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TO : Herman M. Roth, Director, Research and
Medicine Division

DATE: May 19, 1955

FROM : C. S. Shoup, Chief, Biology Branch, Research
and Medicine Division

712303

SUBJECT: ADVISORY COMMITTEE FOR BIOLOGY AND MEDICINE - OAK RIDGE MEETING, MAY 5-7,
1955

SYMBOL: ORB:CSS

The spring 1955 meeting of the Advisory Committee for Biology and Medicine represented the first opportunity for this group to formally review biomedical work in Oak Ridge in five years. All members of the Committee were present including representatives from the Washington Office as follows:

Advisory Committee on Biology and Medicine

- Dr. G. Failla, Columbia University Medical School, Columbia University, N.Y.
- Dr. Edward A. Doisy, St. Louis University School of Medicine, St. Louis, Mo.
- Dr. Curt Stern, University of Calif. Berkeley, Calif.
- Dr. Shields Warren, New England Deaconess Hospital, Boston, Mass.
- Dr. Charles H. Burnett, University of North Carolina, Chapel Hill, N. C.
- Dr. S. T. Cantril, Tumor Institute of Swedish Hospital, Seattle, Wash.

AEC Washington

- John C. Bugher, Director, Division of Biology and Medicine
- Charles L. Dunham, Deputy Director, Division of Biology and Medicine
- Paul B. Pearson, Chief, Biology Branch, Division of Biology and Medicine
- H. A. Stanwood, Chief, Program Analysis Branch, Division of Biology and Medicine
- N. S. Hall, Biologist, Division of Biology and Medicine

Dr. E. C. Stakman, University of Minn., Minneapolis, Minn., Consultant

HIGHLIGHTS OF THE MEETING:

THURSDAY, MAY 5, 1955, 1:30 P.M.

The Committee members (with the exception of Dr. Stern who arrived in the evening) and AEC representatives met at the UT-AEC laboratory building. Mr. Sapirie presented a description of the production, construction, engineering, and research and development programs which are the responsibilities of Oak Ridge Operations. At the conclusion of the Manager's review and welcoming remarks, the meeting was opened for UT-AEC to present their program.

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April, May, June

THURSDAY, MAY 5. 2:30 P.M. UNIVERSITY OF TENNESSEE-AEC PROGRAM

Dean of the College of Agriculture, J. H. McLeod, indicated (a) that UT-AEC feels its interests are closely allied with programs of both the Commission and the University; (b) they seek and appreciate guidance from the Washington Office; (c) believe in professional honesty and feel this will be exemplified by the efforts of the new Acting Laboratory Director and will be seen in their forthcoming progress reports. He further stated that the University desires that the University of Tennessee-AEC Program develop along lines originally designated. Mr. John A. Ewing, Project Leader, stated further that the functions of the UT-AEC Program are to accomplish research objectives within Commission and University interests, to use the external radiation field most effectively and to encourage cooperative efforts with the various departments of the University, with other institutions and experiment stations, and to provide objectives for training of graduate students. He informally presented the UT-AEC organization chart on the blackboard and we noted the omission of an affiliation with ORO in the diagram shown. It was stated efforts are underway to reduce farm costs to the Commission, that whereas net FY 1954 farm costs were near \$60,000, the FY 1956 net farm costs would be \$28,500. It was indicated that UT is supplying support to the program in the amount of about \$40,000, leaving us at a loss to fully account for this estimate since personnel support supplied to the program by the University is indicated by them to be \$24,000. We do not know whether they regard the additional \$15,500 as representing the value of University-owned cattle supplied to the UT-AEC herd or their estimate of absorbed University overhead costs. The Acting Laboratory Director, Dr. Homer Patrick, stated the current budget forms 189 represent a cooperative effort of the UT-AEC staff approved by the University in Knoxville and that the plan of research follows proposals made at the time of our review meeting in Washington on January 27, 1955. The program presentation followed.

1. Homer Patrick - Fission Product Metabolism. Project 2.

This work has included studies on the deposition of Strontium-89 in bone, and Ca-Sr exchange, particularly in relation to the protein intake of experimental animals. Studies of La¹⁴⁰ have been started on laboratory animals and chicks to examine the deposition of several chemical forms of La as they become bound in the liver, spleen and bone.

