ITEM 6

ADVICE TO
THE EXPERT ADVISORY COMMITTEE ON DRUGS
ON:

An overview of BZP

May 2007

Executive Summary

This paper provides members with further documents relating to BZP. These documents provide an opportunity for the Committee to review and determine what additional advice the EACD might want to give to the Minister in light of such developments.

Background

BZP was considered by the EACD in a previous meeting held 29 November 2006. The Committee reviewed a number of documents and gave advice to the Associate Minister of Health that evidence now indicated BZP posed a 'moderate risk of harm' and BZP, phenylpiperazines and related substances would be appropriately classified as class C1 drugs in the Misuse of Drugs Act 1975.

The Minister announced this advice in December and a public consultation closed on April 23. The Ministry of Health has analysed these submissions and a draft report of this analysis is enclosed. Also enclosed are peer reviews of the studies by The Medical Research Institute of New Zealand and the University of Auckland as well as new research by Theron et al, Consumer Link and results from the ESR's testing of "Torque."

Papers

1. *Theron et al (2007) "Benzylpiperazine based party pills' impact on the Auckland City Hospital Emergency Department Overdose Database (2002-2004) compared with ecstasy (MDMA or methylenedioxymethamphetamine), gamma-hydroxybutyrate (GHB), amphetamines, cocaine, and alcohol".*

This research (Attached) reviewed Auckland City Hospital's Emergency Department's overdose database for the years 2002, 2003 and 2004, for 'herbal ingestions' and 'party pills.' The study compared the number of presentations for BZP based 'party pills' to the number of presentations for alcohol, and also the illicit drugs MDMA, GHB and cocaine. The study recorded one BZP presentation in 2002 (0.07% of total overdoses), 4 BZP presentations in 2003 (0.29% of total overdoses) and 21 BZP presentations in 2004 (1.58% of total overdoses). Data is not currently available for presentations during 2005 and 2006.

The study shows an increasing trend of BZP related hospital presentations as would be expected with an increasing prevalence of BZP use. Of note however is that even in 2004 when the highest number of presentations was recorded, the presentation rate (1.58%) was still considerably lower than alcohol (60.87% of total overdoses), GHB (6.4% of total overdoses) and amphetamines (3.69% of total overdoses). The authors of the study note that

"With a consumption of 200,000 tablets/month, a presentation of 21 patients to the emergency department in a year [2004] is relatively small."

The authors also note that of those presenting for a BZP related condition, the most common symptoms were anxiety, palpitations, nausea, and vomiting and that 38% of those presenting required only reassurance, 46% were treated with IV fluids and 23% were given diazepam for anxiety. While data was not given for the treatment requirements of other drugs it might be assumed that more intensive methods would have been required for treating adverse reactions to such substances.

The authors of this study note that their findings contrast that of Gee et al (2005), where presentations to Christchurch hospital appeared to be more common and threatening. With 15 out of 60 people suffering 'toxic seizures' as a result of 'party pill' use. An explanation for this discrepancy is offered that Auckland city retailers and manufacturers of 'party pills' are/were more likely to adhere to the voluntary code of practice provided by STANZ than those in Christchurch. STANZ members self regulate to a maximum of 200mgs per dose. The Committee has previously noted products with up to 500mgs of BZP per pill/capsule commonly available in Christchurch.

STANZ has submitted on the proposed classification of BZP and related substances, noting that this research puts into context the Christchurch reports and indicates a low risk of harm. STANZ has also alleged that the adherence by Auckland city distributors to a code of practice including limiting BZP to 200mgs per pill/capsule justifies the discrepancy in presentations and harms between Auckland and Christchurch hospitals and evidences this argument as a basis for further regulation, rather than classification under the Misuse of Drugs Act 1975.

Dr Chris Wilkins, SHORE, Massey University was approached to provide analysis on harms between Auckland and Christchurch using data from the National Household Survey 2006. Due to restrictions in sample size it was considered unfeasible to compare responses from the two cities and instead a comparison was made between the North and South islands. It was found that:

- Statistical analysis did not suggest South Islanders were more at risk than north islanders

- There were differences between the islands in terms of the 'party pill' most commonly used; "Charge" was the most popular product in both islands while "Kandi" was the second most popular in the North and "Frenzy" in the South.

