

IN – VITRO GENOTOXIC ACTIVITY OF MAINSTREAM CIGARETTE SMOKE

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Aims

1. To establish whether **tobacco blend** influences selected **genotoxic activities**
2. To establish whether certain **cigarette design variables** can be used to *predict* selected **genotoxic activities**

To assess *Genotoxicity*:

- **Ames:** bacterial system
 - Consists of a number of strains of *Salmonella typhimurium*
TA98, TA100
 - Looks at gene (DNA base) changes
- ***In vitro* Micronucleus:** mammalian cells
 - Chromosome damage

Mammalian Activation System

- **Some mutagenic chemicals** are **inactive** unless they are metabolised to **active** forms
- In animals and man enzyme systems in e.g. the liver are capable of metabolising many of these chemicals. **Some of the intermediate metabolites are very potent mutagens in the Ames and Micronucleus tests**
- Therefore part of both these tests includes the addition of a mammalian activation system referred to as **+S9**

Procedure

- Smoked samples on Borgwaldt RM 200 rotary smoke engine
- ISO (35/2/60) regime only
- Trapped **particulate matter** onto Cambridge filter pad

Eluted with dimethyl sulphoxide

Blend Effects

Tobacco type
100% Virginia
100% Burley
50:50 Virginia/Burley mix
Oriental

Constant cigarette design:

