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This paper considers the Group's current allocation of resources across broad areas of tobacco R&D.

Following the major changes in R&D organisation initiated two years ago, we have six R&D centres all of which now classify project activity in a standardised way. This enables us to estimate quite reliably the relative effort allocated to various sub-groups of R&D. We also have details of external contract research undertaken for the six centres.

R&D activity across the six centres costs £30 m and the external supported research costs an additional £1.5 m. Their total is allocated as follows:

OVERHEAD SLIDE I : DISTRIBUTION OF GROUP R&D EFFORT

Classification	Short-medium term focussed R&D	Long term "uncharted" Research
	I	II
R&D aimed at Quality Improvement, Cost Reduction and Innovative Products	65%	16%
	III	IV
R&D in response to S&H related (Regulatory) Issues	12%	7%

General consensus suggests that cigarette development will be evolutionary rather than revolutionary and that we can reasonably plan 5 years ahead. Consequently, short-medium term research spans this period, but of course, is effectively updated annually (a "rolling" 5 year programme) in the light of Group management perception of what either the customer or the Regulatory Authorities will require.

This presentation will focus on the type of work falling into categories I-IV and the rationale for the work.

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Category I

The Group has a major effort in this sector. It is highly market-oriented and projects are selected either to increase market share or to improve margins. Across the Group we have a particularly concerted effort on smoke quality improvement with technical improvements rapidly being transferred to brands, for instance in USA. Production of satisfactory low density cigarettes in terms of both physical and subjective properties is key to many markets.

Development of our own novel expansion process for tobacco and a completely new reconstitution process for use of tobacco waste will generate very significant cost savings for the Group.

In terms of product innovation we have been successful with Barclay and, so far, Capri (the ultra-slim) and we are constantly searching for new products.

Category II

The need for new 'building bricks' for extending our capability to meet quality demands etc. is clearly recognised. In this "seed-corn" area we have work directed towards understanding and modifying the smoke aerosol properties, a fundamental route to taste character. The effective release and transfer of nicotine from tobacco to the smoker is a subject of our longer term research. This important compound contributes not only to the pharmacological sensations but also to taste and flavour. The search for new and more effective flavour materials remains key to our long term needs.

Items I and II have been dealt with briefly. The next two items need more careful consideration since they are a potential source of confusion.

Category III

The evolutionary development of the cigarette in response to S&H issues will be guided by such Regulatory Authorities as the ISC or the US Surgeon General's Report. We believe our role is to be able to have meaningful interaction with such bodies, and, in practical terms, to be ready to provide appropriate products. Thus we must stay closely in touch with such bodies and to some extent anticipate their requirements.

Our work in this category is almost entirely conducted internally since apart from a competence in biological testing, it largely calls for research on the cigarette itself - selection and processing of blend, construction of cigarette including paper, and additives, combustion, filtration and ventilation, and we believe that BAT Group has the appropriate expertise 'in-house'. If we are deficient in this area we have a serious problem.

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Some examples of the in-house projects are:

Reduction of specific 'noxae'

Of the 4,000 or more chemicals identified in tobacco smoke, there are hundreds that, if taken in isolation and in sufficiently high dose, can produce toxic reaction in humans. Which, if any, have serious consequences in smoke with its complex physical structure and its various generally low concentrations, is a truly open question. The two key Regulatory Authorities - the Royal College of Physicians and the US Surgeon General each have commented on relative importance of groups of chemicals, but in most cases, they call for further research.

Our approach has been two-fold. Firstly, we have over 20 years explored means of controlling the formation or selective removal of those chemicals generally classed as important by Authorities, viz nitrosamines, aromatic hydrocarbons, phenols, aldehydes etc.

OVERHEAD SLIDE : OTHER NOXAE

The complex list of possible toxic components in smoke appears to present as much confusion to the Authorities as to the Industry when trying to prioritise. We are aware that at a recent US Conference of Governmental Industrial Hygienists a scheme was outlined for classifying noxae on the basis of their Threshold Limit Values (defined as the concentration for a normal 8-hour working day/40 hour working week to which nearly all workers may be repeatedly exposed, day after day, without adverse effect). This may form a sensible basis for prioritising compounds.

A quite different approach to reducing those components that concern the Authorities is to go for blanket reduction through major smoke modifications rather than aim at selective reduction. The first approach of lowering all deliveries (tar, nic, etc.) by filtration/ventilation appears to have run into controversy due to arguments about compensation.

Current pointers suggest that the Regulatory Authorities will encourage a move to cigarettes with lower tar but normal nicotine deliveries.

OVERHEAD SLIDE 3: POSSIBLE TRENDS IN CIGARETTE  
DELIVERY MODIFICATION

We have research projects exploring the feasibility of making low tar/high nicotine products. One way depends on breeding tobacco with unusually high nicotine levels. One opportunity for establishing quite radically different leaf is through plant biotechnology for which we are well placed in BAT Industries.