2. S. L. Hansard - Calcium-Phosphorus Metabolism. Projects 3-4.

Work in progress on the determination of the endogenous calcium metabolism of the steer with Ca⁴⁵ indicates the proportion of Ca absorbed and retained in the bone and the proportional amounts believed unabsorbed in the G.I. tract or absorbed and excreted. Studies are underway also on the effects of age and dietary protein

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on the calcium and phosphorus absorption in rats. It was stated that some studies were being made of Vitamin D but this appears to have little influence if the available calcium and phosphorus is at the normal intake levels. It is planned that phosphorus availability studies will be made on sheep and swine and will include isotopic fluorine effects.

3. R. L. Murphree - Reproduction and Fertility. Project 5.

Attempts are made to evaluate the effects of total body irradiation from 100 to 400 r. on reproductive functions of the male. A search will be made for the minimum level of radiation exposure that produces changes in the sperm and sperm counts in cattle. It is thought effects may be found at some dose level lower than that producing visible effects on sperm morphology.

4. F. W. Lengeman - Iodine Elimination in Milk. Project 7.

Work on milk secretion using mainly I^{131} was described. It is believed that 4 to 7% of the iodine dose goes to the milk no matter how the dose is administered. The iodine appears to be free iodine and does not seem to be bound. About 1/10 of 1% of I^{131} present in the milk will remain in butter fat. It was interesting that goats do not eliminate the I^{131} dose exponentially as do cattle and sheep.

5. Lt. Col. B. F. Trum - External Radiation Studies. Project 10.

Some aspects of the large animal external radiation studies were covered briefly, and it was pointed out that the need for the project has outlasted the original objectives. Using burros, lethal dose studies have been accomplished at different energies of gamma irradiation and these have emphasized the energy dependency in radiation effects. Recent studies on swine using zirconium-niobium sources and a dose rate of 2 r/hr indicated resistance to radiation effects since to date the swine have shown no radiation syndrome following a total of 600 r.

The College of Agriculture people were called on to describe some of the work the University wants to do on beef cattle breeding in the control herd at UT-AEC. They plan on line evaluation, feeding tests, and detection of potential dwarfism from X-ray photos of vertebrae. Stilbestrol feeding and expanded use of the exposure field are included in their projects.

Dr. George K. Schweitzer, who serves as part-time radiochemist, briefly discussed radiological physics work and indicated UT-AEC regards this phase as a service duty to the program. We believe this attitude is a serious

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error in that the radiological physics and radiochemistry portion of the program is basic to the effectiveness and quality of accomplishments in the laboratory. However, a new radiochemist will join UT-AEC this month and it is hoped that this phase of the work will be improved.

Dr. Paul B. Pearson referred to the use of the exposure field by the Southern Agricultural Stations. He and Dr. Singleton of Brookhaven attended the recent meeting of the southern experiment station directors in New Orleans where Singleton spoke on agricultural uses of external radiation. Pearson expects the UT-AEC field and possibly the Oak Ridge graphite reactor can be used for plant and seed exposures at no cost to the stations. However, this would be under a plan providing for the several stations doing their own planting and follow-up studies under their own individual state support.

At the conclusion of the program presentation, Dean J. H. McLeod requested a closed session with the Committee and Commission representatives. He asked for a criticism of the program. This request was met by expressions that the people presenting the program appear enthusiastic, that there is general approval for their entering into some amount of plant work with the exposure field, and that full advantage might be taken for cooperation with other southern institutions. Dr. Warren stated that UT-AEC represents the only large-animal facility we have, and that the radiation field is unique and the advantages of the field should not be overlooked. One criticism was voiced regarding the size of the UT-AEC technical advisory committee in that too large a committee with too much emphasis might tend to stifle free investigation.

The Dean noted that Dr. Patrick, as acting laboratory director, had been in charge for eight months, and asked the opinion of the Committee regarding his designation as Director. It was called to the Dean's attention that nearly all those present had but short acquaintance with Dr. Patrick and the current developments in the program, and no action would be appropriate on this question at this time. At this stage in the proceedings it was pointed out that a decision regarding a permanent director should be based on experience of the man and the local and regional leadership he could demonstrate and that a director for the UT-AEC Program should be of such stature that he could meet other leading scientists and ORO laboratory directors on an equal basis of leadership and cooperation. At about this point the meeting adjourned in order that the visitors could have time to visit the exposure field.

