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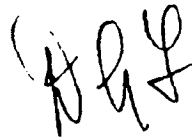
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DGF/VC/46D-2

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I enclose a note summarising suggestions for the long term skin painting tests to be carried out under Project JANUS. These represent the suggestions from R.& D.E. for discussion at the meeting to be held in Millbank on Thursday, 3rd February.



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Project JANUS

1. Introduction

The following suggestions are put forward by R.& D.E. as the result of discussions between C.I.A., D.J.W., I.W.H. and D.G.F. The aim has been to propose a scheme of interlocking experiments in which there are a small number of variables, which are susceptible to control over a limited range. These variables are:

- (a) Temperature
- (b) pH
- (c) Aromatic polycyclic hydrocarbon concentration in condensate

Other factors which are involved are:

- (i) Tobacco change
- (ii) Process changes, e.g., chemical or microbiological
- (iii) Cigarette parameters, e.g., porosity, cpi and packing density
- (iv) Puffing parameters (in practice, these are restricted to puff volume change)

2. The mice which are to be used in JANUS do not originate directly from I.C.I or Harrogate.

The assumption was made initially that their mortality and tumour rates would be similar to those of the Harrogate mice, but this must be established at the earliest time. In view of the possibility that the mice may be different from the Harrogate strain, the orders of difference in specific mouse skin carcinogenicity, which are demonstrable with the numbers of mice available, may have to be larger if the same significance levels as are used at Harrogate are employed at Frankfurt. This point is under examination in R.& D.E.

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3. Standard Tobacco

For the purpose of examining the effect of the interlocking variables on biological activity, it is necessary for a standard tobacco to be chosen. Ideally, this standard tobacco should be one permitting a comparison with the results from Harrogate, although the possible difference in mouse strain may preclude this in practice. In what follows, it has been assumed that the standard tobacco is a flue-cured blend, for the following reasons.

(a) There is some evidence (Bock, Wynder) that a U.K. type cigarette is more carcinogenic than a U.S. blended type.

(b) There is a considerable background of experience in R.& D.E. on the chemistry of flue-cured tobacco smoke.

(c) Inherent in the schemes are chemical treatments which may only apply to flue-cured tobaccos.

4. Scheme 1 (see Fig.1)

This scheme would involve a total of 11 (or possibly 13) samples and, moreover, does not include a repeat test on the standard cigarette, which is thought to be necessary.

The experiments outlined would serve to illustrate the following changes in variables:

- | | |
|------------|---|
| Change 1-2 | Change in APH concentration but probably not temperature or pH. |
| " 1-3 | May change temperature and APH, but not pH |
| " 3-4 | As 1-2? |
| " 1-5 | Change in APH, pH but probably not temperature |
| " 5-6 | ? |
| " 1-7 | Change in APH, pH but not temperature |
| " 7-8 | ? |
| " 1-9 | Change in APH, pH and temperature |
| " 9-10 | ? |
| " 9-11 | ? |

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The following additional points should be made.

- (a) Change in puff parameter. This is important in the context of human smoking where a lower puff volume than 35 ml. should be investigated (10 ml. is suggested). A reduction in puff volume could be achieved by cigarette design.
- (b) Change in cigarette parameters. By change in paper porosity, cpi and packing density, it will be hoped to achieve high puff temperatures. Should the need arise, such changes could be readily made by manufacturers.
- (c) Chemical and microbiological treatments are aimed at producing a tobacco similar in characteristics to an air-cured fermented type. A sample of a commercially available tobacco of this type is included for comparison.

5. Scheme 2 (see Fig.2)

This scheme only requires 10 samples and includes a repeat on the standard tobacco. The interlocking of samples cannot be achieved here and the scheme examines a number of approaches.

The samples which are included in this scheme only are:

- (a) K_2CO_3 treatment - Lowers APH, changes pH and temperature.
- (b) Low Bp. Burley - A filter tip cigarette with low tar and low bp. with normal nicotine.
- (c) BONDEX filter - The viscosity of smoke condensate passing a BONDEX filter is different from that of condensate from plain or acetate or paper filtered cigarettes.
- (d) Added Bp. - An attempt to determine whether smoke is predominantly a carcinogen or a co-carcinogen.