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Finally, on the subject of smoke toxicity based on likely Regulatory standards, it should be mentioned that in our search for factors affecting the biological activity of smoke one of the most important findings is that activity is markedly dependent on cigarette diameter. Capri, the ultra-slim cigarette, recently launched in US by B&W, with a circumference of 17 mm in contrast with the normal 24-25 mm, has a much reduced activity based on the Ames test for mutagenicity. Whilst we must remember that the meaning of this test in relation to human toxicology is highly questionable, based as it is on the fate of bacteria in a laboratory test condition, the result is important in the event that biological indices become mandatory. (Interestingly a similar result was found many years ago in mouse-skin painting tests, a predictor of tumorigenicity).

#### OVERHEAD SLIDE 4: AMES RESULTS V. CIRCUMFERENCE

##### Passive Smoking

Another issue calling for short term action in response to clear targets is passive smoking. Dr. Thornton has covered the main BAT thrust of challenging poor epidemiology. We also have important lines of in-house research on this topic.

The first is largely of an information-gathering nature and focusses on reliable measurement of ambient smoke concentration both for particulate matter and for specific chemical components. At Southampton we have two environmental rooms that are fully controlled in terms of air temperature and humidity and which can have complete atmosphere changes at pre-set frequency (representing different levels of room ventilation). There are also sampling ports for monitoring chemicals or for subjective rating of smell, eye irritation and so on.

Quite separately, we have looked at smoke concentrations in some typical environments, using some ingenious surreptitious atmospheric monitoring devices. Results are:

#### OVERHEAD SLIDES:5

##### CONCENTRATIONS IN FAMILIAR ENVIRONMENTS

The only satisfactory known means of reducing overall sidestream yield is to reduce the total weight of tobacco burned. Once again Capri offers an interesting opportunity since a simple calculation suggests a 35-40% reduction in sidestream relative to conventional 84 mm cigarettes. For general purposes, where slim cigarettes cannot yet be seen as the answer, increased expanded tobacco inclusion offers the next best direction providing puff number can be maintained.

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#### Category IV

Thus far we have considered product evolution in response to S&H issues. Such activities have reasonably clear targets, are practical and have some reasonable probability of success - judged in terms of keeping abreast of Regulatory requirements.

The key question is whether there exists any more fundamental approaches to our major S&H issues? What technical avenues exist for products will not be embroiled in the S&H controversies, of which causality between cigarette smoking and specific diseases is key?

Scientific information currently available suggests few research directions to follow in terms of cigarette modification. Until we know that we have a problem and what it is, how can we react in a rational manner? If, for instance, changes to minor components of smoke were firmly believed by scientific and medical opinion to be the route to an acceptable cigarette, they would apply strong pressure on the Industry and we would willingly respond. This is not the case.

In our view, the most appropriate fundamental research on S&H issues approach is to monitor all publications on Smoking & Health and where information is incomplete, to support further research at external centres of excellence. Much of it is focussed on unravelling mechanisms of disease and the role of various chemicals in these processes.

#### External Research

Molecular biology provides the modern medical research worker with far more precise tools than the crude techniques, mainly limited to animal studies, of the past. The present-day medical researcher is beginning to study changes taking place at the fundamental cell level and to track the changes including the incidence of abnormalities that are taking place within the cell. Not only can we expect medical research to throw light on the interaction of human cell material with specific chemicals but also to show at the molecular level the reason for so-called genetic predisposition of individuals to various diseases.

#### OVERHEAD SLIDE 6 : HUMAN GENETICS, R.L. WHITE

It is essential that we are thoroughly appraised of such research. Let's look at some examples of where we sponsor research or have consulting arrangements with key workers in these areas.

#### OVERHEAD SLIDE 7+8: MECHANISMS OF DISEASE

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Such work may have a variety of outcomes. It may

1. exonerate smoking from key disease processes
2. point to various components of smoke which are undesirable
3. indicate individuals genetically disposed to disease
4. provide a cure or prevention of such diseases.

Additionally such work should lead to bioassays that have true relevance to human disease mechanisms.

The final leg of the Group-supported long term research towards increasing the acceptability of smoking concerns the so-called 'benefits of smoking'. In this area there is little point in doing 'in-house' research since credibility will be low. In any event the techniques appropriate to studies of this kind will be located in universities or institutes since they will be either medical or psychological. The 'benefit' most widely publicised is in relation to Parkinson's disease where smoking is associated with a reduction in incidence. We are now pursuing interesting developments in relation to ulcerative cholitis and Alzheimer's disease, both of which also indicate signs of "benefits".

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Summary

In summary, we have 80% of our £31.5 m expenditure on R&D aimed at market-oriented goals. This is generating some visible achievements for the Group and I believe, at this level of effort, we are competitive.

On the S&H issues, I distinguish between activities which are essential in response to those currently held scientific views that determine Regulatory requirements and influence consumer habits. Specific chemical components and simple biological test standards fall into this category. This accounts for 12% of our expenditure.

Purposeful long term and truly fundamental research on S&H, in my view, can only be done in collaboration with medical scientists/molecular biologists. The majority of our 7% expenditure in this area is directed at the mechanisms of diseases. In my view this is appropriate currently but may need to be escalated if any interesting leads are identified.

I hope this talk has given the impression of a business-like approach to R&D, closely managed and cost-effective. Of course, our scientists have "brainstorming" discussions and will occasionally advance revolutionary ideas for radical product modification. One such example is based on a nicotine-carrying, synthetic aerosol. So far there is little belief that this avenue really represents a realistic direction to pursue.

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