any compound when a commercial firm demonstrates it can make satisfactory synthesis.

   d. The Commission will make clear that its prices are derived from arbitrary costs established without routine production experience. Commercial production may involve costs for laboratory facilities, etc., not considered in the Commission's charges, and prices may be relatively higher.

   e. Synthesis processes which have been developed in Commission laboratories should be made freely available.

   f. The Commission make isotope-labeled compounds which are not of interest or profit to commercial firms but are important for scientific research.

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ENCLOSURE 5

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ENCLOSURE 5

COPY

OFFICE OF [illegible]

UNITED STATES GOVERNMENT

TO : F. G. Jeberson, Chief, Isotopes Branch, Office of Oak Ridge Directed Operations

January 29, 1948

FROM : Russell H. Hall, Chief, Materials Information Branch, Berkeley

SUBJECT: [illegible] DISTRIBUTION OF C-14 LABELED COMPOUNDS [illegible] IN [illegible]

SYMBOL: [illegible] 4

Reference is made to your letter dated December 5, 1947, subject as above. Particular reference is made to paragraph 5 of this letter in which a request is made for a list of labeled compounds which can be synthesized at Berkeley.

In accordance with the above referenced request, please find forwarded herewith two copies of the list of C-14 labeled compounds which have been or could be produced at Berkeley, together with estimated cost data. The term "could be produced" is used to indicate that some compounds on the list have not actually been produced with the labeled carbon in the position indicated but could be produced by using as starting materials labeled compounds which are available. To illustrate: carbonyl labeled potassium pyruvate, $CH_3C{*}OCO_2K$, has been produced from carboxyl labeled acetic acid. Had methyl labeled acetic acid been used, the product would have been methyl labeled pyruvate. Thus both of these compounds are listed.

Inasmuch as we have not to date received from your office a clarification as to what specific labeled compounds Tracerlab is prepared to synthesize, the attached list of compounds does not, as you had suggested, omit such compounds.

As in the case of the cost data submitted by this office in letter of August 14, 1947, the following approximate cost formula has been used:

$$\text{Cost} = \text{Man days} \times 20 \times 1.33 \times 1.85 + \text{m.c. } C^{14} \times 50 \times 0.01$$

For your information you will also find enclosed two copies of the list of compounds which Dr. Calvin has sent to Dr. Becher. The compounds on this latter list are those compounds whose routine or commercial production are considered as especially desirable for organic and bio-chemical research.

