SJG/BGM/16D-2 11th February, 1966.

MINUTES OF MEETING HELD IN MILLBANK ON 3rd FEBRUARY, 1966

Present: S. J. Green (Chairman)
Sir Charles Ellis, F.R.S.
D. G. Felton
D. J. Wood
W. B. Fordyce (Secretary)

Action

Matters arising from previous Minutes

2. The composition of the Committee has been approved and welcomed by Messrs. Laporte, Griffith and Reid. ?

3. It was noted that Dr. C. I. Ayres had the testing of Harrogate mice at Frankfurt in hand.

5. Dr. C. I. Ayres would visit suppliers (of mice) on 8th February, together with Dr. Miedreich of Battelle, Frankfurt.

7. Schemes for the long-term tests were put forward in the course of January by R. & D.E., CDE and LCL; a note was also available from WBF, amalgamating many of the suggestions made in the above schemes. Replies to the effect that the matter was having their consideration were received from WWR and RBG. ?

9. Each of the 10 Frankfurt skin painting tests would be performed on a total of 750 mice, for example each would comprise tests at, say, three dose levels, each on 250 mice. If only one dose level is used for one of the 10 experiments then two condensates would be compared using 375 mice for each. It was also agreed that it is essential to include a second control experiment in the series.

10. The scheme of experiments proposed by LCL was examined. It was pointed out that Test A was already effectively being performed by TRC (using T5 cigarettes) and Test B, by I.T.Co. and TRC in the near future. C, representing the best available selective filter was considered to be a possible candidate and would be considered further at a later stage in the meeting; similar comments apply to Test D. It was not considered that Test E or Test F need be carried out at present on the terms outlined by LCL.

With regard to Test G, it was agreed that puff parameters would be investigated on some basis, to be decided after consideration of the further schemes.

...../2.

Action

11. DGF then outlined the reasoning behind the two schemes proposed by R. & D.E. After examination of the situation it was concluded that a factorial plan could not be applied to such a small number of experiments. As a result two schemes were proposed, the first of which was an attempt to plan the tests in such a way that they would interlock with one another; the second scheme was essentially a list of independent experiments. DGF pointed out that while interlocking experiments were superficially the more potentially useful form, certain disadvantages could well arise once the ten experiments were irrevocably under way. For example, if instant condensate were to become available as a practical technique half-way through the series of tests, it would be extremely unfortunate to be committed to a continuation of the original ten on the basis of present condensate collection techniques. Or, it is possible that the mice could change either in the genetics of the breeding stock, or in their susceptibility.

DGF then went on to explain how they had arrived at the interlocking experiments described in scheme I. These, he said, were based on attempts to change a limited number of determinable variables, namely combustion temperature, smoke pH, and polycyclics concentration. These they sought to change by alterations in (1) the tobacco, (2) the processing of the tobacco, (3) changes in cigarette parameters and (4) changes in puff parameters. With regard to No.4, he explained that, since the Mason machine was being used, only the puff volume could be altered. In choosing a puff volume change from 35 to 10 cc., they had been exercised chiefly by the fact that the polycyclics concentration in smoke, relative to tar and/or nicotine, changes demonstrably at low puff volumes, whereas at high puff volumes no such change occurs.

Scheme I in its present form involved not ten but possibly up to fourteen experiments, (including a second control).

DGF further commented that, with regard to both schemes, they had sought to exclude all experiments which might provide answers already forthcoming from TRC. With regard to the choice of standard, R. & D.E. favour a blend rather than any single grade of tobacco because only in this way could any reasonable continuity of cigarette properties be expected. The choice of flue-cured tobacco as the basic material to be used throughout Scheme I lay in the results obtained by Bock and Wynder, among others, which showed that flue-cured tobacco was, on current evidence, that which gave rise to the most carcinogenic smoke.

12. CDE then explained his own choice of ten experiments. He had come after some thought to the conclusion that it was not possible to devise any set of experiments which were usefully interlocked, and as a result his own scheme was to his mind the best available form of "league table". CDE had very much

...../3.

Action

in mind the possibility that developments in the whole field of biological testing in the next few years could well change the pattern of such tests, and it might, therefore, be unwise to embark at the moment on a set of pre-planned experiments, which one might not be able to change. The developments to which CDE specifically referred were the Leeds investigation by Dr. Eaves "instant condensate", a general reduction in the errors associated with such biological experiments, and finally, the almost certain development of much shorter term tests based on histological examination of appropriate exposed tissues.