FRIDAY, MAY 6, ORINS MEDICAL DIVISION, 9:00 A.M.

The Oak Ridge Institute of Nuclear Studies, Medical Division, covered the following projects in their program on the morning of May 6:

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1. Gould A. Andrews - Clinical Colloid Studies. Reported on recent developments in a long-range program on clinical colloids. Chronic phosphate and Au^{198} with two less familiar ones, Y^{90-91} and Lu^{177} , given as chlorides along with stable carrier but which behave as colloids in the body.
2. G. C. Kyker, Rare Earth Studies. Using animals, has investigated the metabolism and distribution of many rare earths. The metabolism and distribution patterns of carrier free rare earths have also been followed. Carriers from other members of the rare earth family have been added and it has been found that the metabolism and distribution patterns do not change except in minor detail, but advantages are from the different radiations.
3. Ralph Kniseley, Thyroid Pathology. Excretion patterns following iodine administration, the blood levels of iodine-131, and the histological picture in thyroid recovery, were described.
4. C. L. Comar, Low Level Counting. A brief description was given of present work on Iodine-131 determinations in cattle and human thyroids, and on milk and bone, the measurements being at a sensitivity of 5×10^{-5} uc. Milk values are less than 5×10^{-6} uc/ml.
5. Marshall Brucer, Thyroid Uptake Calibration Program. Studies were presented of the mock-iodine spectrum, the plans for evaluation of calibrations, and the proposed presentation for Geneva.
6. Vincent Collins, Teletherapy Evaluation Board. Dr. Collins of the Baylor University School of Medicine, presented the main aspects of the TEB program. A question was raised as to the TEB evaluation of survival, and it was stated consideration of this information would be a part of lung carcinoma studies and some of the bone work.

At the conclusion of the ORINS Medical Division review, the visitors were taken to the Oak Ridge National Laboratory for a luncheon provided by Carbide at the X-10 Cafeteria. The afternoon session covered Program 6000 research in progress at ORNL.

FRIDAY AFTERNOON, MAY 6 - BUILDING 4500, OAK RIDGE NATIONAL LABORATORY

1. K. Z. Morgan, Director, Health Physics Division. The main areas of research in Health Physics were presented, together with a resume' of efforts toward securing additional data relating to calculations for the maximal permissible concentration for various radioelements, a main problem being interpretation of single dose data in terms of

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chronic exposure. ORNL continues to seek further information on the normal base-line of trace elements in the human for boron, cesium, manganese, iron, nickel, copper and strontium. "Operation Boston", the cooperative study with the Massachusetts General Hospital, continues to supply data bearing on the Y-12 model for uranium in blood, bone, kidney and urine. Dr. Failla remarked upon the unique nature of the work in progress, giving due credit to ORNL for its initiation.

2. Stanley Auerbach, Ecological Consideration of Soil Organisms. Attempts are to be made on identification of radiation effects on organisms of the forest floor. Currently studies are being made on the so-called "tree-hole" invertebrate population as representative of a habitat niche, at dose range of 15,000-1,000,000 r. and it is found the range of at least 50,000 r. is required to cause depletion of key organisms.
3. Conrad Straub (USPHS) - Soil Absorption of Specific Isotopes. Saturation and migration capacities of various soils are under study. Evaluation is being made of clays and other materials for pit liners, and studies on pit models include entrainment tests and consideration of possibilities for air-borne escape of activity.
4. S. H. Hurst, Dosimetry. Research in dosimetry includes both experimental and theoretical physics consideration of stopping power and scattering. The fast neutron dosimeter was described and the S-U-Np-Pu threshold detectors. It was noted that Hurst's work has comprised an important contribution to the development and application of new methods of dosimetry, and from this has come more accurate measurements that have improved interpretation of recent data, especially the Greenhouse information from the lead hemispheres.

In concluding the Health Physics phase of the program, Birkoff and Snyder reported briefly on work in progress regarding ionization and stopping power in various media, and securing of depth dose curves for media containing tissue elements. Dr. Elda Anderson reported on the Radiological Physics Fellowships, noting that of the 101 who have completed the program, 62% are in H.P. work, and 20% are in graduate schools or are extension fellows. Further demands for people with this training are anticipated.
5. R. F. Kimball. Cytogenetics. Reporting on the general cytogenetics phase of work at the Biology Division, ORNL, Kimball covered briefly the main outlines of studies on Paramecium, Tradescantia and Vicia, maize, Neurospora, and the insect work.

