ADVICE TO THE EXPERT ADVISORY COMMITTEE ON DRUGS ON:

FURTHER ADVICE ON PIPERAZINES
AN UPDATE ON EVENTS POST FEBRUARY 2004

Executive Summary

This paper presents an overview of recent research findings and significant media events since the Ministry of Health previously provided advice to the EACD on benzylpiperazine (BZP) in February 2004. Available research results are included and an outline is provided for projects due to report to the Committee before the next meeting takes place. Also included are the details of significant media events, as well as petitions and submissions that the Ministry of Health has received regarding the controls upon, and legal status of BZP.

Background

BZP was considered by the Committee in April 2004. It was concluded that, based on the criteria that the EACD must apply before making a recommendation to the Minister, there was insufficient information available on which to base a recommendation to classify this substances in the Misuse of Drugs Act 1975. The Committee considered that "more information on the health effects of BZP and similar substances should be obtained," and the prevalence of BZP use should be investigated.

The Committee further considered BZP in June 2005 and noted that the quantity of the substance imported had increased from a 3 year average of 400kgs to approximately 1100kgs and that doses of BZP contained in 'party pills' had in some products increased to 750mgs. Members also agreed that a priority for BZP research should be to focus on the level of uncertainty around effects of long term, or chronic use, and also to gauge an understanding of the prevalence of polydrug use with BZP and alcohol and/or other drugs.

Substance Identification

Piperazines are stimulant type substances that form the main active ingredients present in almost all 'party pills', and are also available for purchase as a raw powder. In the last 5 years New Zealand has witnessed growth in the industry, both in the quantity of products being consumed and in the number of manufacturers of 'party pills' entering the market. The EACD has previously given advice on BZP, the base ingredient found the majority of 'party pills,' and also considered the significance of triflurophenylmethylpiperazine (TFMPP) in this context. The industry has recently moved to also include the piperazine p-fluorophenylpiperazine (PFPP) in selected party 1-(meta-chlorophenyl)piperazine pill products¹ (MCPP) and 1-(4methoxyphenyl)piperazine (meOPP) may also be currently used for recreation purposes.2

¹ http://www.funkpills.com/index.php?act=viewProd&productId=50

² www.wackyherbs.com

Current Classification

BZP is a 'Restricted Substance' as specified in the Misuse of Drugs Amendment Act 2005. As such the sale of products containing BZP are confined to those over 18 years of age and restrictions have been placed on the nature in which products containing BZP may be advertised or distributed. Other piperazines including TFMPP and PFPP have not been placed in either controlled or restricted drug schedules and therefore are subject only to industry self-regulation.

Research

Massey University (SHORE)

Earlier this year the Centre for Social and Health Outcomes Research and Evaluation (SHORE) at Massey University published a report titled "Legal party pill use in New Zealand: Prevalence of use, availability, health harms and 'gateway effects' of Benzylpiperazine (BZP) and Triflurophenylmethylpiperazine (TFMPP)." The study conducted a random sample of 2,010 people aged between 13-45 years. Findings that may be of interest to the Committee are:

- 20% of the sample had ever tried legal party pills and 15% of the sample had used legal party pills in the last year. Of this last year use, nearly half of the sample had only consumed party pills 1-2 times in this period.
- One user (0.6% of the sample) reported they typically injected their party pills
- The mean number of party pills taken on a typical occasion was 2.6 pills; 10.9% of the sample had taken 8 or more pills at one time.
- 32% of the sample stated that they 'drink more alcohol' than normal when using legal party pills.
- The physical problems most commonly experienced by users from legal party pills use were 'insomnia,' 'poor appetite', 'hot/cold flushes', 'heavy sweating,' 'stomach pains/nausea' and 'headaches.' 4 users reported 'fainting/passing out' and 1 user reported having 'fits/seizures'.
- Psychological problems most commonly reported by users were 'strange thoughts,' 'mood swings,' 'confusion' and 'irritability'.
- Of the sample that consumed party pills in the last year, 2.2% could be classified as dependent upon them by scoring greater than 4 on the Short Dependency Scale, a measure that had previously been validated for detecting amphetamine dependency.³

University of Auckland (School of Pharmacy)

A second study funded by the National Drug Policy Discretionary Fund has been conducted by Sheridan and Butler (2006) and is titled "Legal party pills and their use by

³ Wilkins et al (2006) Legal party pill use in New Zealand: Prevalence of use, availability, health harms and 'gateway effects' of benzylpiperazine (BZP) and triflourophenylmethylpiperazine (TFMPP).