Russell H. Hall

2 Encls.:
1. List of 33 compounds (in dup.)
2. List sent to Becher (in dup.)

Hall/mjc

Encl 5

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	Compound name	Compound formula	Man Days per batch	Millicuries used per batch	Batch Yield %	mc	Approx cost per batch: Synthesis only	Approx cost per batch: Total cost incl. C-14	Approx. cost per mc.: Synthesis only	Approx. cost per mc.: Total cost incl. C-14
1.	Methyl alcohol	C^*H_3OH	4	40 mc	90%	36 mc	$217.00	$2217.00	$6.00	$62.00
2.	Methyl iodide	C^*H_3I	5	40 mc	85%	34 mc	$266.00	$2266.00	$7.[illegible]0	$67.00
3.	Sodium acetate	$CH_3C^*O_2Na$	2	40 mc	90%	36 mc	$115.00	$2115.00	$3.[illegible]	$59.00
4.	Sodium acetate	$C^*H_3CO_2Na$	6	40 mc	60%	24 mc	$315.00	$2315.00	$13.00	$97.00
5.	Ethyl acetate	$CH_3C^*O_2C_2H_5$	3	40 mc	85%	34 mc	$168.00	$2168.00	$5.00	$64.00
6.	Ethyl acetate	$C^*H_3CO_2C_2H_5$	7	40 mc	55%	22 mc	$365.00	$2365.00	$16.[illegible]	$108.[illegible]
7.	Methyl alcohol	$CH_3C^*H_2OH$	4	40 mc	80%	32 mc	$217.00	$2217.00	$7.00	$6[illegible].00
8.	Ethyl alcohol	$C^*H_3CH_2OH$	8	40 mc	50%	20 mc	$415.00	$2415.00	$21.[illegible]	$121.0
9.	Methyl iodide	$CH_3C^*H_2I$	5	40 mc	75%	30 mc	$26[illegible].00	22[illegible].00	[illegible].00	$76.00
10.	Ethyl iodide	$C^*H_3CH_2I$	9	40 mc	45%	18 mc	$463.00	$2465.00	$26.00	$137.0
11.	Methyl bromide	CH_3CH_2Br	5	40 mc	75%	30 mc	$266.00	$2266.00	$9.00	$76.00
12.	Methyl bromide	$C^*H_3CH_2Br$	9	40 mc	45%	18 mc	$465.00	$2465.00	$26.00	$137.0
13.	Chloroacetic acid	$ClCH_2C^*O_2H$	4	40 mc	70%	28 mc	$217.00	2217.00	$7.75	$79.00
14.	Chloroacetic acid	$ClC^*H_2CO_2H$	8	40 mc	50%	20 mc	$415.00	2415.00	$21.00	$121.0
15.	Glycine	$H_2NCH_2C^*O_2H$	6	40 mc	45%	18 mc	$315.00	$2315.00	$17.50	$129.0
16.	Glycine	$H_2NC^*H_2CO_2H$	10	40 mc	30%	12 mc	$512.00	2512.00	$42.00	$210.0
17.	Tetramethyl ammonium iodide	$(C^*H_3)_4NI$	5	40 mc	80%	32 mc	$291.00	$2291.00	$9.00	$71.50

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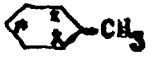
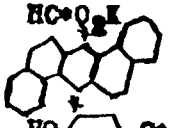
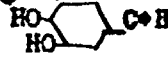
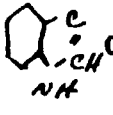
	Compound Name	Compound Formula	Man Days per batch	Millicuries used per batch	Batch yield %	Approx. cost per batch: Synthesis only	Approx. cost per batch: Total cost incl. C-14	Approx. cost per mc. Synth. only	Approx. cost per mc. Total cost incl. C-14
18.	Potassium pyruvate	$CH_3C^*OCO_2K$	5	40 mc	10-35%	9 mc $266.00	$2266.00	$29.50	$252.
19.	Potassium pyruvate	$C^*H_3COCO_2K$	9	40 mc	6-20%	5.2mc $463.00	$2463.00	$89.00	$474.
20.	Lactic acid	$CH_3C^*H_2OHCO_2H$	7	40 mc	5-17%	3.8 mc $365.00	$2365.00	$96.00	$622.
21.	Lactic acid	$C^*H_3CH_2OHCO_2H$	11	40 mc	3-10%	2.6 mc $561.00	$2561.00	$216.00	$985.
22.	Acetone	$CH_3C^*OCH_3$	4	40 mc	35%	14 mc $217.00	$2217.00	$15.50	$158.
23.	Acetone	$C^*H_3COC^*H_3$	8	40 mc	40%	16 mc $414.00	$2414.00	$26.00	$151.
24.	Toluene		10	40 mc	10%	4 mc $512.00	$2512.00	$128.00	$628.
25.	Propionic acid	$CH_3CH_2C^*O_2H$	1	40 mc	90%	36 mc $ 69.00	$2069.00	$ 2.00	$ 57.
26.	Propyl alcohol	$CH_3CH_2C^*H_2OH$	3	40 mc	80%	32 mc $168.00	$2168.00	$ 5.25	$ 68.
27.	Propylene	$CH_3CH=C^*H_2$	5	40 mc	60%	24 mc $266.00	$2266.00	$ 11.00	$ 95.
28.	Propyl bromide	$CH_3CH_2C^*H_2Br$	4	40 mc	70%	28 mc $217.00	$2217.00	$ 7.75	$ 79.
29.	Potassium formate	HC^*O_2K	2	40 mc	90%	36 mc $111.00	$2111.00	$ 3.00	$ 59.
30.	Dibenzanthracene		15	40 mc	10%	4 mc $758.00	$2758.00	$190.00	$690.
31.	Di hydroxyphenyl alanine		20	40 mc	10%	4 mc $1000.00	$3000.00	$250.00	$750.
32.	Tyrosine		15	40 mc	10%	4 mc $758.00	$2758.00	$190.00	$690.
33.	Tryptophan		20	40 mc	10%	4 mc $1000.00	$3000.00	$250.00	$750.

