CIA/VEC/461-2

18th February, 1966

Dr. A. Hofmann,
Battelle Institut e.V.,
Frankfurt am Main 13,
Wiesbadenerstrasse,
W. Germany.

Dear Dr. Hofmann,

I am enclosing photocopies of some results from the Hyperplasia test which you left in Southampton on your recent visit. I am also sending photocopies of the following papers:

1. "On the significance of the mouse hair cycle in experimental carcinogenesis". Andreasen and Engelbreth-Holm, Acta. Path. Microbiol Scand. 32, 165, (1953).

2. "Comparison of the epidermal hyperplasia in the skin of mice after application of carcinogenic and noncarcinogenic irritants". Berg, Acta. Path. Microbiol. Scand. 25, 34, (1948).

3. "Mitotic frequency in methylcholanthrene epidermal carcinogenesis in mice". Cooper and Keller, J. Nat. Cancer Inst. 2, 335, (1941).

4. "The first effects on mouse skin of some polycyclic hydrocarbons". Pullinger, J. Path. and Bacteriology 50, 463, (1940).

5. "Correlation between carcinogenic potency and the first skin reaction to certain hydrocarbons". Pullinger, J. Path. and Bacteriology 53, 287, (1941).

6. "A histological and cytological study of different methods of skin tumorigenesis in mice". Dammert, Acta. Path. Microbiol. Scand. 53, 33, (1961).

7. "Hair pattern and hair succession in the albino mouse". Borum, Acta. Path. Microbiol. Scand. 34, 521, (1954).

8. "An experimental analysis of the air cycle effect in mouse skin carcinogenesis". Berenblum, Haran-Ghera and Trainin, Brit. J. Cancer, 12, 402, (1958).

9. "Cutaneous tests on mice to determine the carcinogenic activity of the smoke tars of cigarettes". Guerin and Cusin, Bull. Ass. Franc. et Cancer, 48, 112, (1961).

10. "Tests sur la peau de souris pour la determination des activities carcinogenes". Lacer, Libermann, Chouroulinkov and Guerin, Bull. du Cancer 50, 567, (1963).

11. "Mitotic activity in mouse epidermis during the induction period of papillomas". Decoust, Acta. Path. Microbiol. Scand. 45, 159, (1959).

I will look through some other reprints which I have and either send you photocopies or the references if I think they will interest you.

Yours sincerely,

C.I. Ayres

Encl:

c.c. Dr. W. Schwick
Dr. S.J. Green
Sir Charles Ellis
JANUS File

CIA/VEC/46D-2

18th February, 1966

Dr. W. Miedreich,
Battelle Institut e.V.,
Frankfurt am Main M13,
Wiesbadenerstrasse,
W. Germany.

Dear Dr. Miedreich,

Thank you for your letter of 14th February addressed to Dr. Felton.

In general we agree with all the points you outlined, although we have a few minor comments.

Point 4

The exact distribution of the animals and experiments throughout the four animal rooms is a problem which will require a lot of thought. At this stage I doubt if our plans can be finalised. It is essential, of course, that we have your views on any scheme which might be suggested and I will let you have our ideas as soon as possible.

Point 8

We agreed that in the first calibration experiment with benzpyrene and dibenzanthracene the number of mice will be doubled.

Point 9

We agree that the control group will consist of 250 mice, 125 of which will be shaved and painted with acetone/water. It still has to be decided, however, whether the remaining 125 animals will be kept unshaved and unpainted or whether they will be shaved but not painted.

Yours sincerely,

C.J. Ayres

C.I. Ayres

c.c. Dr. Schwick

Dr. S.J. Green
Sir Charles Ellis
JANUS File ✓

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CIA/CAL/[illegible]D 18th February 19[illegible]

Visit to B. & D.F., Southampton of Drs. Miedreich, Hofmann and Kramer (Battelle Institut, Frankfurt, 4th February 19[illegible])

Discussions were held on the progress with Projects CONQUEROR and JANUS. The main points covered were:

Project CONQUEROR

Clam Gill and Rabbit Trachea Tests

The samples examined during November and December had shown an unexpectedly high toxicity. Battelle now have evidence that this was probably due to contamination of the cigarettes during conditioning. Members of the Battelle staff, not connected with either Project CONQUEROR or JANUS, had contaminated the conditioning chamber with acetone-methylene chloride and di-cyclohexyl ketone. Battelle will probably buy a new conditioning cabinet to be used exclusively for cigarettes.