13. After considerable discussion, it was decided that the unrelated experiment approach offered sufficient advantage over the other to justify planning the experiments on this basis.

Discussion then turned to a number of points fundamental to the whole exercise, such as the calibration of the mice, the question of cross checking with TRC, the type of cigarette to be used as the standard, etc. It was agreed that an established fluo-cured blend should be the standard throughout, and that while every effort should be made to ensure that TRC experience should be utilised to the full, it was not necessary to use the same cigarettes.

It was finally agreed that the superior accessibility of TRC results would make them a first choice of background experience.

14. Ten experiments to be carried out in Frankfurt were then outlined:

Experiment 1.
This will be one of two control experiments, will be carried out at a puff volume of 35 cc. using a flue cured blend cigarette, and will be performed at three dose levels (25, 50 and 100 mg). These levels ought to provide sufficient insurance with regard to the as yet unknown susceptibility of the mice being used.

Experiment 2.
This is planned as an experiment on the effect of puff volume, the volumes suggested being 10, 25 and 50 ml. The same single dose level will be employed throughout, namely 75 mg, unless there are, at the inception of experiment 2, strong indications from experiment 1 that this particular dose level would be wrong with regard to the susceptibility of the mice employed. The same cigarettes would be used as in experiment 1.

Experiment 3.
It was first decided that the next four experiments should be

...../4.

Action

allocated to different tobacco types. Having made this decision, the Committee found itself in some disagreement over which tobacco types should be given priority.

After much discussion, it was finally decided that experiment 3 should be conducted on straight Burley cigarettes, smoked under standard condition, at three dose levels, probably 25, 50, and 100 mg.

Experiment 4.
Experiment 4 should be carried out as for experiment 3, but using a normal B.A.T. American Blend (but not including PCL).

Experiment 5.
Experiment 5 will replicate experiments 3 and 4, but will be carried out on the same blend modified to contain a high proportion of PCL made from that blend.

Experiment 6.
The decision in this case was that it should be a cigarette made from dark air-cured tobacco, possibly a standard blend, and that it should be carried out at the same dose levels as used in experiments 3-5.

Experiment 7.
It was generally agreed that by this stage in the programme a re-check of the standard cigarettes and the relevant controls should be carried out.

The remaining experiments were left open at this stage but it was felt likely that they might be allocated to tobacco treatments e.g. Airferm, St. Paul, etc.

It was felt that any experiment involving filter cigarettes would best be carried out once techniques for the production of instant condensate became available. In the light of this SJG suggested that by 1969 we should produce what might be termed "the best possible cigarette", which would incorporate all advances made towards the development of a "safe" cigarette. CDE made the further point that if any Company, whether in the Group or not, should produce a cigarette which was desirable both from a taste point of view and from a health standpoint, then consideration should be given to testing its biological activity. He also made the point that behavioural studies should be undertaken both in the U.S.A. and in the U.K. within the next fifteen months in order that a proper evaluation of those experiments involving changes in puff parameters might be made.

SJG stressed that the Committee must, of course, remain open to advice, comments and suggestion from the corresponding members of the Committee, particularly in those areas which correspond most closely with their specific interests and

...../5.

Action

problems.

15. There was some discussion on the testing of cigar type tobacco in cigarette form and vice versa and it was mentioned that Canada might well be able to help in providing cigars made from non-fermented flue-cured tobacco. It was agreed that DGF should inform SJG of the sizes required and of any other relevant data. — DGF

16 It was agreed that none of the cigarettes in experiment 1 or indeed in any other experiments should bear a commercial brand name and should be coded, e.g. J1, 2, 3 etc. It was also decided that steps should be put in hand to have the cigarettes for experiment 1 made available by the end of May, even though some doubt still attaches to the question of whether or not the Frankfurt buildings will be ready in time.

17. When comments have been received from overseas members a further meeting will be held to re-assess the validity of this programme. — RBG, LCL, WWR

Distribution:

Sir Charles Ellis.
S. J. Green.
D. G. Felton/D. J. Wood. ✓
L. C. Laporte.
R. B. Griffith.
W. W. Reid.

105610856