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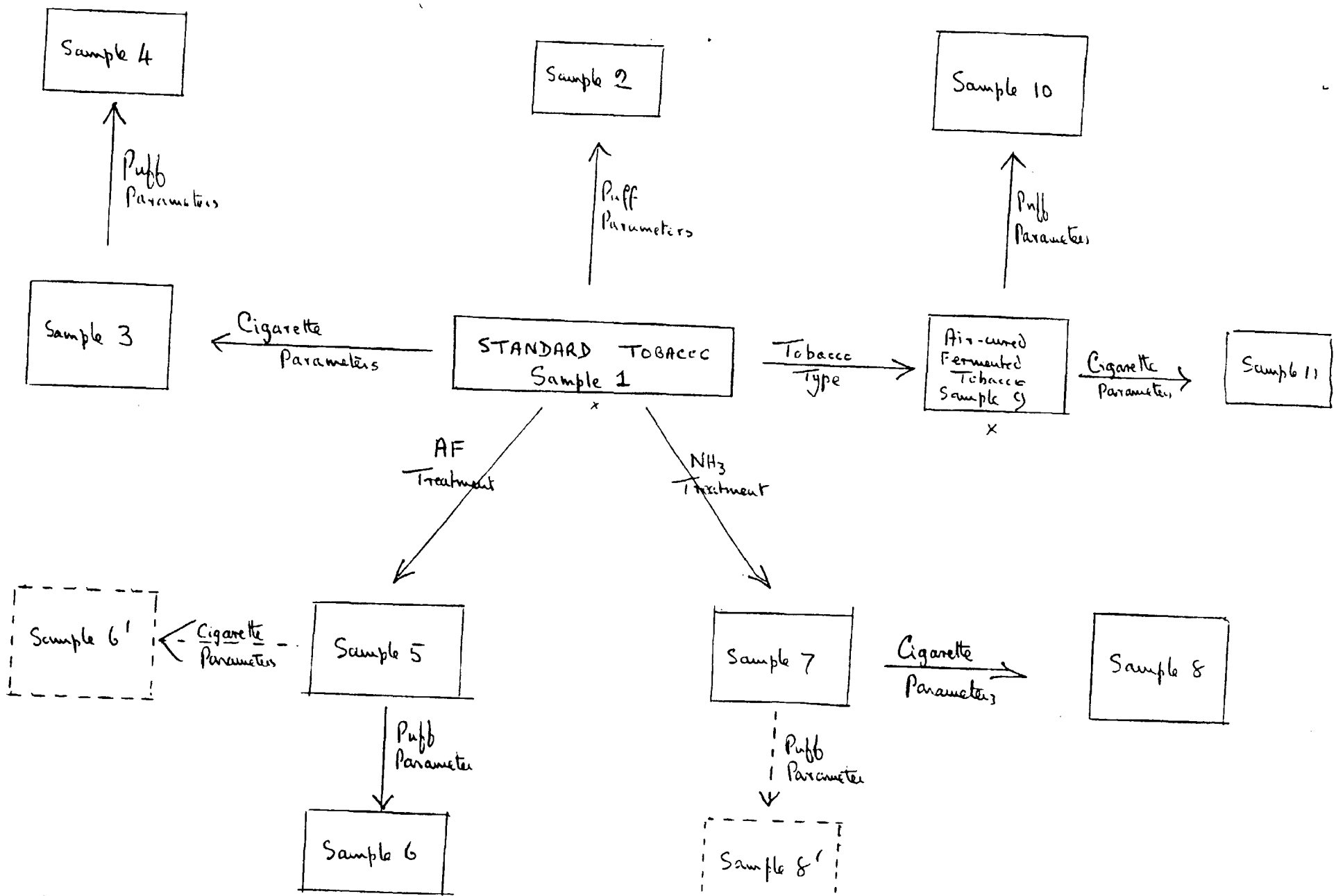