young people". This study employed a qualitative research design and obtained results from both young people aged 16-24 years, and also key informants including representatives from alcohol and other drug services, health services, education, youth organisations, health promotion, the legal party pill industry, event organisation and national drug organisations.⁴ The Secretariat has obtained a recent draft report of the study. Key results include:

- BZP use, as well as being linked to the 'dance party' culture for the purpose of 'staying power' and 'increased socialization', is also being consumed for 'functional means' such as for studying assistance and weight loss.
- The same similarities in use patterns of MDMA (ecstasy) are being found with BZP, including the use of other substances to manage the 'comedown' period and also negative effects such as 'mood fluctuations' and 'depression' in the period after taking the drug.
- Young people appear to be engaging in risky behaviors with regard to legal party pill use. Examples include: mixing substances, driving whilst under the influence and taking larger doses than recommended. However, the study found limited evidence of significant harms being experienced as a result of such activities.
- Young people were generally aware that certain behaviors could lead to increased risk with taking legal party pills and were considered to be well informed in regard to harm reduction messages such as not mixing BZP with alcohol.
- Young people were more likely to seek advice from their friends rather than consulting packaging or leaflets for information on safe use, appropriate dosage, etc.
- Given the 'inferior high' and unpleasant comedown, legal party pills were not generally considered a viable substitute for ecstasy amongst ecstasy users.

The authors have agreed that a final version of this study will be made available for consideration by the EACD.

National Poisons Centre

The National Poisons Centre at the University of Otago are in the final stages of compiling research into cases of poisoning due to piperazine-based party drugs (PBPD) in New Zealand. The results, which are expected to be made available to the EACD, will provide information on:

• Specific toxicology knowledge of PBPD, their effects, toxic doses and medical management of poisoning.

⁴ Sheridan, J and Butler, R., (2006) Legal party pills and their use by young people. *School of Pharmacy, The University of Auckland.*

- Recommendations on the safety of PBPD to relevant groups such as the Ministry of Health, health professionals, and the general public.
- Advice to the public on the issue of PBPD poisoning, including prevention education.

University of Auckland (Dr Bruce Russell)

A further study is taking place at Auckland University to investigate the effects that both BZP and TFMPP, either in combination or alone, have on memory and neurological function. This study will be the first controlled trial to investigate the effects of TFMPP and will also extend the limited literature available on BZP.

It is expected that a report detailing preliminary results will be made available for consideration by the EACD.

Medical Research Institute of New Zealand

This study conducted by the Medical Research Institute of New Zealand (MRINZ) aimed to investigate the effect of BZP, either alone or in combination with alcohol, on driving performance. An interim safety analysis was undertaken after 35 subjects had completed the investigative models and due to concerns about the frequency, nature, and severity of the side effects that participants had reported, a decision was made to halt the study. 41% of participants in the BZP/TFMPP group (with or without alcohol) suffered an adverse event following use of the piperazines. No severe events were reported in the placebo, or alcohol only groups. Examples of adverse events reported include:

- Severe agitation, anxiety
- Severe headache, fatique
- Severe anxiety, panic attack (required medical treatment)
- Hallucinations, agitation & anxiety
- Severe vomiting, confusion
- Severe migraine ('worst ever')⁵

The authors of the study have indicated that a revised report on the safety effects of party pills containing BZP and TFMPP will be made available for consideration by the EACD.

Ministry of Health Pill Testing.

The primary rationale for this research was to pharmaceutically test a number of legal party pills for consistency in levels of piperazines between doses of a given product. A

⁵ Thompson et al (Unpublished report) (2006) The safety effects of party pills containing Benzylpiperazine (BZP) and Trifluoromethylpiperazine (TFMPP) with and without alcohol.

secondary aim was to identify what, if any piperazines other than BZP and TFMPP are now being included in legal party pills. The need for this testing has come from the realisation that certain internet sites⁶ are distributing the piperazines 1-(metachlorophenyl)piperazine (MCPP), 1-(4-methoxyphenyl)piperazine (meOPP) and p-fluorophenylpiperazine (PFPP) along side BZP and TFMPP for recreational use. The products to be tested were identified by studies from SHORE, the University of Auckland and the Ministry's knowledge base and represent the products most commonly reported as being used by participants from each of the seven major manufacturers.