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6. Waldo E. Cohn. Biochemistry. The sequence of work on nucleic acid and nucleotide identification in heterogeneity and function, and relationship with coenzymes and DNA, RNA, was described. D. G. Doherty's enzyme-substrate complex studies and synthesis of protective compounds was described briefly, together with Totter's work on labelled precursors such as glycine, leucine and formate, and Arnold's studies of plant bioluminescence. Dr. Doisy, who had a two-day visit previous to the current meeting, remarked that he so enjoyed talking with ORNL biochemists that he felt he could sit down and talk with them for another full day with pleasure because of the quality of the work being accomplished.
7. Stanley F. Carson. Microbial Metabolism and Plant Biochemistry. Carson briefly covered the work of his own group dealing with incorporation of carbon compounds and their intermediates in microbial metabolism, and also the work under Tolbert's program in plant biochemistry, emphasizing the seven-carbon sugar studies, metabolism of glycolic acid and the side reactions that may give rise to glycine and serine, the energy-transfer systems under study, especially the identification and isolation of the flavoprotein peroxidases.
8. C. W. Sheppard. General Physiology and Biophysics. Membrane permeability, ion-exchange across the red cell, isolation of cell components and the separation of nuclei, mitochondria and microsomes by Anderson, were described, particularly with bearing on the recovery program, and work of the groups interested in cytogenetics.
9. Arthur C. Upton. Radiation Injury. The problems of hemorrhage, escape of haemoglobin into the lymph, and role of platelets and platelet recovery after irradiation were covered. The rates of platelet formation, megakaryocyte formation, effects of platelets on vascular permeability, are under study. Present cataract studies seem to show RBE for thermal neutrons to be about 3.0. RBE for fast neutrons is about this value also for cataract production at the 86" cyclotron, but fast neutrons from point sources such as Po-Be or the Cockcroft-Walton seem to have RBE near 9.0. Leukemia studies were mentioned, pituitary tumor incidence, and the nephrosclerotic lesions due to radiation that are under further study.
10. W. L. Russell. Mammalian Genetics and Development. The time schedule after whole-body or half-body irradiation of the male was described with reference to the sterile period, mating, mutations in the seven specific loci, for the doses, 300, 600,

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and 1000 r of x-rays. Possibly the non-linearity at 1000 r may be due to the heterogeneity of the spermatogonia and killing of sensitives with survival of the more resistant cell groups. If dominant lethals adversely effect a heterogeneous population, then lower dose studies seem warranted on populations with respect to litter size, productivity of first-generation females, general first-generation damage, with regard to both fractionated and chronic doses. Oakberg's studies of spermatogonia show the Type B cells are extremely sensitive, with an LD/50 of about 20 r and detectable X-ray effects as low as 5 r.

11. Alexander Hollaender. Protection and Recovery program. The earlier bacterial studies showed glutamate uracil and guanine were almost as helpful as complete media in promoting recovery after irradiation. Recovery could be augmented by cystamine, and in proper treatment the obtaining of more and more surviving cells could be shown to be accompanied by a lesser mutation rate as well. The studies on bacteria, including modification of the media and use of such materials as b-mercaptoethylamine, led directly to the new recovery SH-compounds.
12. Charles Congdon. Mammalian Protection and Recovery Program. The new material, S-beta-aminoethylisothiuronium bromide-HBr, is found not to be very toxic, although further tests are under way to determine if a small neurotoxicity is shown. Efforts under the new program will be centered on how to keep animals alive after lethal doses of radiation. The work will include follow-up regarding all aspects of tumor production cataracts, hair changes, etc., as well as simply recovery. A problem will be the cell-recovery situation in bone marrow and questions of immunology and cell compatability associated with infusion.
13. Alexander Hollaender. Education. University contacts and general educational aid from ORNL Biology Division were described under the following headings: (a) Traveling lectureships, (b) Research participation, (c) Teaching at the University of Virginia and at Duke, (d) Oak Ridge graduate fellowships, (e) the plan for temporary employees as research associates in the Division, and (f) loan of employees for teaching aid in establishment of radiobiology courses at southern college and universities. In the discussion afterwards it was remarked that ORNL has shown a considerable interest along educational lines, probably more than the other laboratories, and in general this meets with approval.

