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NOTE FOR THE TOBACCO STRATEGY REVIEW TEAM

TRANSDERMAL NICOTINE

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1. THE PRODUCT

Nicotine patches are a system of delivering nicotine into the blood stream. Nicotine patches were introduced onto the market as a pharmacy-only product in New Zealand in 1991 and in the U.S.A. they were approved by the Food and Drug Administration for prescription-only sales from 1992.

Pharmaceutical companies manufacturing nicotine patches are currently marketing them for "treatment of nicotine dependence--as a smoking cessation aid, claiming for example, the psychopharmacological stimulant effects of nicotine underlie the tobacco nicotine addiction". This paper also considers issues relating to other potential uses of the transdermal nicotine patch, i.e: dual usage by smokers of patches and cigarettes and choice of the patch solely for nicotine intake.

2. AS A METHOD OF ADMINISTERING NICOTINE

Guidelines for use of nicotine patches issued by the manufacturer Ciba Geigy recommend that the subject should stop smoking completely and use patches for no longer than three months (as treatment period and doses above 52mg per patch have not been evaluated). The guidelines advise against use by non-smokers, occasional smokers and subjects with certain medical conditions.

Neither the standard nicotine patch (e.g. Nicotinell) nor the "Stowic" patch match the delivery pattern or impact of nicotine that is obtained when smoke is inhaled from a cigarette. They do, however, match more closely the pattern of some other forms of tobacco usage, e.g. pipes, cigars, and snuff, although there is some debate on the actual importance of the peaks and troughs in nicotine levels associated with inhaling cigarette smoke.

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Tobacco companies market cigarettes to smokers who enjoy smoking. Part of that enjoyment may relate to intake of nicotine but the smoker decides by the way he smokes whether he receives from 0 to 3 mg nicotine per cigarette. This is quite unlike the steady stream from the nicotine patch which is somewhat akin to an intravenous drip.

While delivering nicotine, patches do not mimic any of the other facets of smoking cigarettes. In addition, as presently developed, they are a totally automatic delivery system and have none of the flexibility of tobacco usage, both as to amount and timing of delivery.

In certain circumstances nicotine-containing patches are potentially dangerous: they can be easily misused or tampered with and, as currently manufactured, can be mistaken for plasters by the elderly or the young. The total nicotine content of individual nicotine patches can be as high as 51 mg, roughly equivalent to the lethal dose for a man of average weight.

Whether by multiple patching, ingestion, or inadvertent nicotine extraction, nicotine availability in patches is sufficient to give rise to the concern that acute toxicity in adults and possible child fatality could occur. Salient questions are: What would be the effect of wearing more than one patch at a time? If patches were discarded carrying significant residuals of nicotine what would be the effect of accidental ingestion by children? What would be the effect of inadvertent extraction of the nicotine in a patch by spilled alcohol (drinks for example)?

3. EFFECTIVENESS OF PRODUCT IN SMOKING CESSATION

The evidence produced by the makers of Nicotinell (Ciba Geigy) is not convincing and does not indicate substantial advantages compared to a placebo. A report by the New York Times (8th April 1992) suggested that those who quit using patches relapse at about the same rate as anyone else. In one series of follow-up studies, six months after having stopped using the patches, the share of subjects not smoking ranged from 0 to 48% compared with a rate of 0 to 40% of those who did not use them.

It has also been suggested that the patches are relatively ineffective unless used in conjunction with some form of behavioural therapy. A consumer group is now complaining to the U.S. Federal Government that advertisements for the patches are misleading by implying that the patch is all that is needed to quit smoking. The group

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is petitioning for requirement of labels warning smokers of the risks of smoking while wearing the patch and that they may also need counselling to help overcome "psychological addiction" of smoking.

4. NICOTINE IN RELATION TO NEURODEGENERATIVE DISORDERS AND OTHER DISEASES

Current advice from consultants to BAT is that the epidemiological basis of a negative association between smoking and incidence of Alzheimer's disease is hardening. There is also good evidence that smoking alleviates the symptoms of Alzheimer's disease. The situation with regard to Parkinson's disease is similar but rather more certain.