A second round of testing is currently being proposed to the target the party pills in which the effects claimed are not consistent with traditional use of BZP and/or TFMPP, and which may contain comparatively high quantities of active ingredients. The Ministry has also received allegations that some products may potentially contain controlled drug analogues. The Ministry will consult with ESR on this, and include these products in future tests if appropriate.

The results from the first round of this testing, which is being undertaken by the Pharmaceutical Division of ESR will be available for consideration by the EACD at the upcoming meeting.

Medical cases

Dr Paul Gee (Christchurch Hospital)

A report has been published by Gee et al (2005) titled "Toxic effects of BZP-based herbal party pills humans: a prospective study in Christchurch, New Zealand". The study documented all presentations associated with piperazine use between 1 April and 1 September 2005 and reported: "A total of 61 patients presented on 80 occasions to the Emergency Department of Christchurch Hospital and patients that had an adverse reaction had taken an average of 4.5 tablets/capsules. Patients with mild to moderate toxicity were classified as experiencing symptoms such as insomnia, anxiety, nausea, vomiting, palpitations, dystonia and urinary retention. Some adverse reactions persisted up to 24 hours after ingestion and 15 toxic seizures were recorded with 2 patients suffering life-threatening toxicity". This study concludes by stating that BZP "can have a narrow safety margin" and may cause "unpredictable and serious toxicity in some individuals".

⁶ www.wackyherbs.com

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⁷ Gee, P. Richardson, S. Woltersdorf, W and Moore, G., (2005) Toxic effects of BZP-based herbal party pills in humans a prospective study in Christchurch, New Zealand. *The New Zealand Medical Journal*, 118

Dr Mohammed Alansari (Waikato Hospital)

Alansari and Hamilton (2006) have published a report investigating the nephrotoxicity of BZP. The study investigates the case of a 17 year old male who consumed 5 BZP-based party pills and a small amount of alcohol. A few hours after ingestion the subject developed bilateral loin pain that worsened over the next 24 hours. 36 hours after ingestion he was admitted to hospital and then later transferred to a specialised renal unit. The subject was discharged in due course and his kidney function returned to baseline levels after 3 weeks. The authors conclude that "the acute renal failure observed here may be related to a direct toxic effect of the party pills on the kidneys".8

Petitions

On 23 March 2006 Jacqui Dean, MP and 7,500 others presented a petition requesting that

 "Parliament review the classification of Party Pills with that review encompassing the health, psychological, social and community safety impacts of these substances."

On 13 September 2006 Roy Ramsey from Drug Arm (Blenheim) Youth Workers Forum and 3,600 others presented a petition requesting that:

 "Parliament legislates banning the use, manufacture and sale of party pills due to the negative health, psychological, and social impacts of these substances upon our community's safety."

The Ministry of Health has provided reports to the Health Select Committee on the above two petitions and the Clerk of the Committee has indicated that the Committee will consider both petitions in tandem early in 2007.

Submissions

Subsequent to the petition presented by Jacqui Dean, the Member has also provided the EACD with a submission expressing her concerns over the way in which party pills are affecting New Zealand. The Secretariat notes that the EACD is considering this submission as an agenda item.

Media Events

BZP has continued to receive attention in the media with coverage now extending to international agencies. Examples of some recent media stories are attached as appendices to this report.

⁸ Alansari, M and Hamilton, D., (2006) Nephrotoxicity of BZP-based herbal party pills: a New Zealand case report. *The New Zealand Medical Journal, 119*

References

Alansari, M and Hamilton, D., (2006) Nephrotoxicity of BZP-based herbal party pills: a New Zealand case report. *The New Zealand Medical Journal, 119*

Gee, P. Richardson, S. Woltersdorf, W and Moore, G., (2005) Toxic effects of BZP-based herbal party pills in humans a prospective study in Christchurch, New Zealand. *The New Zealand Medical Journal, 118*

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Sheridan, J and Butler, R., (2006) Legal party pills and their use by young people. School of Pharmacy, The University of Auckland.

Thompson et al (Unpublished report) (2006) The safety effects of party pills containing Benzylpiperazine (BZP) and Trifluoromethylpiperazine (TFMPP) with and without alcohol.

Wilkins et al (2006) Legal party pill use in New Zealand: Prevalence of use, availability, health harms and 'gateway effects' of benzylpiperazine (BZP) and triflourophenylmethylpiperazine (TFMPP). Centre for Social Outcomes Research and Evaluation. Massey University.