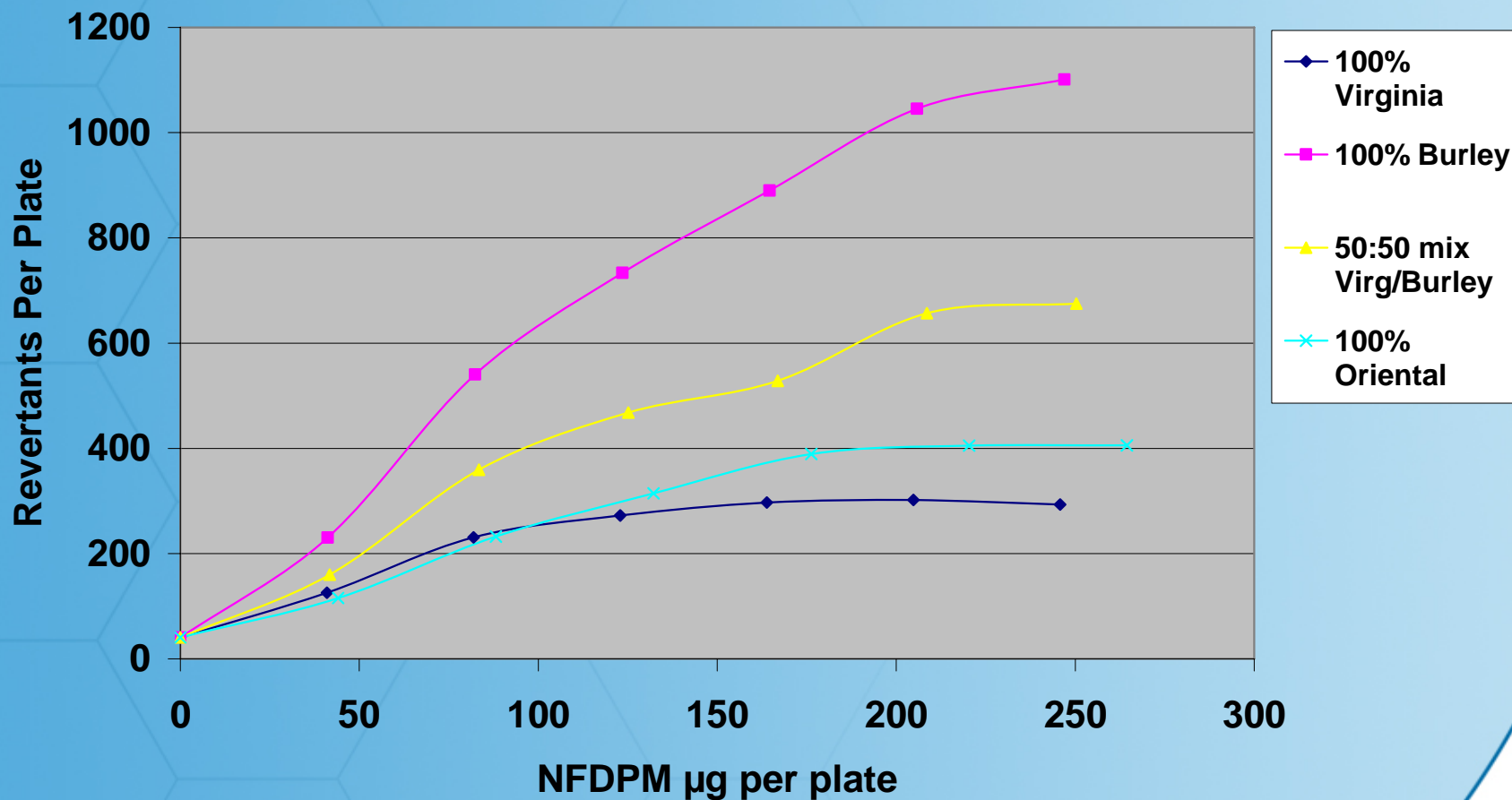
Filter ventilation: **35 %**

Paper permeability: **55 CU**

Pressure drop: **80 mmWG**

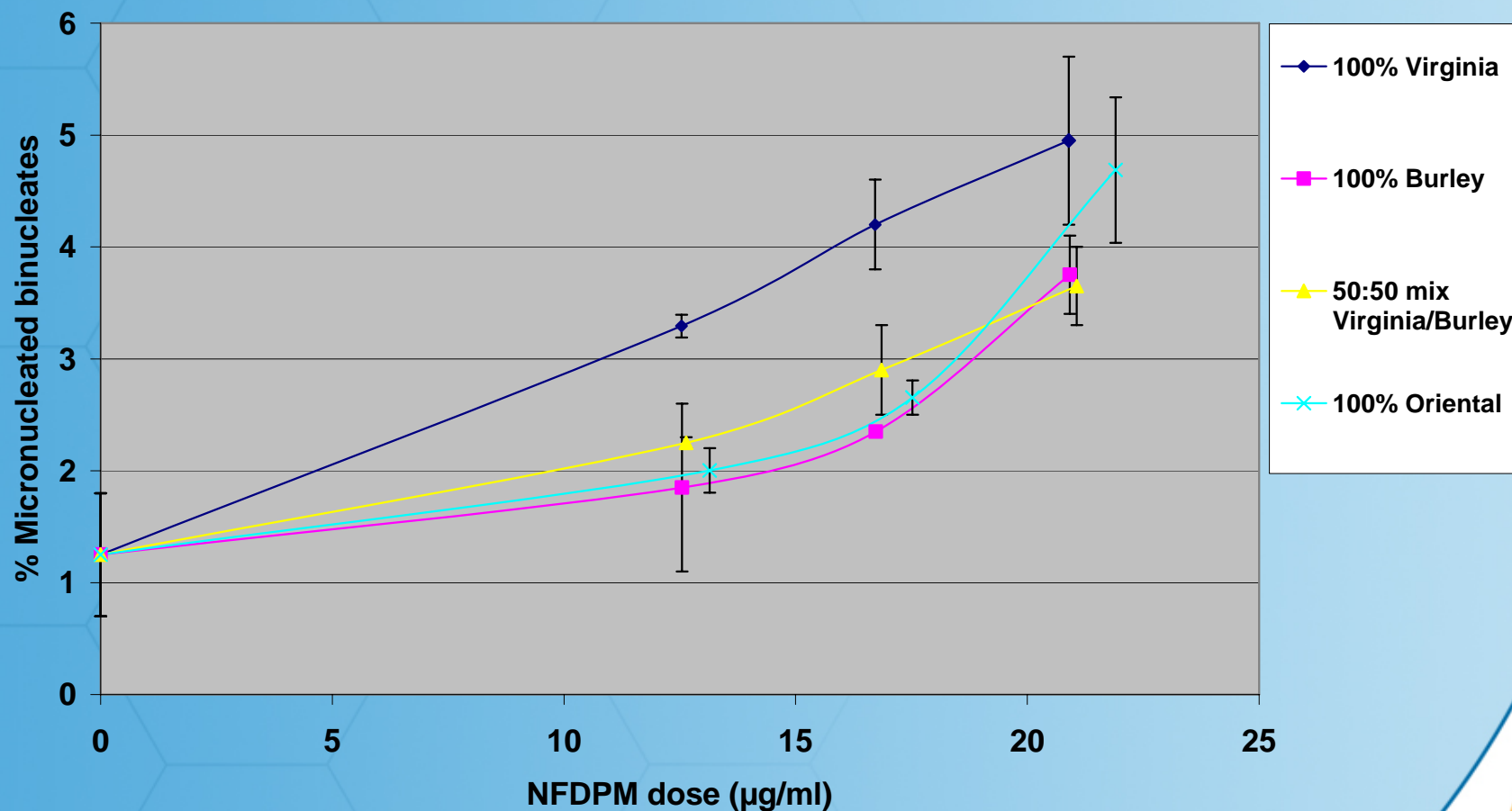
Blend Effects : Ames

Centrepoint samples: TA98 +S9



Blend Effects: Micronucleus

Micronucleus Induction minus S9