Goblet Cell Test

Battelle will prepare an official report on this work as quickly as possible.

Project JANUS

Short-Term Hyperplasia Test

1. There is some confusion over the age of the ICI type mice from Huntingdon. B-A.T. information was that the mice were 5 months old whereas Huntingdon had told Battelle that the mice were at least 7 months old. The mice were unusually heavy (30-45 g as opposed to the 28-30 g recorded at Harrogate).

2. The results were available from experiments using a dose of 100 mg stale condensate from T4 cigarettes. It appears that:

(i) The results obtained by Battelle with "Harrogate" and "Battelle" mice were significantly different.

(ii) The results obtained by Battelle with "Harrogate" mice were similar but not identical to those obtained at Harrogate.

3. A rapid hair-growth has been observed on some of the mice: the skin sections from these mice preclude reliable measurements being made.

4. The February experiments were planned:

Mice:	"Battelle". i.e., ex ASL Ltd., January delivery.
Cigarette:	27bR. i.e., the control CN102 blend.
Smoking conditions:	B-A.T. standard conditions.
Number of paintings:	Five
Condensate:	Fresh i.e., 24 hours old.
Dose:	Experiment 1 12.5 mg
	Experiment 2 25 mg
	Experiment 3 50 mg
	Experiment 4 100 mg

A fifth experiment, designed by Hofmann, using "Harrogate" mice and involving three paintings each day instead of the single application of the dose, will also be carried out.

5. Battelle will examine the feasibility of a "planimetric" method for the measurement of the width of the epidermis.

Long-Term Tests

1. The building is approximately 6 weeks behind schedule. It was agreed that the starting dates would be:

1st June	Mice and cigarettes to reach Battelle
1st July	Start of the first long-term experiments.

2. The delivery of mice would be re-scheduled into a quarterly basis. Additional mice (100) would also be ordered to serve as replacements for any mice which died during the early weeks of the long-term test.

3. In the first calibration experiment, the number of mice required would be doubled so that the Harrogate technique could be duplicated.

4. The distribution of the experiments throughout the four animal rooms was discussed. Both Battelle and B-A.T. will consider the implications of the various distributions which are possible.

DISTRIBUTION

Dr. S.J. Green
Sir Charles Ellis
Janus File
Conqueror File
File No. 46D

bee: Dr. S. J. Green
Sir Charles Ellis
Conqueror file
Janus file

CIA/sml/461-2

18th February, 1966.

Dr. A. Hofmann,
Battelle Institut e.V.,
FRANKFURT am Main W13,
Wiesbadenerstrasse,
W. Germany.

cc: Dr. W. Schwick

Dear Dr. Hofmann,

Thank you for your letter of 14th February in which you confirmed the main points of our recent discussions on the Hyperplasia test and Project Conqueror.

I Short term Hyperplasia test

Point 1 Whilst I would agree that we have not reproduced the Harrogate results in the experiment with the T4 stale condensate and "Harrogate" mice, I would suggest that the results obtained are similar. It will be of interest to see whether the results with fresh condensate are also similar.

Point 3 Next time I am in Frankfurt, I would be interested in your assessment of the effort which would be involved if the "hair cycle" of the A.S.L. Ltd. mice was mapped.

Point 5 As you know, interest has been shown in the possibility of a "planimetric" measurement of the thickness of the epidermis. We understood that you would examine the feasibility of such a technique in the next few weeks.

Point 6 I will send you our information on new publications.

II Conqueror

I will be sending the samples of cigarettes you requested as soon as possible.

Yours sincerely,

C. T. Ivens

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