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7-04-113

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OAK RIDGE, TENN.

TO Dr. C. E. Larson
LOCATION Bldg. 9704-1

DATE June 14, 1958 **UNCLASSIFIED**

ANSWERING LETTER DATE

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SUBJECT Proposed Toxicological Studies

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Introduction

One of the principal functions of any Health Physics group is that of collecting information relative to degrees of personnel exposure and making it available to the physician for use in providing the proper clinical safeguards. Up to the present time this information has consisted largely of monitored data such as air concentration measurements, surface measurements, clothing counts, hand counts, etc., but lacking in concrete evidence as to dosage, or the amount of active material deposited in body tissues.

It has been known for some time, in the case of uranium and other radioelements, that certain tests of urine and feces can be used to determine whether or not a "tolerance" amount of the element has accumulated in the body. Hundreds of these measurements are made daily within the Atomic Energy Commission project in view of their importance as a means of controlling potentially hazardous exposures, but little has been done or can be done to interpret these findings in terms of a long range effect on the genus Homo. It has been felt that some effort to correlate excretion findings with exposure monitoring, in an area where exposure levels and materials are relatively constant, might prove worthwhile in helping to establish the effectiveness of presently accepted tolerance levels in air, clothing and body contamination.

Two opportunities for detailed toxicological study of uranium metal and its compounds present themselves at this plant. They are: (1) chemical processing and handling of product material appurtenant to the electromagnetic separation of U^{234} , and (2) continuous and measurable exposure of machinists and operators in the Sunflower and Daffodil programs for the next few years.

The two problems should be studied cooperatively since they are related. Because of the greater activity present in enriched U^{234} , the first study will offer opportunities for developing micro quantitative analytical data directly applicable to the second. Moreover, the results of the second study should establish clearly that measurable physiological injury either does, or does not occur as a result of long term exposure.

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The U²³⁴ Study

Recent attempts at this site to obtain medium level concentrations of U²³⁴ by electromagnetic separation have been quite successful. In an effort to determine the extent of the hazards involved in the handling of this highly active material, it was definitely established that some uranium is absorbed in spite of precautions taken to prevent it. That is, complete protection is not afforded by elaborate ventilation facilities and respiratory protective devices.

Now a further effort to obtain higher concentrations is being planned. And it is this project to which the proposed study has reference. Only one or two subjects are involved in the study and, in view of the potential benefits to personnel in this plant and others which may result, it is felt that full advantage should be taken of this opportunity. The plan is outlined as follows:

1. Determining Kidney Function. Inasmuch as there will be but one or two individuals involved, every effort must be made to validate the test results. Since uranium has its primary toxic effect on the kidney tubules, it becomes important then to determine the presence or absence of abnormal physiological conditions in the kidneys of those who are to participate in the test. This imposes the need for performing certain kidney function tests (inulin clearance, urea clearance and others) on these subjects prior to the period of the test. Inulin clearance, being a medical research procedure, requires hospitalization and will probably have to be performed at some hospital associated with a School of Medicine.
2. Determining Uranium Intake. To determine the amount of uranium taken in by inhalation a "dummy" respirator, backed by a cascade impactor and a suitable trap to capture all material which passes the respirator filter, will be run at breathing level along side the subject while work is in progress. Two or three runs followed by careful analysis of the filter, impactor slides and trap should establish the relationship between the amount of uranium on the respirator filter and the amount which passes through. The uranium intake can then be determined by application of the proper factor to the amount of uranium on the respirator filter. Following this, all of the respirator filters will be analyzed daily to determine the daily uranium intake. Such precautions as are thought to be necessary will be taken to prevent possibilities of intake by other modes of entry.

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3. Determining Uranium Absorption. Assuming that all uranium intake is by inhalation and that that which is not absorbed (owing to particle size, density, solubility, etc.) is caused to enter the gastro-intestinal tract by ciliary action in the bronchioles, then complete stool, sputum, and nasal excretion analyses for uranium content daily should reveal the following:

$$(\text{Uranium Intake}) - (\text{Uranium in Stool, Sputum and Nasal Excretion}) = \underline{\text{Uranium Absorbed}}$$

4. Determining Uranium Deposition. Knowing within certain limits the amount of uranium absorbed and the concentration of uranium in urine to a fraction of a part per billion, then 24 hour urine samples analysed for uranium content daily should give:

$$(\text{Uranium Absorbed}) - (\text{Uranium in Urine}) = \underline{\text{Uranium Stored}}$$

All of these data have been determined on small animals for values of air concentrations in the range of several milligrams per cubic meter. The lower limits of sensitivity of chemical methods of analysis have precluded any attempts at lower level exposures. The high alpha activity of U^{234} makes possible the practical use of counting methods which thus may reveal the missing physiological data for exposures of the order of micrograms per cubic meter.