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COPY COPY

Copy of list sent to Dr. L. I. Lacher

C^{14} labeled compounds whose routine or commercial production would be desirable to organic and bio-chemical research.

1. Potassium cyanide, $K\overset{*}{C}N$

2. Barium carbide, $Ba\overset{*}{C}_2$

3. Methyl iodide, $\overset{*}{C}H_3I$

   a) Methyl alcohol, $\overset{*}{C}H_3OH$

4. Sodium acetate, $CH_3\overset{*}{C}O_2Na$

5. Sodium acetate, $\overset{*}{C}H_3CO_2Na$

6. Ethyl alcohol, $CH_3\overset{*}{C}H_2OH$

   a) Ethyl iodide or bromide, $CH_3\overset{*}{C}H_2X$

7. Ethyl alcohol, $CH_3CH_2\overset{*}{O}H$

   a) Ethyl iodide or bromide, $\overset{*}{C}H_3CH_2X$

8. Potassium formate, $H\overset{*}{C}O_2K$

9. Malonic ester (diethyl ester), $\overset{*}{C}H_2(CO_2Et)_2$

10. Toluene (1) CH_3

    a) Benzoic acid CO_2H

    b) Bromo benzene Br

11. Glycine $CH_2NH_2\overset{*}{C}O_2H$

12. Glycine $\overset{*}{C}H_2NH_2CO_2H$

13. Alanine $CH_3\overset{*}{C}H_2NH_2CO_2H$
    or $\overset{*}{C}H_3CH_2NH_2CO_2H$

14. Potassium pyruvate $CH_3\overset{*}{C}OCO_2H$
    or $\overset{*}{C}H_3COCO_2H$

15. Lactic acid $CH_3\overset{*}{C}H_2CHOCO_2H$
    or $\overset{*}{C}H_3CH_2CHOCO_2H$

1019476

16. Acetamido malonic ester (Acetylaminomalonic ester)

$$CH_3CO.NH\overset{*}{C}H(CO_2Et)_2$$

17. Chloroacetic acid $Cl\overset{*}{C}H_2CO_2H$

a) Cyano acetic ester $N \equiv C \cdot CH_2CO_2Et$

18. Glucose (photosynthetic - either uniformly or non-uniformly labeled)

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(1) The symbol ⟨*⟩ is used here to mean a benzene ring in which one or more carbon atoms are labeled at known positions and concentrations. All ring positions should not be labeled.

19. Urea. $H_2N\overset{*}{\overset{O}{C}}.NH_2$

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ENCLOSURE 6

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ENCLOSURE 6

RESUME OF MEETING ON FEBRUARY 9, 1948, OF TRACERLAB, INC.
PRODUCTION POTENTIAL OF C 14-LABELED COMPOUNDS

Attending:

Dr. F. C. Henriques, Jr., Technical Director, Tracerlab, Inc.

Dr. Melvin Fields, Chief, Organic Division, Tracerlab, Inc.