Appendix one

Pill casualties down 50% 27 September 2006 By ANNA CLARIDGE

The number of party-pill users going to Christchurch Hospital's emergency department has halved in the past year.

Doctors are seeing just two patients a week, compared with a high of six a week at this time last year, and the number arriving with seizures and blackouts has also dropped.

Emergency medicine specialist Dr Paul Gee said that while numbers were down, the department was still seeing patients as young as 14 with overdose symptoms.

In one case, a two-year-old had consumed his mother's supply of party pills.

"I think (the numbers have dropped) because people realise that it can be dangerous and are using it a bit more cautiously," Gee said.

"Also, most people who want to try, have, and as (the Massey University) study shows, more than half don't like the experience and will stop.

"In fact, most who use are of the opinion that BZP should be banned."

Party pills, marketed as herbal but containing the drug benzylpiperazine (BZP), leave many users feeling agitated, dehydrated and strung out.

The pills caught the headlines two years ago after several overdoses prompted medical professionals to speak out. The drug is banned in the United States.

Gee said the fall in the number of Christchurch patients may be a reflection that the herbal-high craze has passed. His comments are backed by a study released this year by Massey University's Centre for Social and Health Outcomes Research and Evaluation that showed one in five young people had tried the pills and 50 per cent said they would not try them again.

The Government last year created a class D classification for BZP-based pills and restricted their sale to people aged over 18, but Gee said this was not behind the drop in patient numbers.

The Government had commissioned three studies into the pills, and Associate Health Minister Jim Anderton said he would not make a decision on whether to ban them until the results were in.

Mairead Harnett, a researcher with the National Poisons Centre in Dunedin, said staff were just finishing a study of the known BZP poisoning cases treated at hospitals in the past three years. "We are focusing on dose, symptoms and the medical management," Harnett said.

"Our ultimate aim is to be able to provide more accurate and comprehensive poisoning management advice to the public and hospitals."

Over a two-year period, the centre had about 180 calls and at least 120 suspected cases of poisoning.

Appendix Two

Medics advise total avoidance of party pills

10.30am Wednesday November 1, 2006

Party pills containing the ingredient Benzylpiperazine (BZP) can cause seizures, paranoia and hypothermia, and people should stay away from them altogether, the New Zealand Medical Association says.

People with a history of psychiatric illness in particular should avoid taking the pills, which should not be mixed with alcohol, other drugs or prescription medicines.

The legal status of pills containing BZP, originally developed as a drug to treat cattle with worms, is under question, and the association recommended in a statement today that people should not take them until their status is determined.

NZMA chairman Ross Boswell said there were growing concerns about the safety of BZP-based party pills.

A recent study at Christchurch Hospital had examined 61 patients, presenting 80 times to the emergency department.

Patients with adverse effects had taken an average of 4.5 tablets or capsules and suffered symptoms including insomnia, anxiety, nausea, vomiting, palpitations, and muscle spasms.

Fifteen toxic seizures were recorded and two patients suffered life-threatening conditions.

Dr Boswell said if people did take the pills they should make sure they stuck to the manufacturer's recommended dose of one or two pills, and not combine them with other stimulants.

While the pills were often marketed as "herbal", there was nothing herbal about them, he said.

Further research on the effects of BZP is soon to be released by the Health Minister, Dr Boswell said.

NZPA

Appendix Three

Legal high: the party pills stronger than ecstasy

The selection of legal, mind-altering drugs, similar to cocaine, ecstasy and speed, are being legally sold over the counter to anyone aged over 18, in at least 13 so-called 'head stores' around the country, as well as stalls outside big music festivals and gigs.

Support groups are becoming increasingly concerned about the recent explosion of pep pills because they contain the dangerous substance benzylpiperazine (BZP) which acts as a substitute for MDMA, the banned substance in ecstasy and speed pills.

Despite warnings from experts that they cause heart problems and panic attacks, the Government said it has no plans to ban them. However, it is backing a new drugs awareness campaign being launched to warn young people of the dangers of these "legal highs".

The Department of Health said BZP is not a scheduled substance under the Misuse of Drugs Act, but its status is kept under constant review. However, it is banned and classified as a Class A substance in the US since 2002.

In a statement, the Department of Health said it "reviews any evidence that substances are being abused and are causing significant harm to public health. For example, earlier this year the law surrounding pyscho- tropic mushrooms in their raw state was clarified in the light of evidence of increased availability and significant harm being done".

