

Battelle-Institut e.V.

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Dr. C.I. Ayres
Research and Development Establishment
British-American Tobacco Company Ltd.
Regent's Park Road
SOUTHAMPTON
England

IHR ZEICHEN:

IHRE NACHRICHT:

UNSER ZEICHEN:

DATUM:

101-11/AHO/rdt

14th February, 1966

Dear Dr. Ayres,

This letter is to confirm the main points concerning Janus A and Conqueror which were discussed during our recent visit at Southampton. The points concerning a) the Janus contract in general and b) our visit at the Roebuck Farm, Welwyn, Herts (Animal Suppliers, London) will be covered in a separate report by Dr. Miedreich.

I. Short-Term Hyperplasia Test (Janus A)

1. We reported on the first results of the comparative tests between "Harrogate" and Battelle mice (T 4, 100 mg stale condensate, three times) performed in January 1966. The two tests furnished different results. The Harrogate results, as far as they are known to us, could not be reproduced with either "Harrogate" or Battelle mice.
2. We emphasized that the treatment has partly led to extended inflamed areas and epithelial lesions (necrosis) with both Battelle mice and "Harrogate" mice. Reliable measurement of the thickness of the epidermis is not possible in the case of such slides (mostly slides of mice which were sacrificed after 48 or 72 hours).
3. The fact that the Harrogate results could not be reproduced and that Harrogate, as far as we know, has never reported on the occurrence of skin lesions, gave rise to the question as to whether the animals supplied to us by Huntingdon are really Harrogate mice. Between these

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GEMEINNÜTZIGE LABORATORIEN FÜR VERTRAGSFORSCHUNG

TELEGRAMM-ANSCHRIFT:
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"Harrogate" mice and the Battelle mice there are the following conspicuous differences: The "Harrogate" mice received from Huntingdon are much bigger and heavier than the Battelle mice; they are less lively, their food intake is higher, and their body weight scatters over a wider range (scattering range: $58 - 28 = 30$ g as compared with $29.5 - 21 = 8.5$ g for lots of 50 mice). In the case of about 40 per cent of all "Harrogate" mice, but less than 20 per cent of the Battelle mice, the hair-growth cycle was in the active phase. Moreover, islands of hair growth were observed with numerous "Harrogate" mice. These differences were discussed. The question of the actual age and the actual origin of the "Harrogate" mice will be examined again by B.A.T.

4. In consideration of the results obtained so far, the question was raised as to whether the Janus A test is of any value for our purposes. Although we know today much more than is reported in the Note on the Beckett-Day Test, we considered it doubtful whether the test is appropriate to provide the information required for Janus B.

Therefore we shall try again to obtain a "dose-response curve". To this end, the following tests will be performed: R 276; 12.5, 25, 50, 100 mg fresh condensate, 5 paintings, January batch of the Battelle mice. Moreover, it was agreed to make a multi-painting test, in which selected "Harrogate" mice are treated each with 25 mg fresh condensate three times a day on five successive days. These tests have been started on 7th February, 1966.

5. It was discussed whether a method of evaluation other than the usual one would furnish additional or better information. On the basis of the results obtained, we shall examine this question in due time.
6. In order to obtain a most complete survey of the literature on this subject, we shall exchange information on new publications. Dr. Ayres will soon send us some copies and further references. This applies also to Janus B.

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II. Consequeror

Some of the samples tested in November 1965 showed an unexpectedly high ciliary toxic effect. The results could not be explained; therefore it had been decided to repeat the tests on the occasion of Dr. Ayres's visit in December. In the course of these tests we found out that accidentally several experiments with solvents had been made in the airconditioned room which up to the completion of our new building has to be used for conditioning the cigarettes. We showed you a graphic representation of all the results obtained between November 1965 and February 1966 with indication of the dates on which the individual samples had been tested. It was found that ciliary toxicity was always high when solvents had been used in the air-conditioned room during the storage of the samples.

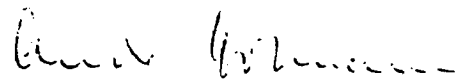
Since after exclusion of the use of solvents it was possible to reproduce previous results, we came to the conclusion that the unexpected results have very probably to be attributed to the solvents. Provisions have been made against the repetition of an incident like this.

The following programme has been agreed upon for CA₁ and CA₂:

1. First of all the measurements with samples C 5 and C 103 will be repeated.
2. Dr. Ayres will again send us samples of the types C 109 and C 111, so that the tests with these samples can be repeated, too.
3. In addition to the tests with R 305, tests with R 276 will be made.
4. The above-mentioned tests will be completed by the end of March, 1966.
5. We shall see to it that a sufficient number of clams is available also in the following months.

The urgency of the report on our work concerning the goblet-cell count was stressed by B.A.T. The report is being prepared at present. The German draft will be sent to you immediately after completion, and four copies of the English report will be submitted to you shortly afterwards.

Yours sincerely,
BATTELLE-INSTITUT E.V.


Dr. A. Hofmann

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