Dr. Paul C. Aebersold, Chief, Isotopes Division

Dr. N. H. Woodruff, Isotopes Division

Dr. S. A. Lough, Isotopes Division

A discussion of the Tracerlab production potential of C 14-labeled compounds was held in Oak Ridge on February 9. In this meeting, Dr. Henriques indicated that they could make the following labeled materials available:

1. Barium carbonate, 70% purity, within one week after receipt of purchase order.

2. Acetylene, one week after receipt of purchase order.

3. Amorphous carbon, within one week after receipt of purchase order.

4. Potassium cyanide, stocked by February 28, 1948

5. Methyl alcohol and methyl iodide, by May 1, 1948

6. Double labeled ethyl alcohol, ethyl iodide and acetaldehyde, by July 1, 1948.

7. Benzene, low specific activity, by May 1, 1948.

8. Carboxyl labeled and methyl labeled acetic acid, acetyl chloride and ethyl acetate, by September 1, 1948.

After review of the production facilities and other commitments of Tracerlab, it appears that this production schedule may be satisfactorily met.

1019479

ENCLOSURE 7

1019480

DRAFT

Enclosure 7

To: Manager, Chicago Directed Operations
Attention: A. P. Pollman, Manager, Berkeley Area
From: Carroll L. Wilson, General Manager

Subject: PRODUCTION OF ISOTOPE-LABELED COMPOUNDS BY BIO-ORGANIC DIVISION AT BERKELEY

Approval is hereby given within the limitations listed below for the program for "Synthesis and Distribution of C 14-Labeled Compounds" originally presented by A. P. Pollman to W. J. Williams, then Manager, Field Operations, July 24, 1947.

Authorization of budget allowance for the program shall not exceed $50,000 to the end of the fiscal year June 30, 1949. Charges made on the budget shall include charges for C 14, man-days, expendable materials and overhead on the same schedule as used in estimating costs, but not to include charges for research and development, capital equipment and rental of facilities.

The choice of quantity and quality of synthesized compounds should be flexible, although ten compounds are suggested by the Isotopes Division, ORDO, in enclosure "Cost Estimates of Suggested C 14-Labeled Compounds Based on Estimated Demands". The final decisions on such production for off-Commission distribution are to be made by the Isotopes Division, ORDO, after weighing advice from interested Commission and commercial sources.

Compounds produced will be handled in the customary manner of other radio-isotope material, shipments and charges being made by Clinton National Laboratory, Materials are to be shipped to the Isotopes Office at Clinton National Laboratory with adequate labeling concerning content and credit for production.

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Labels on all such compounds should give (1) structural formula showing labeled atoms, (2) net weight, (3) activity present, (4) water content and all other data which would be pertinent for further synthetic and biological work. In regard to the last item, Dr. Calvin should be free to exercise judgment on the extent of the included data.

The compounds will be sold according to the approved cost estimate schedule in use at Clinton National Laboratory (cost = man-days x 20 x 1.33 x 1.85 + cost of isotope content in labeled compound and in unrecoverable form + cost of rare or expensive chemical consumed). It will be necessary to supply data to the Isotopes Division on (1) man-hours consumed, (2) isotope content in labeled compound and in unrecoverable forms and (3) cost of rare or expensive chemical consumed. Note that charges will not be made for research and development phases of syntheses, capital equipment and rental facilities. Charges for individual compounds will be set by the Isotopes Division.

Requests for radioisotopes to be used in the production should be filed with the Isotopes Division on intra-Commission Request Form 558 in the usual manner.

The Isotopes Division may be contacted directly for recommendations of other syntheses to be performed.

Encl.:
Cost Estimates of....

CC: J. C. Franklin, Manager, ORDO.
J. C. Franklin, Manager, ORDO, Attn: Isotopes Division

