

7th April, 1956

Dr. W. Niedreich,  
 Battelle Institut e.V.,  
 Frankfurt am Main W13,  
 Wiesbadenerstrasse,  
 W. Germany.

Dear Dr. Niedreich,

I am sending, under separate cover, 10,000 cigarettes coded E75R for the work under Projects JANUS and CONQUEROR. These are identical to the earlier batches of E75R cigarettes which have been sent to you. All the cigarettes coded E75R were produced in a single manufacturing run, i.e., the different batches are not samples taken from different manufacturing operations.

A major problem which has to be solved in the immediate future is the large variation in the delivery of dry condensate from the cigarettes smoked on the Mason machines.

You recently summarized the position as:

Batch Number	Date	Delivery of Dry Condensate mg/cig
1	11.10.55	26.9
2	17.1.56	36.5
3	7.2.56	34.4
4	14.3.56	17.2

Despite the correlation between Batch Number and Delivery, I think we can eliminate variations in the cigarettes from batch to batch as the factor responsible for the change in delivery, since

(a) A two-fold change in the delivery of smoke from a cigarette cannot be achieved by any change in the weight, pressure drop, paper porosity or tobacco blend which might conceivably have occurred during the manufacture of the cigarettes.

(b) The results Dr. Kiehl obtained with Flayers 'Medium' M/C cigarettes smoked at different puff volumes also indicated that low deliveries of condensate were being found in March.

Since my return to Southampton, the problem has been discussed at length but, as yet, no definite solution has been put forward. I am therefore listing a variety of points, which in combination may explain the observed change in delivery, although I am sure that most of them have already been considered.

100610/12

7th April, 1956

Presumably, a low delivery means:

- (a) The condensate is being lost during the work-up
- or (b) the smoke is not being trapped
- or (c) the smoke is not emerging from the cigarette.

(a) Work-Up of Condensate

Although I agree that a 50% loss of condensate during the evaporation would be visually obvious, is it worthwhile to determine the nicotine content before and after evaporation?

I believe that Dr. Kienzl has checked the effects of changing the size of the flask used in the evaporation and I understand that there has been no change in temperature or vacuum conditions.

(b) Smoke Trap

Again I would expect a 50% trapping efficiency to be readily noticed but if there are any doubts, presumably the nicotine content of the cotton-wool plug behind the cold-trap could be checked.

(c) Cigarette Smoking

This, I think, is the most probable source of trouble. The fact that two Mason machines have been used would suggest that mechanical failure of the machines is not the explanation. Nevertheless, it might be worthwhile to check with a third or fourth machine.

At Southampton, we have experienced three minor faults with a Mason machine.

- (1) During the day, the wheel carrying the 24 ports 'progressed' so that the cigarette port and the 'suction port' were not in complete alignment.
- (2) The wheel was mounted at a slight angle to its usual position so that the ports at one side made good contact but a leakage occurred at the opposite side.
- (3) Immediately behind the suction port, the smoke-stream is turned through 90°. This part of the machine was inadequately cleaned and although the machine took the correct puff volume at the beginning of the smoking run, the tube rapidly blocked.

On each of these occasions, a low delivery of condensate was recorded.

However, the most likely cause of the change in delivery is a change in the volume of the puff taken on the cigarette. I am assuming that we are completely sure that the cigarettes are smoked to a RJ mm butt. Another factor which I assume can be eliminated is that the 'bubble-stick' used to measure the puff volume is not giving erroneous readings.

105610773

7th April, 1966

Although the puff volume is sensitive to the impedance of the cigarette, it is not extremely sensitive. To assess whether your Mason machines are behaving in an 'unusual' manner, it would be interesting to:

- (1) Set up the machine to puff a 35 ml puff through a 10 ohm W.G. impedance.
- (2) Measure the puff volume without an impedance being used.
- (3) Measure the volume when a 15 or 20 ohm W.G. impedance is used.

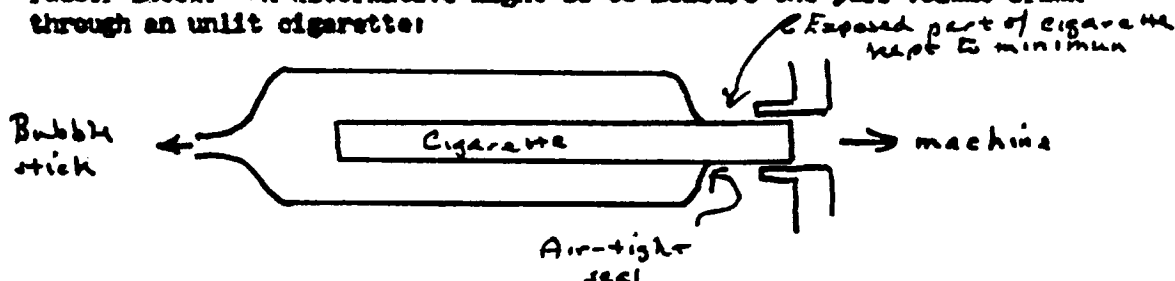
The Mason machines can take a certain amount of time before a steady vacuum is established inside the smoke-trap. Consequently the puff-volume can be affected by the number of cigarettes inserted in the ports, i.e., a different puff-volume is recorded if

(a) No cigarettes are in the ports

or (b) 23 cigarettes are in the ports and the 'bubble-stick' is connected to the 24th port.

On our machines, this effect is only large if the machine has not recently been cleaned. It would appear worthwhile, however, checking with your machines.