- North Islanders (16%) were more likely to have used party pills in the last year than South Islanders (12%)

- There were no differences between the islands in terms of having used 'party pills' for 24 hours or more continuously, the amount of pills used on

a typical occasion and the greatest amount of pills used on a single occasion.

- There were no differences in the average potency of 'party pills' between the islands

- The analysis did not indicate there was any difference between the islands in terms of experiencing negative events through the use of 'party pills.'

Initially these statistics show little variation in use and harms between the two islands. However, the Ministry understands that a more popular product in the North Island ("Kandi"), is a STANZ product, while the more popular product in the South Island ("Frenzy") is not. When the Ministry arranged for testing of "Kandi" it was found that the level of BZP did not deviate above the stated dose of 90mgs. "Frenzy," however, stated 85mg of BZP but the actual quantity found ranged up to 157mgs.

The EACD has previously expressed concern in regard to the robustness of the results of this testing which were undertaken by the pharmaceutical division of ESR, therefore the results in this paper may need to be treated with caution. However when taken at face value the testing indicates that STANZ members are producing more consistent products. While the data above note that there were "no differences in the potency of the pills between the islands", the deviation between stated content and actual content of a product may result in South Islanders taking a larger dose of BZP than North Islanders, due to discrepancies in the manufacturing between two prominent products in each island.

2. ESR Testing of "Torque"

There has been recent heightened media interest in BZP related harm concerning the admission of Greymouth 'disk jockey' Ben Rodden to Christchurch hospital after he collapsed at a dance party. It was initially alleged that Mr Rodden had consumed a BZP based 'party pill' called 'Torque' and that this 'party pill' may have been the cause of his collapse. There was also speculation in the media that the 'party pill' may have contained controlled substances such as MDMA. The Ministry of Health contracted ESR to test a sample of 'Torque' for the presence of illicit substances, and also to assess the consistency of BZP levels between doses of the product. Results from the testing which are attached to this paper indicated that "Torque" did not contain any illicit substances and the BZP content was low with a range of 20-40mgs per pill. The ESR also noted that there were comparatively very high levels of caffeine present although were unable to quantify this finding.

3. *Consumer Link survey (2007) Comparative risks of legal party pills, alcohol and illegal drugs.*

This study commissioned by STANZ employed a survey of 200 individuals aged between 18 and 29 years with 60% of responses received from Auckland, 20% of responses received from Wellington and 20% of responses

received from Christchurch, New Zealand. The rational for the survey was to contrast adverse effects from 'party pills' with that of alcohol and illicit drugs. Key findings from the survey allege that 'party pills'

- produce fewer adverse health effects than alcohol
- are less likely to result in physical injury
- are much less likely to provoke aggressive behaviour
- are not identified with traffic accidents
- create far fewer issues of dependency of loss of control.

When interpreting these findings it may be appropriate to consider the possibility of bias or leading questions. Firstly this survey concludes that 'party pills' produce fewer adverse health effects than alcohol. This appears to be cantered around an analysis of questions relating to vomiting, memory loss, physical injuries and visits to accident and emergency. The survey does not take into account the possibility of seizures as noted by Gee et al (2005) going unnoticed, nor does it consider that despite party pills being legal, they are still stigmatised and viewed unfavourably by some. As such, presentations to hospital or even admittance of harm in general are arguably less likely to be disclosed in relation to the consumption of 'party pills' that in comparison to use of alcohol. This may bias an accurate comparison of negative effects between the two substances.

This study also notes that '50% of respondents believed illegal drug use would increase should party pills be banned.' In interpreting this finding it should be noted that respondents believing this increase would happen, and respondents disclosing that they would use more illicit drugs themselves, are separate issues. With the potential classification of BZP gaining such widespread coverage in the media, a common rebuttal by the 'party pill' industry has been to publicise the likely hood of a shift towards the use of illicit stimulants should a classification occur. The finding that 50% of respondents believed illegal drug use would increase may not indicate any potential for this trend, instead it shows that the respondents surveyed have potentially been influenced by ongoing debate in the media.

4. <u>Analysis of Submissions</u>

The Ministry of Health received 64 submissions regarding the potential classification of BZP, phenylpiperazine and related substances. One of the submissions included a petition with over 9000 signatures and three petitions were considerably complex. The submissions have been analysed by Allen and Clark and a draft report is attached to this paper. The Ministry intends to bring a final version of this summary to the table for this meeting.