1019482

COST ESTIMATES OF SUGGESTED C 14 LABELED COMPOUNDS ESTIMATED DEMANDS*

BERKELEY SYNTHESIS PROGRAM

	SYNTHESES BATCHES					
	No. of Batches	C 14 to be used	Batch Yield	Approximate Cost per mo per Batch	Estimated Requirements to 6/30/49	Total Cost
1. Methyl labeled glycine NH_2C*H_2COOH	1	40	12	210.00	12	$2510.00
2. Carboxyl labeled glycine $NH_2 \cdot CH_2 \cdot C*OOH$	1	40	18	129.00	18	2322.00
3. Carbonyl labeled pyruvate $CH_2 \cdot C*O \cdot COOK$	2	40	9	252.00	18	4530.00
4. Beta-labeled pyruvate $C*H_3 \cdot CO \cdot COOK$	1	40	5.2	474.00	5.2	2464.80
5. Carbonyl labeled acetone $CH_3 \cdot C*O \cdot CH_3$	1	40	14	158.00	14	2212.00
6. Methyl labeled acetone $C*H_3 \cdot CO \cdot C*H_3$	1	40	16	151.00	16	2416.00
7. 2,4,6-ring labeled toluene CH_3	2	40	4	628.00	8	5024.00
8. Carboxyl-labeled propeonic acid $CH_3 \cdot HCOH \cdot C*OOH$	½	20	18	59.00	18	1062.00
9. Propylene $CH_3 \cdot CH \cdot C*H_2$	½	20	12	104.00	12	1226.00
10. Potassium formate $CH*COOK$	½	20	18	62.00	18	1116.00
11. Syntheses to be determined at later date, up to						25117.20
						50000.00

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* Estimates based on latest data from memorandum from Russell H. Ball, Chief, Materials & Information Branch, Berkeley, to P. C. Aebersold, Chief, Isotopes Division, Oak Ridge Directed Operations.

1019484

ENCLOSURE 8

D R A F T

TO: Manager, Chicago Directed Operations
Manager, New York Directed Operations
Manager, Santa Fe Directed Operations

FROM: Carroll L. Wilson, General Manager

SUBJECT: PRODUCTION OF LIMITED QUANTITIES OF ISOTOPE - LABELED COMPOUNDS FOR ISOTOPE DISTRIBUTION PROGRAM

You are authorized to approve the production by Argonne National Laboratory (Brookhaven National Laboratory) (Los Alamos Scientific Laboratory) of quantities of radioactive labeled compounds in excess of the needs of your operations for distribution under the established Commission's isotope distribution program provided

a. The production of excess quantities can be made in the same batch with quantities required for Commission research or the syntheses have been previously performed and facilities for production are readily available.

b. The production is made upon the recommendations of the Isotopes Division, Oak Ridge Directed Operations, coordinator of the isotope distribution program.

Compounds produced will be handled in the customary manner of other radioisotope material, shipment and charges being made by Clinton National Laboratory. Materials are to be shipped to the Isotopes Office at Clinton National Laboratory with adequate labeling concerning content and credit for production.

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Labels on all such compounds should give the structural formula showing labeled atoms, (2) net weight, (3) activity present, and (4) water content and all other data which would be pertinent for further synthesis and biological work. In regard to the last item, the synthesizer should be free to exercise judgment on the extent of the included data.

The compounds will be sold according to the approved cost estimate schedule in use at Clinton National Laboratory (cost = man-days x 20 x 1.33 x 1.85 + cost of isotope content in labeled compound and in unrecoverable forms + cost of rare or expensive chemical consumed). It will be necessary to supply data on (1) man-hours consumed, (2) isotope content in labeled compounds and in unrecoverable forms, and (3) cost of rare or expensive chemical consumed. Note that charges will not be made for research and development phases of syntheses, capital equipment and rental facilities.

You are to notify the Isotopes Division of compounds labeled with distributable radioisotopes which are being produced at present or whose production is anticipated in the near future. Communications on this matter should be addressed directly to the Isotopes Division, Oak Ridge Directed Operations. Requests for radioisotopes to be used in the production should be filed with the Isotopes Division on intra-Commission Request Form 558 in the usual manner.

1019486

Dr. Holland

Contract AT-30-1-Gen-150

RADIOISOTOPE ADULTERATION

W. H. Ray

One gram of air irradiated by one roentgen will dissipate 83. ergs of the radiant energy.

8.3 ergs/day = 3.6×10^3 eMV/minute = 1.64×10^{-9} curies @ 1 eMV/disintegration.