The National Advisory Committee on Drugs (NACD) discussed the emerging trend for the first time at a meeting two weeks ago. It said it will gather information on BZP and consult with its EU counterparts before making any recommendations to the Government.

Support groups say Jax pills and Smileys — both containing BZP and five times the strength of any other dance pills — are becoming the drug of choice for college-goers and even Leaving Cert students, who see them as a more accessible and safer alternative to drugs such as speed, Ecstasy and LSD.

Dr Des Corrigan from the Trinity College School of Pharmacy, said BZP is no safer than any other drug. "The main concern would be dehydration and the risk of heat stroke. The other concerns would be head- aches and a flu like hangover that lasts a few days. There is also the risk of panic reactions and high blood pressure. It would surprise me if anyone would think they are getting anything safer," Dr Corrigan said.

Michael McDonagh of the Drugs Awareness Programme (DAP) said caffeine and herbal tablets have been around for a long time, but since May they are getting more and more calls about these pills, which are a bit more serious in what they contain.

"We are concerned that they will become a big story at exam time next year," Mr McDonagh said.

DAP and the Health Service Executive (HSE) are planning an awareness campaign for early next year, which will advise young people, their parents, and professionals about the dangers of these drugs.

DAP said since the ban on magic mushrooms earlier this year it has received thousands of calls relating to Salvia, a more dangerous but legal hallucinogen.

DAP is calling for the regulation of the socalled 'head stores' which sell these pills, along with growing kits, pipes and other accessories.

Appendix Four

David Braithwaite October 10, 2006 - 4:18PM

The online purchase of a New Zealand-made drug touted as the "strongest energy pill legally available in the world" could land NSW residents in jail, police have warned.

The benzylpiperazine-based products are legal in New Zealand and marketed online under names such as "Dark Angel", "Grin", "Red Hearts", "Majik", "Kandi", "Frenzy", "Altitude" and "Humma", police said.

Paul Dillon, information manager at the National Drug and Alcohol Research Centre in Sydney said the drug was a stimulant.

"It basically gives you a buzz," he said.

New Zealand had created a new classification of drug to cover benzylpiperazine-based products, he said.

"Some are like amphetamine and some are like ecstasy, in a milder form," he said.

Research into the drugs, along with lobbying to legalise them, was driven by NZ entrepeneur Matt Bowden, because he was concerned about the rise in methamphetamine, or "speed", use in NZ.

Mr Dillon said the problem was, like with all drugs, they could be harmful and some people were taking more of them to get a high.

NSW residents in possession of the synthetically produced drugs faced two years' jail, the commander of the Drug Squad, Detective Superintendent David Laidlaw, said.

"We have identified a number of New Zealand-based companies advertising on the internet, which are supplying residents across Australia with these products," he said.

"Law enforcement agencies in both countries are liaising with the companies to make management aware of the legalities of providing a drug of this type to NSW residents.

"While these companies have not broken laws in New Zealand, NSW residents receiving packages of tablets containing benzylpiperazine face prosecution and possible jail time."

Smh.com.au was able to find three New Zealand-based websites selling benzylpiperazine-based pills online within minutes.

One pill, called "Bolts", was "like a lightning bolt of pure energy straight to your brain", a website said.

"Bolts are guaranteed to make your jaws clench, your hair stand on end and your feet want to hit the dance floor.

"Bolts are the strongest energy pills legally available in the world today."

The site included usage instructions for the pills, such as "do not redrop for at least two hours", and noted they were not "herbal highs" but "semisynthetic legal highs".

The pills could not be shipped to Australia, Sweden, Greece or the US, the website said, warning buyers they should check with their local customs department before ordering.

But another website, for an Auckland-based sports nutrition store, did not mention any restriction on the sale of benzylpiperazine-based pills to Australia.

The website sells a two-pack of "Majik" pills, described as "great for more experienced users wanting a strongly altered perception" for \$NZ20 (\$17.70).

Police said benzylpiperazine was a synthetic drug developed as a potential antiparasitic agent and listed as a prohibited drug in NSW.

Superintendent Laidlaw said benzylpiperazine could produce an increased heart rate, nausea, headaches, fatigue, insomnia, seizures, confusion and mild memory loss.

Police said at least one death has been officially linked with the use of benzylpiperazine.

"We are concerned that NSW residents ordering these tablets via the internet are unaware of it being illegal to possess," Superintendent Laidlaw said.

"People are also jeopardising their lives by using these tablets and we strongly warn residents against purchasing or using them."