Long Range Study of Sunflower & Daffodil Workers

For the past year a rather intensive effort has been put forth by the Health Physics Department and the Chemical Division to identify the hazardous conditions inherent in the two processes and to correct them. Vast improvements have resulted from this effort to the extent that present thought questions the wisdom of proceeding further in this direction. About all that can be done has been done, short of installing elaborate and probably unnecessary local ventilation facilities.

Effective as these improvements appear to be, however, present measurements continue to indicate the possibility of minimal exposure via contaminated air, hands, clothing, et cetera. This fact has led to the thought that additional protection is needed by these employees, ever and above that which is presently afforded, viz., exposure monitoring of the workers and their surroundings together with annual physical examinations. Moreover,

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concomitant with an improved program of health protection, there is an opportunity to secure the type of medical information required by the physician to interpret, in terms of human experience, the toxicological findings of small animal research.

The following study of the effects of minimal exposures to the machinists and operators in the Sunflower and Daffodil programs is proposed:

1. General. All monitoring techniques and devices presently used by the Health Physics Department will be investigated, revised and improved in accordance with the experience and advice of several research workers at the University of Rochester who are expert in problems relating to uranium exposure. Much of this has already been accomplished.

All sampling techniques and frequencies will be studied with a view to collecting data that is statistically valid. Some assistance from the Material Control Department has been obtained in the past and indications point to the possibility of additional aid in this regard.

In addition to setting up an adequate system of recording scientific data, a diary method of recording attendant incidents and events will be inaugurated.

Contacts with the University of Rochester School of Medicine and Dentistry are anticipated for the purpose of obtaining the necessary information, suggested revisions, shifts in emphasis, etc., that are needed to make this study worthwhile.

2. Body Tissue Analyses. Dr. Harold C. Hedge, head of the Division of Pharmacology and Toxicology at the University of Rochester, suggested the need for securing samples of soft and hard tissues for purposes of analysis whenever possible. This will involve making arrangements with various hospitals and dental clinics in the vicinity so that when these employees have an appendix removed, a tooth extracted, or some similar medical service performed, these tissue samples will be available for analysis. Furthermore arrangements should be made to secure samples of hard tissue, i.e., rib, sternum, vertebra and femur, on post mortem examinations when such an opportunity is presented.

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3. Sunflower Routine.

- a. Routine 24 hour samples of urine will be collected once per week (Thursday or Friday) and analyzed for uranium content by the Fluorimetric method.
- b. Routine air sampling will be carried out so as to give as accurate an index of inhalation exposure as is possible. This will include determinations of particle size and composition of the airborne contaminant.
- c. Routine hand counts and periodic clothing and surface measurements will be taken with a view to controlling rather than monitoring exposure by ingestion, skin absorption or skin punctures.
- d. The Medical Director will arrange for an Industrial Health Recheck of each employee once every three (3) months. In addition to the clinical procedures prescribed by him the following additional tests will be made:
 - (1) Urinary Catalase.
 - (2) Urinary Protein.
 - (3) Urinary Amino Acid Nitrogen/Creatinine Ratio.
 - (4) Urinary Uranium.

4. Daffodil Routine.

- a. Routine 24 hour urine samples will be collected once per week (Thursday or Friday) and analyzed for uranium content by the alpha count method.
- b. Routine air sampling will be carried out so as to give as accurate an index of exposure by inhalation as is possible.
- c. Routine hand counts and periodic clothing and surface measurements will be taken with a view to controlling exposure by ingestion and skin absorption.
- d. The Medical Director will make arrangements for an Industrial Health Recheck of each employee once every three (3) months. Only those clinical observations prescribed by him will be required for the subjects in this group.

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Conclusion

The problem of increased health protection to the machinists and operators in the Sunflower and Daffodil programs, and the opportunity for a comprehensive study of the long range effects which may or may not occur as a result of minimal exposures to uranium, has been under consideration for some time.

The proposed studies which have been outlined here were discussed with representatives of the University of Rochester Atomic Energy Project by Dr. A. G. Kammer and the author during a recent visit to that site. All who were present at this conference expressed genuine interest in the proposal because of the quick and close opportunity presented here to apply the fruits of research labor to human experience in an industrial environment. Their valuable assistance was proffered and recommendations made by them are included herein.

The advice of several of the Rochester scientists was obtained on problems pertaining to the techniques and equipment related to the study, viz:

- | | | |
|---|---|--------------------------|
| Particle Size Determinations | - | Dr. Sidney Laskin |
| Uranium Analysis in Biological Material | - | Dr. Aser Rothstein |
| Air Sampling Technique | - | Dr. Herbert E. Stokinger |
| Alpha Counting | - | Dr. Jean B. Hursch |
| Urine Analyses | - | Dr. William F. Bowman |

It is recommended that the proposed studies be approved and inaugurated as soon as possible.

jwe

E. G. Struzness

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By (Originating Authority) E. G. Struxness

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