Fig 1. Scheme I

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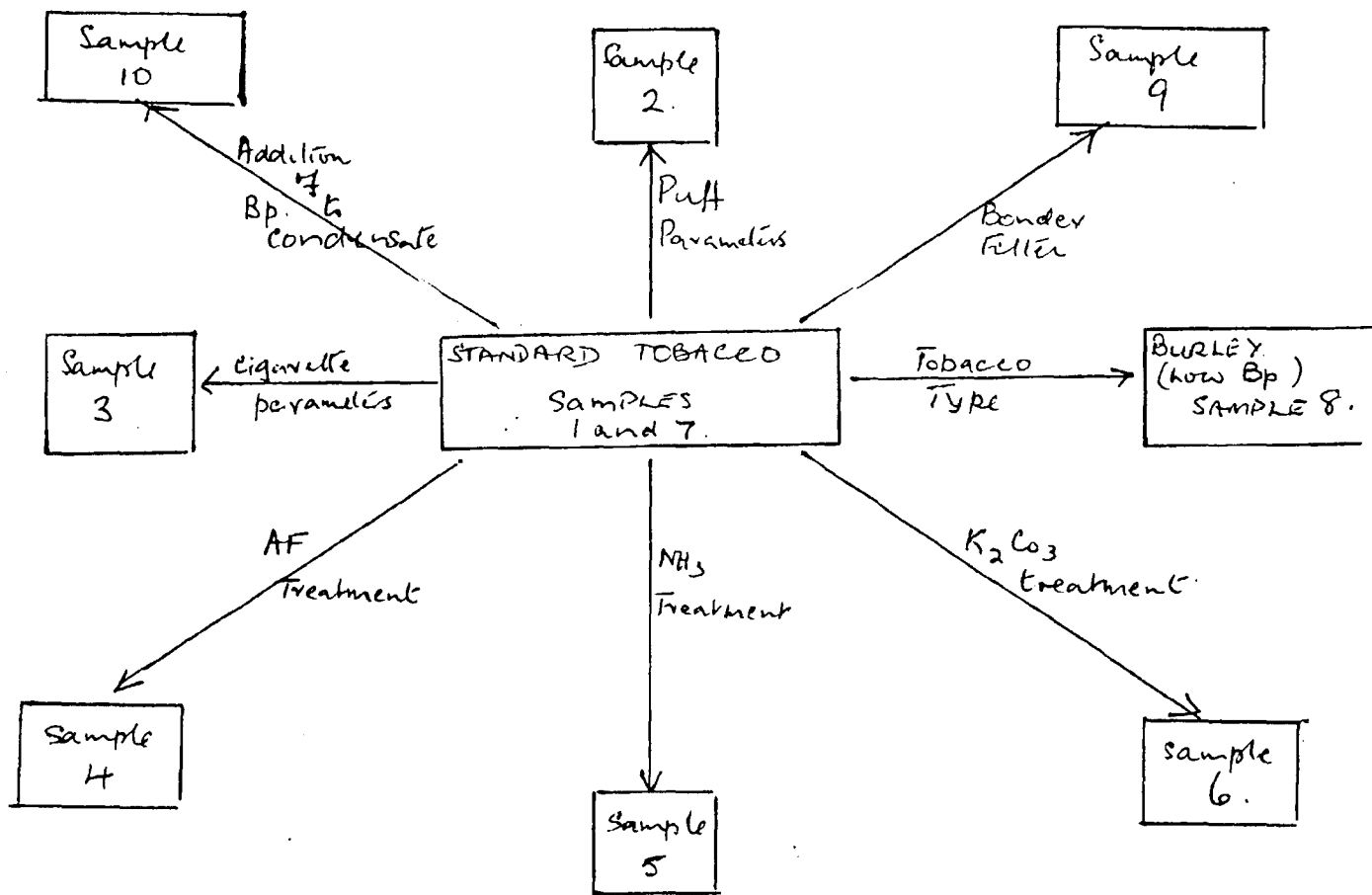


Fig. 2. Scheme 2.

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