These observations are widely believed to be due to nicotine but this has not been substantiated--although the view is consistent with current pharmacological knowledge. One adviser, Dr. S. Wannacott (University of Bath), is of the opinion that nicotine has unique properties and 'protects' nerve cells against damage leading to neurodegenerative disorders. On this basis she believes that the pharmaceutical companies will not easily be able to develop a drug to replace nicotine in relation to Alzheimer's disease. In relation to alleviating symptoms of Parkinson's disease the position is different and another material (l-dopa) is preferred. This is because different regions of the brain are involved.

It has also been suggested over the years that nicotine may be implicated in some smoking-associated diseases, more especially cardiovascular disease. This possibility has not been disproved although Wald and Froggatt (1989) do not find the evidence persuasive.

Generally speaking this area of work is likely to increase the interest in nicotine administration, especially since Alzheimer's disease is likely to be a major health issue in the next century, as life expectancy increases and birth rates fall.

5. POSSIBLE DEVELOPMENTS

The possible development of more sophisticated patches can be foreseen, for example in which compounds other than nicotine could be co-administered. Patches containing reduced amounts of nicotine (and shorter useful contact times) are obviously possible, as are user-controllable patches.

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Such developments would be expected to make the product more acceptable to potential consumers and, possibly, lessen some of the safety concerns associated with it.

6. FUTURE PRODUCT RESEARCH ARRANGEMENTS

The following arrangements have been put in place as part of BATCo's continuing review of transdermal nicotine patches ("TNPs").

- a] Meeting with Stowic Resources (May 19th) - to ascertain their views on their product.
- b] Informal meeting on May 21st with the Chairman of the U.K. Committee on Safety on Medicines (Professor M. Rawlins, University of Newcastle) to hear his views on the probable approach to nicotine patches in the U.K.
- c] Brief behavioural study to compare the efficacy of nicotine patches with smoking in a vigilance task. (Summer 1992 - subject to approval from the University of Reading).

7. PRODUCTION AND PROFITABILITY POTENTIAL

Patches are a low-technology manufacturing challenge probably associated with a low capital investment threshold.

Although TNPs and cigarettes have a common element only in that they both deliver nicotine, the possible diversification of Tobacco manufacturers into the production and marketing of TNPs is not supported by synergistic benefits:-

- i. The technologies involved are distinct.
- ii. The fabrication processes are different.
- iii. There is little commonality in terms of raw materials used.

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- iv. The channels of distribution are different.
- v. Any potential advantage arising from the use of common brand names would be constrained by the fact that TNPs are likely only to be available on prescription.

It is believed that profitability on a unit basis is likely to be substantially greater than cigarettes. Patches will probably be marketed at a retail price closely equivalent to a pack of cigarettes, are most likely to be cheaper to manufacture, and attract no excise duty.

8. MARKETING CONSIDERATIONS

Sales of patches in New Zealand are said to have been better than the makers expected and it is reported that demand is "amazing" in the U.S.A. Analysts have said that the combined sales of the three brands in the U.S. could reach US\$1 billion annually.

The products have only been on the market for five months and the early findings of research on the products' effectiveness as a smoking cessation aid are inconclusive. It is, therefore, difficult to predict their long term sales potential.

Freedom of Choice. It could be argued that patches represent an alternate product for nicotine users (along with gums, snuffs and inhalants), and thus having the potential to be marketed as a cessation aid or a means of cutting down smoking. They would however need to be clearly positioned as not being an alternative to cigarette smoking, since this would erroneously suggest that the cigarette itself is a simple nicotine delivering device.

Erosion of smoking franchise. By topping up the wholebody nicotine reservoir, patches might be expected to reduce daily consumption of cigarettes. We currently

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know insufficient about the potential demand for such products and, hence, the potential business trade-off value between patches and cigarettes is unknown.

Dual Usage Risks. Patches do not appear to be an effective cessation aid in the medium term. There is, however, the possibility that people will use them in addition to cigarettes, with the possibility of:-

- (a) nicotine overdosing for regular smokers;
- (b) habituation to continual body reservoir nicotine requirement; and
- (c) consequential debate that patches actually synergise rather than antagonise the smoking habit.

Patches would therefore not appear to be immediately appropriate for marketing for use by smokers as an alternative product in circumstances where smoking is proscribed e.g. airlines, theatres, etc.

Association with Poison/Drug. However insulated from cigarettes the patch alternative may be, it shares a known common feature, nicotine. Patches may focus debate on nicotine as a psycho-active component of cigarettes, diverting attention from other valid aspects of smoking satisfaction (taste, texture, visual/tactile stimuli) and potentially focusing on nicotine as a drug and a poison.