Amongst themes raised in the analysis of submissions there were concerns regarding the EACD process, including that the Committee:

- recommendation relied on unpublished and un-replicated research/reports that had not been under a robust peer review process (7, 37, 44, 54, 61/61a)

- has not defined moderate risk and has not undertaken a formal risk assessment (37)
- was asked only to evaluate harm not potential benefits (42, 54)
- has not evaluated other harm minimisation options such as tighter regulation (19, 54)
- has relied on information from two sources (letter from the National Poisons Centre and report form the MRINZ) that are subject to serious challenge (7, 37, 54)
- has formed conclusions from results of recent studies in which there has been inaccuracies as well as misinterpretation and misrepresentation of the facts. (7, 37, 54)
- has relied on research where the researchers could be viewed as having been compromised by the need to bid for funds or having a conflict of interest because of funding source (35, 55)
- does not appear to have considered and provided recommendations, as required by legislation, on the practicalities of imposing restrictions or the ability to enforce those restrictions and requirements (61/61a).
- A drug policy/law reform agency (42) recommended change to the makeup of EACD to include lay people.

The full draft report of the analysis of submissions is 100 pages long. The Ministry of Health expects to receive a final report by 30 April inclusive on an executive summary detailing the main findings and recommendations in the analysis. This summary will be made available to committee members for consideration and comment at the meeting on 3 May.

5. *Peer review of studies*

"Legal Party Pills and their use by young people: summary report of findings" Sheriden and Butler (2006), University of Auckalnd.

Since this study was considered by the Committee on 29 November 2006, peer reviews have been conducted by Dr Marc Wilson, Deputy Head of School of Psychology, Victoria University and Melissa Girling and Lanuola Asiasiga, qualitative researchers at SHORE, Massey University. The Reviews are generally supportive of the methodology used in this study however some feedback is given relating to;

- Screening of participants
- Recruitment techniques
- Interview methods, and
- Reporting style

These peer reviews are attached to this paper. Comment has also been sought on these reviews by the authors of this study, and is expected to be made available to the Committee at the meeting on 3 May.

"The benzylpiperazine (BZP) / trifluoromethylphenylpiperazine (TFMPP) and alcohol safety survey" Thompson et al (2006),Medical Research Institute of New Zealand.

This study was also considered by the Committee at the 29 November 2006 meeting. The Ministry of Health has recently received a peer review of this study by Andrew Jull, research fellow and doctorial candidate at the Clinical Trials Research Unit, University of Auckland. The review raises a number of issues with the study relating to:

- Reporting style
- Sample size calculation
- Definition of serious adverse events
- Early stopping of the trial
- Fasting, Tobacco and Caffeine abstinence

The study concludes that 'given the many concerns noted about the design, conduct and analysis of the trial the conclusion reached by the authors that party pills commonly cause severe adverse reactions cannot be supported' and 'there are insufficient grounds for drawing any conclusions wither in support of the hypothesis that party pills cause adverse events, or against it.' The review is attached to this paper.

Another peer review of this study was supplied by STANZ in their submission on the proposed classification of BZP. The review is conducted by Associate Professor Michael Dawson, Head of Department Chemistry, Materials and Forensic Science, University of Sydney and Dr Alex Wodak Director, Alcohol and Drug Service, St Vincent's Hospital. The review notes methodological flaws relating to:

- Co administration of BZP and TFMPP
- Time of study
- The unnecessary insertion of a venous cannula
- Fasting of participants
- Use of commercial 'party pill' products

The review concludes that 'the design of the study is fundamentally flawed to the extent that it is incapable of establishing that BZP poses a moderate risk of harm and should not be relied on by the EACD and/or the Minister as basis for making any scheduling changes.' The review is attached to this paper.

The Ministry of Health is also awaiting a peer review of this study by Dr Peter Black, Department of Pharmacology University of Auckland. It is expected that all peer reviews and comment from the authors will be made available to the Committee at the meeting on 3 May.

References

Theron, L, Jansen, K, Miles, J (2007)., *Benzylpiperizine-based party pills' impact on the Auckland City Hospital Emergency Department Overdose Database (2002–2004) compared with ecstasy (MDMA or methylene dioxymethamphetamine), gamma hydroxybutyrate (GHB), amphetamines, cocaine, and alcohol.* Accessed 24 April 2007 from http://www.nzma.org.nz/journal/120-1249/2416.