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In the Committee's discussion following presentation of the formal program, it appeared that probably two general considerations were brought out regarding more mouse genetics work: (a) question of whether it would be suitable to go to quite low total dose studies, perhaps 75 r now, or whether to do the 150 r work first, and (b) whether all this mouse work should be done at ORNL or if some phases might be farmed out elsewhere, perhaps even some dose ranges being done at Harwell. It was evident that many more animals and great difficulty would be encountered with the very low doses. For example, the English have now about 10,000 matings in a 40 r group of animals, and there are more mutations in the controls than in the experimentals. Some hesitancy was shown regarding a marked growth of the program at one location because of past experience with epidemics, fire, or other disasters that might wipe out a total experiment. It was remarked that perhaps we are a little too excited regarding the effects of low doses, but Russell stated he is worried a bit over the marked sensitivity of spermatogonia and thinks a 150 r experiment is needed. Using 150 r, he can check on the linearity of dose vs. mutation rate in about two years.

The meeting adjourned about 5:30 P.M. We heard a number of favorable expressions from the Committee members regarding the Laboratory's presentation of its program.

SATURDAY MORNING, MAY 7, 1955. MEETING OF THE ADVISORY COMMITTEE.

The Committee met on Saturday morning in the ORINS Administration Building conference room. A major portion of the Committee's program included review of the ABCC and coverage of some of the Division of Biology and Medicine's activities and interests in Nevada.

Portions of the discussion in which we had most interest, were of course the comments on work in Oak Ridge, which can be summarized as follows:

UT-AEC: The consensus seemed to be that the UT-AEC Program has done good work in the past, and it is hoped this can be continued along the same lines. The newly-constituted group at UT-AEC seems enthusiastic and it is urged full exploitation can be made of the exposure field, especially with respect to large animal research. In order to aid the program, it was recommended that an ad hoc committee be appointed to appraise the external and internal studies planned, to make recommendations to avoid overlap with other programs. In a brief discussion of who might serve on such a committee, no definite word was forthcoming save that Dr. Bond of Brookhaven might be considered as one appointee.

ORINS: Commenting on the ORINS Medical Division, it was stated that in general the ORINS Program is serving as a training and development ground and a coordinating program in its field. The iodine studies, and the low-level

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counting studies now under way are needed and should be so channeled that they coordinate with what is being done elsewhere by Van Middlesworth, Hardin Jones, and others. Less emphasis seems necessary on strontium since this element is being extensively worked on in the low-level counting field by at least three other laboratories, and Brucer has been so advised. In terms of program balance, it is urged that ORINS not undertake programs that detract from its main purpose, namely continuation and emphasis on cancer research and therapy. Further exploration studies of the internal emitters are urged.

ORNL: The biomedical programs of the Oak Ridge National Laboratory are regarded as outstanding. It was noted in the area of chemical protection, that Argonne and a pharmaceutical house had initiated some work of this kind but that it had moved slowly. Now, however, ORNL strikes out in this field, and it is appreciated by the Division of Biology and Medicine. It is hoped that the additional genetics work, if done, will include additions of major personnel to safeguard survival of the program. In general, it appeared that the Committee felt inclined toward the 75 r study being done first, rather than the 150 r. and that since so few people are available elsewhere to conduct such a program, it may fall in the province of Russell to continue this phase here. Although no real settlement was made regarding preference toward the 150 r experiment or the 75 r experiment, the Committee placed itself on record as recommending the mouse genetics expansion, expressing favor for the program and emphasizing it as of great importance.

With regard to the mammalian protection and recovery program at ORNL, the committee felt here again that a move of major importance is under way, and expressed themselves as desirous of supporting this program on protection and recovery agents with view of the work being expanded as planned.

The general session entered into recess about 3:30 P.M., following which the Committee reconvened for Executive Session. Prior to the recess, however, we gave a brief review of the present status of Mound Laboratory personnel placement and the scheduled Mound Laboratory reports now being prepared for scientific literature.

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