Another source of trouble could be leakage around the cigarette due to inadequate seating in the cigarette port. As a check experiment, leakage could be avoided by sealing every cigarette into the port with rubber latex. An alternative might be to measure the puff volume drawn through an unlit cigarette:



One final point - in this letter I have inferred that the delivery found in March was 50% low. This might not be correct. A delivery of 35 mg (January and February) appears to me, to be on the high side. The October figure of 27 mg is approximately the value I would expect. Thus the problem might be not "why is the March delivery 50% low" but "why are the January and February deliveries 30% high and the March delivery 35% low".

I apologise for the rather long and laborious letter, but, as you will agree, this is an important problem which has to be overcome. If in the next few weeks the problem has not been resolved, we will expect Dr. Kiedrich to visit us in Southampton during the first week of May.

Yours sincerely,

*C.I. Ayres*

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

C.I. Ayres

105610774

CI/VHC/450-2

7th April, 1966

Dr. W. Niedreich,  
Battelle Institut e.V.,  
Frankfurt am Main W13,  
Wiesbadenstrasse,  
W. Germany.

Dear Dr. Niedreich,

I am writing to confirm the various points raised during our recent discussions in Frankfurt.

Consolidation of Contracts for JANUS and CONQUEROR

It was proposed that JANUS and CONQUEROR be consolidated in future and that the estimate of costs foreseen for 1966-67 should include an element to cover the following CONQUEROR studies:

- (a) 3 tests per month using clam-gill eiliated tissue (Test CA<sub>2</sub>)
- (b) 4 tests per month using rabbit trachea preparation (Test CA<sub>2</sub>)
- (c) 6 tests per year using goblet cell proliferation test, with an apparatus modified for intermittent smoking.

The suggestion was made that the balance of funds for CONQUEROR remaining at the end of March 1966 should be appropriated to the joint JANUS/CONQUEROR account to help finance this part of the tests. Battelle will raise this point when a letter is written to B.A.T. A further point which will need consideration in due course is the extension of the contract period from 31st March 1970 to 31st January, 1971.

Project JANUS

Long-term Skin-painting Tests (JB)

The mice and cigarettes are scheduled to arrive at Battelle by 1st June and the first long-term test will start on 1st July, 1966.

The following points were discussed:

1. Building

The estimated date for completion of the building is 15th May, 1966.

2. Staff

About 12 assistants have joined Battelle to work on the JANUS project and it is planned to recruit 3 or 4 more in the next three months. You have obtained the assistance of Professor Müller in your efforts to locate a second pathologist.

100010/11

7th April, 1956

3. Cigarettes

The cigarettes will be coded B0, B1, B2 etc. and will be shipped to Battelle at three-monthly intervals. You will be obtaining a cold chamber for cigarette storage.

10,000 cigarettes (coded B0) will be sent, as soon as they are available, to be used in the training of the smoking machine operations.

4. Rice

You have confirmed with Edwards of ASL Ltd. that we will be using rice from the current line of animals.

We had already agreed upon the distribution of the experiments throughout the animal rooms. It was confirmed, however, that the 'unpainted controls' will be shaved, inspected and weighed each week and re-shaved as necessary.

5. Autoclave

You told us that the supplier is unable to deliver sterilized food before September.

This point was discussed at a recent meeting in London. The result of this meeting was that we should do everything in our power to ensure that sterilized food is available by 1st June 1956. I understood that the main difficulty was the long delivery quoted on a suitable steam-jacketed autoclave. If this is so, could you let Dr. Felton know your requirements as, if necessary, it may be possible to obtain suitable equipment in England.

6. Condensate Preparation

Battelle will devise a scheme for the preparation of the condensate solutions for the long-term tests which is consistent with:

- (a) the solvent being acetone-water (9:1)
- (b) evaporation of the solutions of condensate being at a minimum.

I am enclosing a copy of a memo to Dr. Felton on this topic which may be of interest to you.

Inherent in this approach is the assumption that we can overcome the large variation in delivery of condensate which has recently been observed. I have written a separate letter to you on this point.

Short-term Hyperalacia Test (JA, and JA.)

1. Method of Measurement

In view of Dr. Hofmann's recent comparison of three methods of

105610776

Dr. W. Miedreich

-3-

7th April, 1956

measurement, we agreed that in future experiments the original method would be used, i.e., direct measurement of the width using a microscope fitted with a screw micrometer eyepiece.

2. April Experiments

The detailed design of the experiments will be planned by Dr. Hofmann. In principle the effects of treating the mice with solutions of benzo(a)-pyrene is to be examined.

3. Excess Mice

I can now confirm that the disposal of the excess mice (approximately 500) can now go ahead.

Project CONQUEROR

Clean Oil and Rabbit Trachea Tests (CA. and CA.)

The immediate experiments will include

- (1) Completion of the list of 'check-experiment' samples of cigarettes.
- (2) Repeat examination of the Cambridge Filter effect.

In all future experiments, care will be exercised to prevent contamination of the coil during one test from interfering with the result of a second test.


Goblet Cell Test (CB)

Battelle will examine the possibility of attaching a Mason smoking machine to the exposure chamber. The aim is to expose the rats to smoke which is generated from a cigarette smoked under the normal smoking regime.

Preliminary experiments will also be carried out on the methods of assessing the 'average goblet cell count' of the rats.

Please let me know if there were any additional items covered in our discussions which I have failed to mention in this letter.

Yours sincerely,



C.I. Pyres

c.c. Dr. W. Schwick

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

105610111