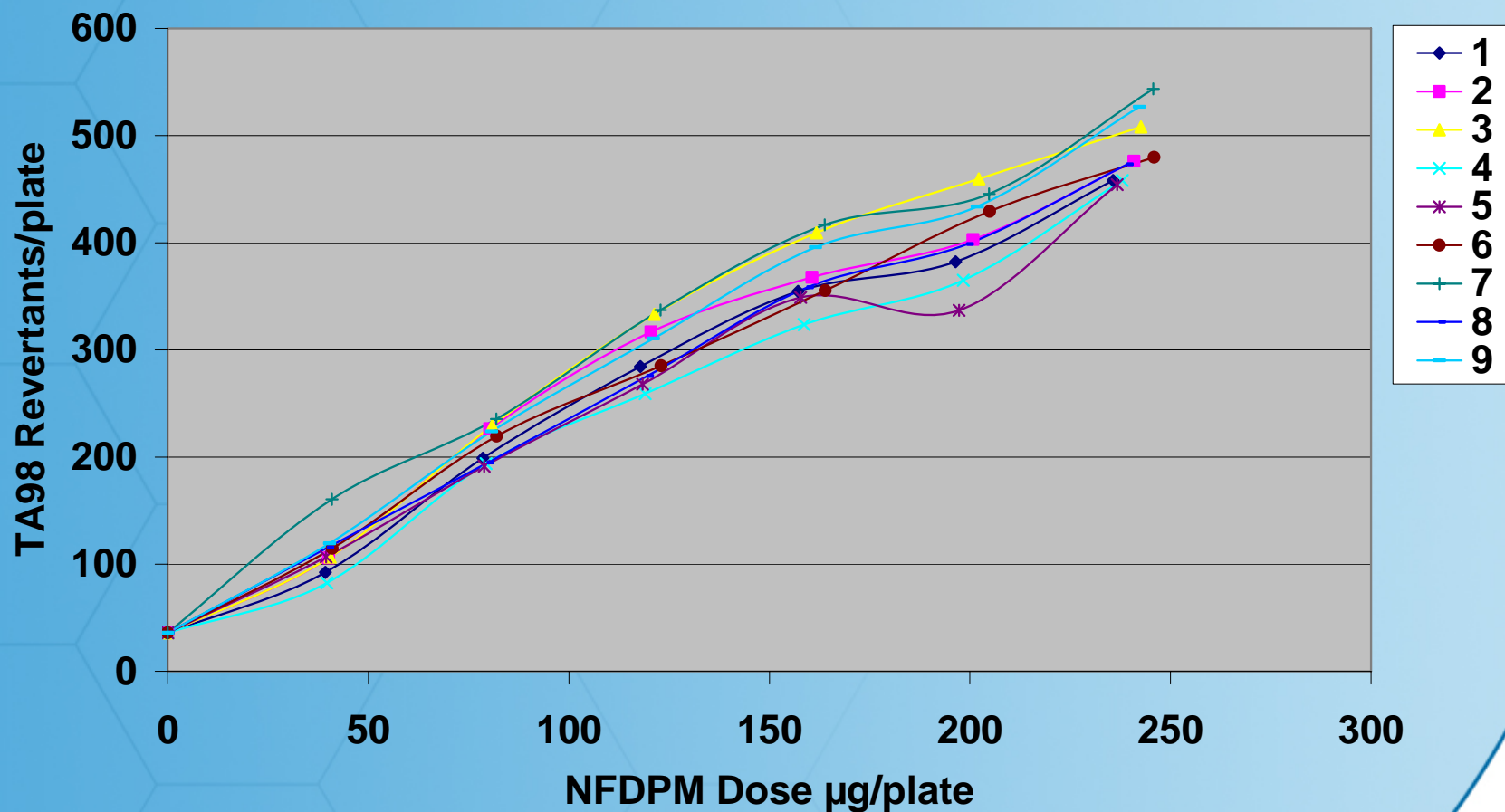
Corner Point Designs

Corner point samples and the **Centre point**

- | | | | |
|--------------------------|-----------|-----------|------------|
| •Filter ventilation (%) | 15 | 25 | 55 |
| •Paper permeability (CU) | 35 | 55 | 75 |
| •Pressure drop (mmWG) | 60 | 80 | 100 |
- Used these experimental design points from the **Virginia** and **Burley** blends

Virginia Corner Points & Centre Point: Ames

Virginia Cornerpoint: TA98 +S9



Corner Points Summary

Filter ventilation (%)	15	25	55
Paper permeability (CU)	35	55	75
Pressure drop (mmWG)	60	80	100

For both Virginia and Burley:

Ames: No significant differences with TA98 +S9
and TA100 +S9

Micronucleus: No significant differences with + S9
or - S9

Star Point Designs

Star point samples and **Centre point**

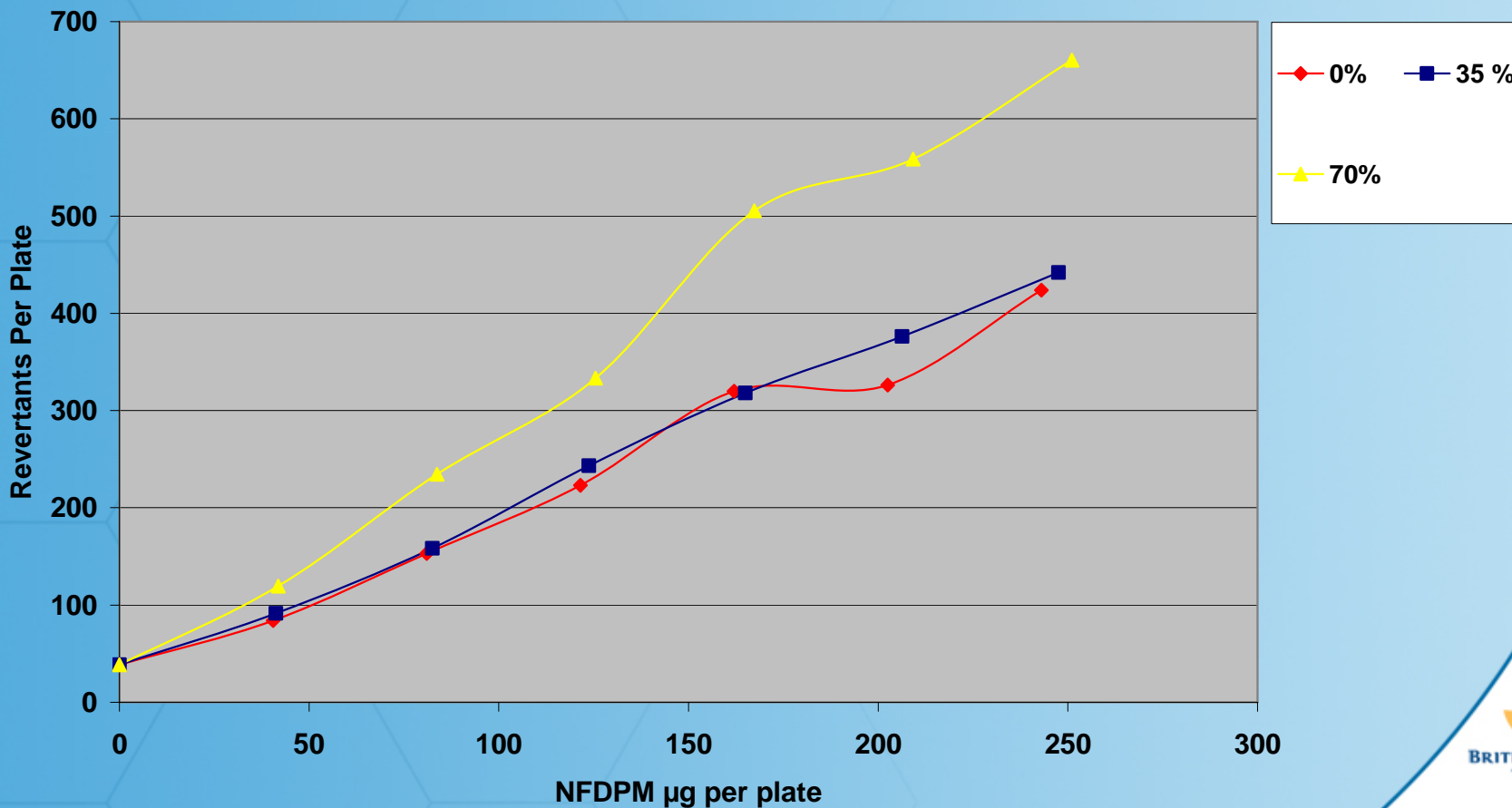
•Filter ventilation (%)	0	35	70
•Paper permeability (CU)	10	55	100
•Filter pressure drop (mmWG)	40	80	120

- Used these experimental design points from the **Virginia** and **Burley** blends