Erosion of Brand Value. Patches do not offer great marketing flexibility in terms of product and brand image differentiation since the only variables currently available are amount and relative speed of dosing. If the nicotine centrality argument generalises back to cigarettes, which are in themselves relatively homogeneous at product level, some consequential brand value erosion could follow.

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Marketing Competence. Patches are most likely to be controlled as prescription-only drugs which is not an area of marketing competence for BAT. Given the 'drug' profile of patches it would also be important to separate the business completely from cigarette marketing.

9. OTHER CONSIDERATIONS

The classification of nicotine patches as a drug delivery system may or may not apply in all countries. In the U.S.A., tobacco products are not regulated by the F.D.A. unless health claims are made, e.g. "Premier" came under the scrutiny of the F.D.A. If tobacco companies were to market nicotine patches, this could be seen as a move towards tobacco companies being regarded as pharmaceutical companies. The anti-smoking lobby has in the past offensively referred to the tobacco industry as "no better than drug pushers".

The issue of addiction has been widely debated in respect of smoking and the potential use of nicotine through patches is likely to lead to further public interest in that issue. The 1988 U.S. Surgeon General's Report observed that nearly half of all living adults who ever smoked have quit but still concluded that nicotine is addictive. The tobacco industry's response is that addiction is a frequently misused term that has become a catch phrase for many habits. In product liability litigation tobacco companies assert that people continue to smoke because they enjoy it and that it is not appropriate to term smoking as addictive when millions of smokers have given up voluntarily and without assistance.

10. SUMMARY

In view of the different product characteristics of TNPs and smoking, current designs of TNPs would not appear to be a serious threat to the tobacco industry. It is, however, difficult to make confident predictions about the likely success of TNPs although there are clearly some major issues associated with their widespread use.

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On the assumption that they are viewed by consumers as an acceptable and valuable method of nicotine intake, TNPs have the potential to be a highly profitable business activity. This is because the likely retail price of such patches is similar to that for a pack of cigarettes whilst the manufacturing costs are likely to be lower than those for cigarettes and TNPs attract no excise duty.

Arguments against an extension of business activity into the production and marketing of TNPs are:-

- i. TNPs are commodity products, differentiated by very little except perhaps speed of action. They will, therefore, be very difficult to invest credibly with product/brand image differentiation.
- ii. BAT would be placed in an invidious and legally difficult position if it promoted the product:-
 - (a) As an aid to stop smoking - if, as preliminary studies suggest, the patches are not effective as a smoking cessation aid, marketing it would be likely to lead to an allegation of misleading claims being made for the product. It should be noted, however, that if the product is ineffective as a cessation aid this is consistent with the tobacco industry position that smokers are not physically "addicted" to nicotine but choose whether to smoke or not, and therefore they have no need for such an aid.
 - (b) As a product which consumers freely choose in order to satisfy their desire for nicotine uptake, given the fact that TNPs are likely to be available only on prescription.

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- (c) As a dual-usage product for smokers given the lack of research done on the safety of use of the patches in conjunction with smoking
- iii. Patches are capable of being misused, and this is likely to lead to their distribution being restricted and/or potential litigation.

There are no significant technological or processing synergies between tobacco manufacturing and the production of patches other than the use of tobacco waste as a source of nicotine.

Thus, from a business opportunity viewpoint, TNPs should be viewed as a high profit potential but high risk venture.

Committee

11. RECOMMENDATIONS FOR FURTHER ACTION

If it is decided that further investigation of the role of the nicotine patch is to be made, it is recommended that:-

1. The potential of nicotine patches should continue to be investigated, particularly against the possibility that improved patches are developed
2. Consideration should be given to supporting research projects in relation to Alzheimer's disease and Parkinson's disease in view of the probable therapeutic value of nicotine with regard to these conditions and leverage of the positive perception of nicotine.
3. The likelihood of a scenario emerging where people consume both TNPs and tobacco products should be evaluated and estimates made of the business trade-off value therein.
4. Qualitative consumer research on the scope for insulating cigarette perception/usage from patch perception/usage and the scope for branding differentiation of patches should be investigated.

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5. If the production of TNPs were considered to be an acceptable proposition, the business potential and viability should be reviewed by a project team specifically brought together for this purpose under the auspices of BAT Industries rather than being based within one of the BAT tobacco operations.

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