To adulterate one curie so that the energy dissipated per gram of element = 8.3 ergs/day would require $\frac{E}{1.64 \times 10^{-9}}$ or 6.1×10^8 E grams of the adulterated element. (E = electron megavolts average energy per disintegration.)

Isotope	$\overline{E}$	elemental adulteration kg/millicurie to achieve 8.3 ergs/gm/day
${}_1H^3$	6.5×10^{-3}	3.97
${}_6C^{14}$	5.8×10^{-2}	35.4
${}_{11}Na^{24}$	4.61	2.82×10^3
${}_{15}P^{32}$	0.7	4.27×10^2
${}_{20}Ca^{45}$	8.3×10^{-2}	50.6
${}_{26}Fe^{59}$	1.32	8.05×10^2
${}_{38}Sr^{89}$	0.5	3.05×10^2
${}_{38}Sr^{90} + {}_{39}Y^{90}$	0.94	5.74×10^2
${}_{53}I^{131}$	0.645	3.94×10^2

1019487

Concentration Levels of S^{35} in Tracer
Experiments Under Field Conditions

The problem differs from that of Ca^{45} in three important ways, namely:

1. A half life of 87 days restricts an experiment to about three years.
2. Essential absence of sulfate in soil and of a fixation process reduces dilution of applied radioactive materials.
3. Leaching becomes an important process of loss from treated plots.

Plant material might be assumed to contain an average of 0.20% SO_3/gram dry matter. The sulfur should have a minimum activity of 2000 disintegrations/sec/gram of SO_3 corresponding to about 4 disintegrations/sec/gram of dry matter or an activity of approximately 10^{-7} millicuries/gram of dry matter at the time of measurement.

If the sulfur is to be followed for ten half lives, the maximum activity of the foliage the first year of an experiment would be about 1×10^{-4} millicuries/gram of dry matter which is approximately the same as for calcium although the specific activity of the sulfur is higher. An average yield of 1000 lbs. dry matter/acre might be assumed which thus should contain 45 millicuries of sulfur at this rate.

The initial activity of sulfur in an experiment to be followed for three years should be of the order of 100 millicuries/acre or 4 millicuries in an experiment as was the case for Ca^{45}.

Activities given in the above paragraph could be reduced to 1/16 in case an experiment of two seasons' duration was desired. This would probably be the best type of experiment to undertake at first.

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Arrangements would have to be made to prevent loss of leachate from a plot. This could take the form of exchange with ordinary gypsum at the plot boundaries, placed for instance in a trench. Leaching could be used for decontamination of a plot at the end of an experiment.

1019489

Concentration Levels of Ca^{45} in Tracer Experiments Under Field Conditions

A basic assumption is made that experimental plant material after drying should give 20 disintegrations/sec/gram. Thus if these can be detected with 10 percent effectiveness, 2 counts/sec/gram can be obtained. This corresponds to an activity of 5×10^{-7} millicuries/gram at the time of measurement.

Let us assume that the material is to be followed for three years, i.e., six half-lives. The initial level of the basic quantity then must be $5 \times 10^{-7} \times 2^{6} = 3.2 \times 10^{-5}$ millicuries/gram. If the plant material contains 3 percent Ca, the activity must be 1.0×10^{-3} millicuries/gram Ca.

An average eastern soil might contain 600 lbs. Ca/acre in the plow depth. If equilibration of applied calcium is assumed with one-third of this calcium, then the 1.1×10^{5} grams Ca/acre involved must have an activity of 1.0×10^{-3} millicuries/gram Ca or a total initial activity of 110 millicuries. The activity below one square foot on the surface would be 2.5 microcuries.

An experiment involving six types of treatments, replicated six times, on plots of 50 square feet would require 0.04 acre to be treated. This would correspond to use of 4 millicuries Ca^{45} in an experiment.