Virginia Star Points & Centre Point

Ventilation Effects: Ames

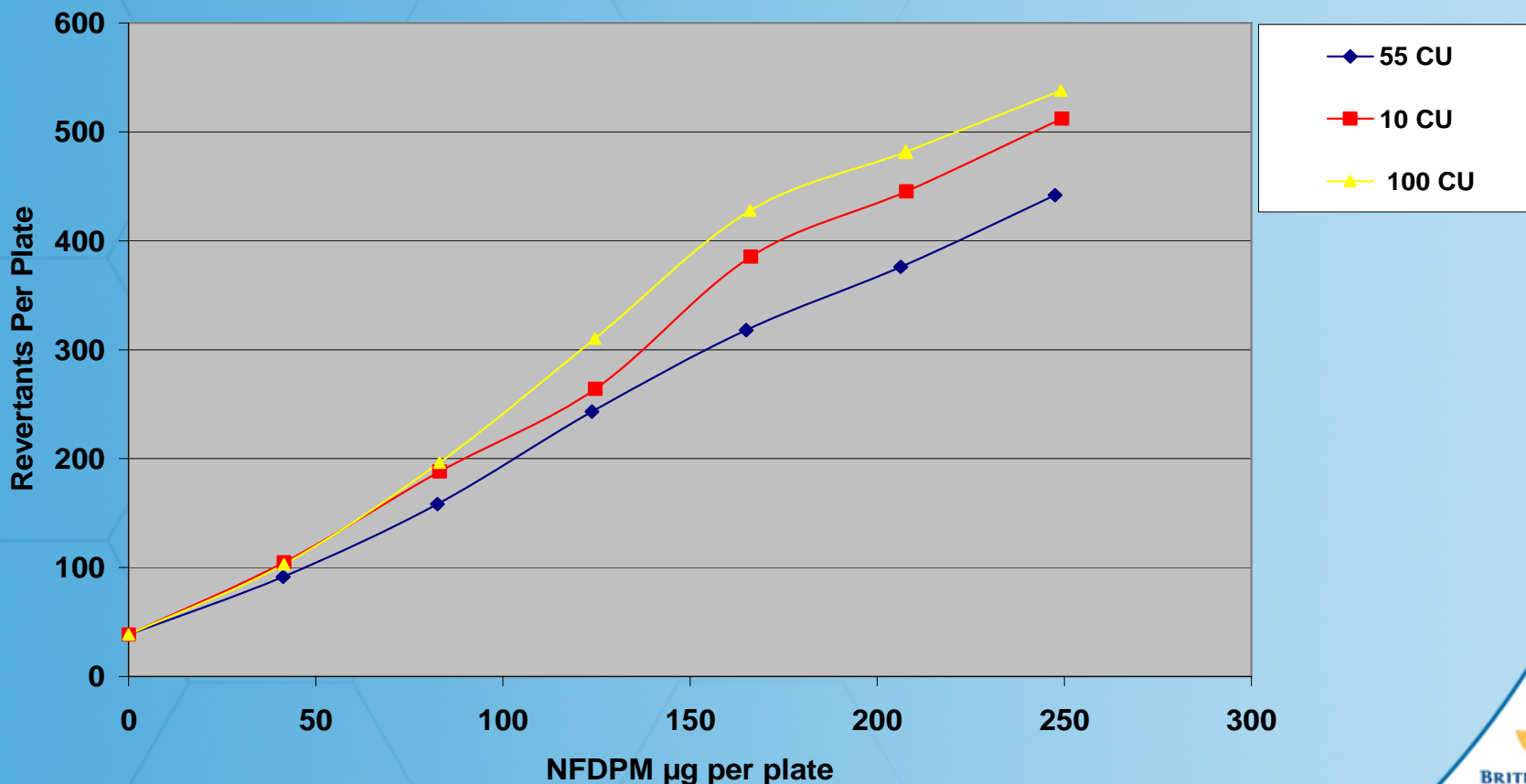
TA98 +S9



Virginia Star Points & Centre Point

Paper Permeability Effects : Ames

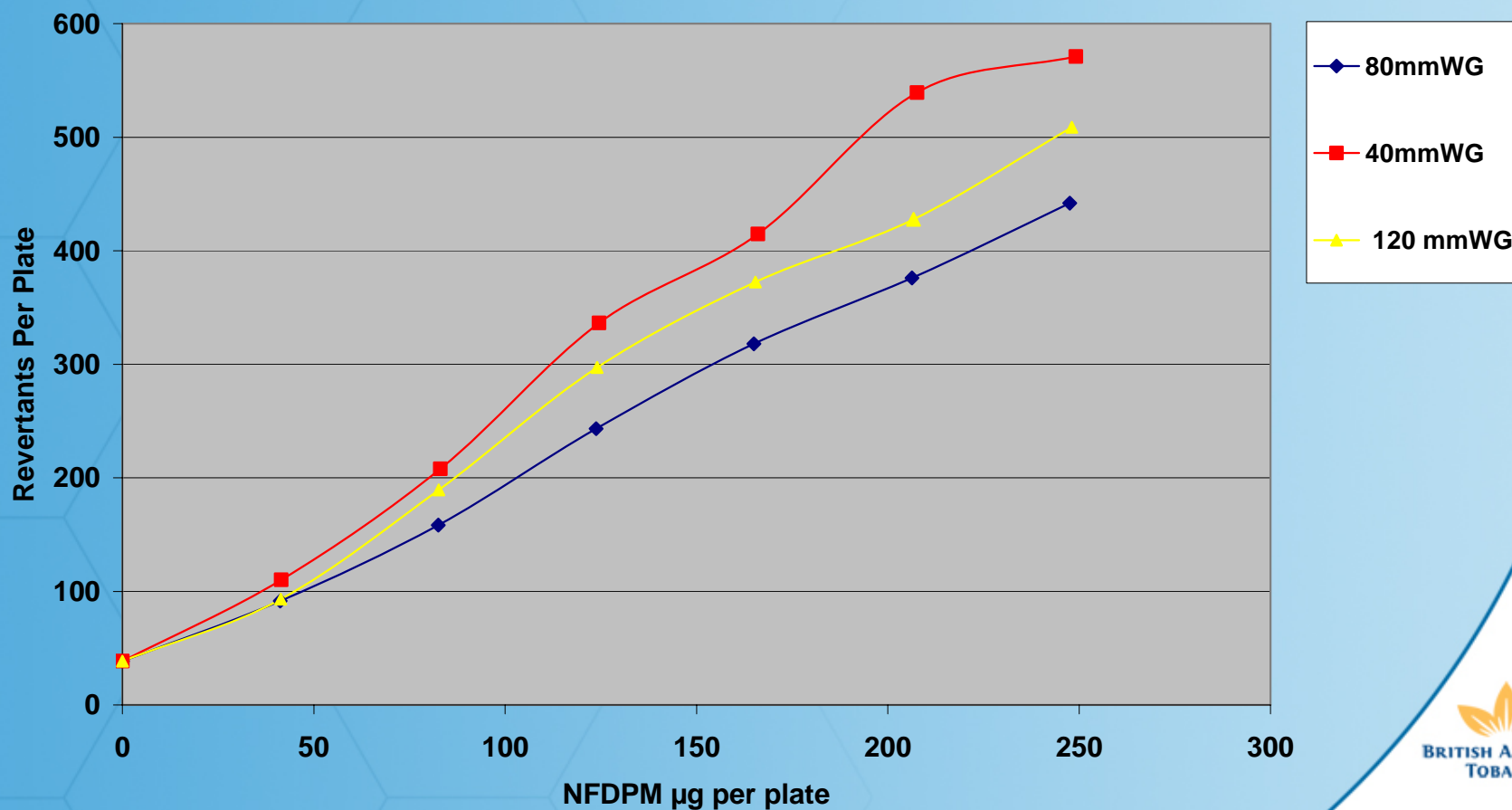
TA98 +S9



Virginia Star Point & Centre Point

Filter Pressure Drop Effects: Ames

TA98 +S9



Star Point Summary

Filter ventilation (%)	0	35	70
Paper permeability (CU)	10	55	100
Filter pressure drop (mmWG)	40	80	120

For both Virginia and Burley:

Ames: Significant differences with TA98 +S9
for: 70% ventilation, 100 CU paper,
40 filter pressure drop
No significant differences with TA100 +S9

Micronucleus: No significant differences with +S9
or -S9

Conclusions

The **genotoxicity** of the **particulate phase** of mainstream smoke is effected by the type of **tobacco blend**

Changes in: filter ventilation from **15-55 %**
paper permeability from **35-75 CU**
filter pressure drop from **60-100 mmWG**

have no effect on the genotoxicity of the particulate phase

The following **cigarette design parameters** of: filter ventiaction of **70 %**
paper permeability of **100 CU**
filter pressure drop of **40mmWG**

do increase the genotoxicity of the particulate phase