The maximum activity in foliage might be taken as 1.0×10^{-4} millicuries/gram of dry matter. Accidental consumption of foliage by farm animals could thus be hazardous, particularly for the first year. The second year level due to decay and further equilibration in the soil would not exceed 1.0×10^{-5} millicuries/gram of dry matter.

1019490

Information supplied to the Geriatrics Division for Isotope Exhibit at the A.M.A. in June -

RADIO-PHOSPHORUS (P-32)

DIAGNOSTIC USES

DISEASES:-- 1. Cancer of the breast.

2. Other superficially located cancers.

METHOD:-- Tracer dose IV, followed by comparative Geiger-Counter readings over normal and diseased tissue.

DOSE:-- 300 to 500 microcuries IV.

INTERPRETATION:-- Radiation levels over surfaces of benign tumors reveal no significant difference from readings taken over normal breast tissue. Malignant breast tumors concentrate radio-phosphorus with a marked increase in the level of radiation over the tumor surface.

THERAPEUTIC USES

DISEASES:-- 1. Polycythemia vera.

2. Chronic myelogenous leukemia.

3. Chronic lymphatic leukemia.

4. Of questionable benefit in other miscellaneous blodd dyscrasias, lymphomas and bone tumors.

METHOD:-- Divided therapeutic dose administered IV or orally, followed by repeated blood counts, sternal marrow studies and careful clinical observation. Excretion studies are desirable.

1019491

DOSE:-- Always requires individualization, based on response - but average total doses for IV administration are:

1. Polycythemia vera 4 - 14 mc
2. Chronic myelogenous leukemia 4- 12 mc
3. Chronic lymphatic leukemia 2 - 12 mc

ABSORPTION:-- 75% (approximately) by oral route, 100% by IV route.

EXCRETION:-- When given orally, 15 - 50% excreted in urine and stools in 4 - 6 days.

When given IV, 5 - 25% excreted in urine and stools in 4 - 6 days.

TOXICITY:-- Limited to hematopoeitic system.

1. Leukopenia.
2. Thrombocytopenia.
3. Aplastic anemia.

CLINICAL RESULTS:--

1. Most effective B/ for polycythemia.
2. Equals X-radiation in chronic myelogenous leukemia.
3. Equals X-radiation in chronic lymphatic leukemia in most cases, but X-ray more effective in rapidly reducing size of spleen and lymph nodes.

ADVANTAGES:--

1. Practically eliminates radiation sickness.
2. No toxic manifestations (G.I., skin, liver).
3. Less burdensome to the patient.

1019492

RADIO-IODINE (I-131)

DIAGNOSTIC USES

DISEASES:-- 1. Hyperthyroidism.

2. Thyroid Carcinoma.

METHOD:-- Tracer dose administered orally, followed by radiation survey of the thyroid region and general body survey for metastatic lesions.

DOSE:-- 100 microcuries.

INTERPRETATION:-- Significant concentration of radio-iodine appears in hyperactive thyroid tissue. Approximately 10% of thyroid cancers will selectively absorb radio-iodine. In these cases, location of metastatic lesions is often possible.

THERAPEUTIC USES

DISEASES:-- 1. Hyperthyroidism.

2. Thyroid carcinoma.

METHOD:-- Administered as sodium-iodide in water given orally, followed by radiation measurements taken over the thyroid and other active areas, repeated blood counts and careful clinical observation. Excretion studies are desirable.

DOSE:-- Always requires individualization, but average total doses vary from 10 millicuries to 50 millicuries.

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ABSORPTION:-- Almost 100% from G.I. tract.

EXCRETION:-- Almost exclusively in urine.

TOXICITY:--

1. Thyroid Crisis.
2. Hypothyroidism.
3. Leukopenia.

CLINICAL RESULTS:--

1. Effective B/ for hyperthyroidism.
2. Effective palliation for susceptible thyroid malignancies and bone metastases.

ADVANTAGES:--

1. Larger radiation doses can be delivered directly to thyroid tissue than by any other mode of therapy.
2. Radiation therapy can be delivered to distant metastatic lesions.

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