ACMD

Advisory Council on the Misuse of Drugs

GBL & 1,4-BD: Assessment of Risk to the Individual and Communities in the UK.

Executive Summary

ACMD Recommendation:
The ACMD provisionally recommends that GBL and 1,4-BD are brought under control of the Misuse of Drugs Act 1971 and licensing arrangements are made for their legitimate industrial use.

The ACMD considers that the harms and misuse of GBL and 1,4-BD are commensurate with Class C of the Misuse of Drugs Act 1971; classified in Schedule 1 of the Misuse of Drugs Regulations (having no recognised medicinal use).

However, the ACMD is conscious of the potential impact of control upon the legitimate use of GBL and 1,4-BD and therefore also recommends that the Government consults specifically on this aspect, and that the Council has an opportunity to reconsider its conclusions following the outcome of the consultation.

Summary
Gamma-butyrolactone (GBL) and 1,4-butanediol (1,4-BD) are precursor chemicals that are rapidly converted (half-life approximately 1min) to the intoxicant gamma-hydroxybutyrate (GHB) when ingested into the human body. GHB occurs naturally in small amounts in the brain, and is recognised by specific receptors. It may be an inhibitory neuromodulator, involved among other things in the control of glucose metabolism, oxygen consumption and temperature regulation.

The intoxicant dose for each chemical is approximately 1ml, and intoxication includes euphoria and loss of inhibitions; higher doses may lead to sedation and sleep. There have been reports of emergency room admissions of patients overdosing on GBL or GHB, with coma, bradycardia and hypothermia. 11 GHB-related deaths were reported in the EU in the period 1995-2000. There is little evidence for widespread misuse of GBL or 1,4-BD, but as they are rapidly converted to GHB it is difficult to distinguish the misuse of these chemicals with that of GHB as only the latter compound can be detected in body fluids. Since the repeated use of GHB is known to lead to a dependence syndrome, it is likely that chronic use of GBL or 1,4-BD would carry a similar risk of dependence. There is some evidence for an increasing use of GBL as a “club drug”, and it has allegedly been used in drug-facilitated sexual assaults, although GHB was only detected in 2 of 344 such cases examined by the Forensic Science Service recently. GBL and 1,4-BD are readily available, at a cost of less than 10p per intoxicant dose.

The Advisory Council on the Misuse of Drugs (ACMD) recommended that GHB be regulated as a Class C drug under the Misuse of Drugs Act, 1971 and this has been the case since July 2003. GBL and 1,4-BD are not controlled, although as

drug precursors they are subject to the EU Voluntary Monitoring list by which imports and exports are monitored.

Both GBL and 1,4-BD are used in large quantities by the chemical industry, as precursors for the synthesis of plastics and industrial solvents. The UK Chemical Business Association reported that 1000 tons of GBL and 5000 tons of 1,4-BD are used annually in Britain – almost all imported from manufacturers in Germany. The ACMD's Technical Committee asked the Home Office for information regarding mitigating options for any negative impact control may have on the industrial use of GBL and 1,4-BD. The ACMD understands that a licensing framework could be implemented that would not be overly burdensome for industry.

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1. Introduction

1.1 The Advisory Council on the Misuse of Drugs (ACMD) is established under the Misuse of Drugs Act (1971) and its terms of reference and current membership are shown in Annexes 1 and 2 (respectively). In January 2006 the then Home Secretary requested the Council to consider the issue of Drug Facilitated Sexual Assault. As part of their consideration, the Council identified the need to undertake a more comprehensive assessment of gamma-butyrolactone (GBL) and 1,4-butanediol (1,4-BD).

1.2 GBL and 1,4-BD (also abbreviated at BDO, BD or 1,4-B) are prodrugs of gamma-hydroxybutyrate (GHB). This means that they are rapidly converted to GHB in *vivo* (i.e. when the substance is ingested). Other related compounds with similarities to GHB include gamma hydroxyvalerate (GHV) and gamma valerolactone (GVL).

1.3 There has been concern that users of GHB may have switched to using GBL and 1,4-BD since GHB was controlled under the Misuse of Drugs Act 1971, as a class C substance on 1st July 2003. The potential change in drug using patterns and concerns that GBL and 1,4-BD have recently been implicated in drug facilitated sexual assault have triggered this report.

1.4 The ACMD had considered GHB on several occasions prior to reaching its provisional decision to advise on the control of the drug. The ACMD had previously advised that, given the nature of the relationship between GHB and GBL, consideration should be given to the position of GBL under the Misuse of Drugs Act 1971 as a 'loop-hole' would be created if different action were taken in respect of GHB and GBL.

2. Background

2.1 GBL is a prodrug of GHB which is a naturally occurring compound found in humans. GHB was isolated in 1960 and developed as a sedative medication and an anaesthetic. It is also used as a treatment for narcolepsy (Xyrem®), a rare neurological condition that is characterised by excessive daytime sleepiness.

2.2 Reports of GHB misuse was first highlighted in the 1990s among bodybuilders who used it for its purported growth hormone stimulating effects. It was also bought as a sleep aid and as a dietary supplement. Gradually, reports of adverse events involving the use of GHB came to light.

2.3 Reports that GHB could produce euphoria without hangover effects helped promote GHB as a ‘club drug’. It was also purported to enhance the effects of alcohol and stimulants as well as enhancing libido. This type of promotion helped GHB to become a popular niche drug as part of the night-club scene.

2.4 GHB was classified as a Schedule I substance in the USA in 2000, and as a class ‘C’ drug (listed in Schedule 4, Part I of the regulations) in the UK in 2003. Since then there has been concern that users have switched to GHB prodrugs such as GBL and 1,4-BD. Evidence of the use of GBL and 1,4-BD has only recently come to public attention.

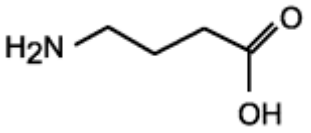
3. Pharmacology and Harmful effects

Pharmacodynamics

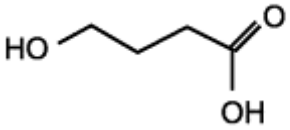
3.1 GBL and 1,4-BD are rapidly converted to GHB, therefore the pharmacology of GHB must be reviewed in order to understand the effects produced. Furthermore, as the consequences of GBL and 1,4-BD ingestion are the same as GHB, studies do not usually characterise the drug ingested. This is further hampered as GBL and 1,4-BD are rapidly converted and are not detectable in plasma and urine samples. Therefore, information about the drug ingested is entirely reliant on a users self-report.

3.2 GHB was initially synthesised in order to produce analogues of the inhibitory neurotransmitter GABA, which could cross the blood, brain barrier. GABA is the precursor for GHB in human brains and the enzyme responsible for this reaction is GABA aminotransferase (Gonzalez and Nutt, 2005).

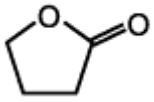
Structures of neurotransmitter GABA, GHB and prodrugs GBL and 1,4-BD.



GABA



GHB



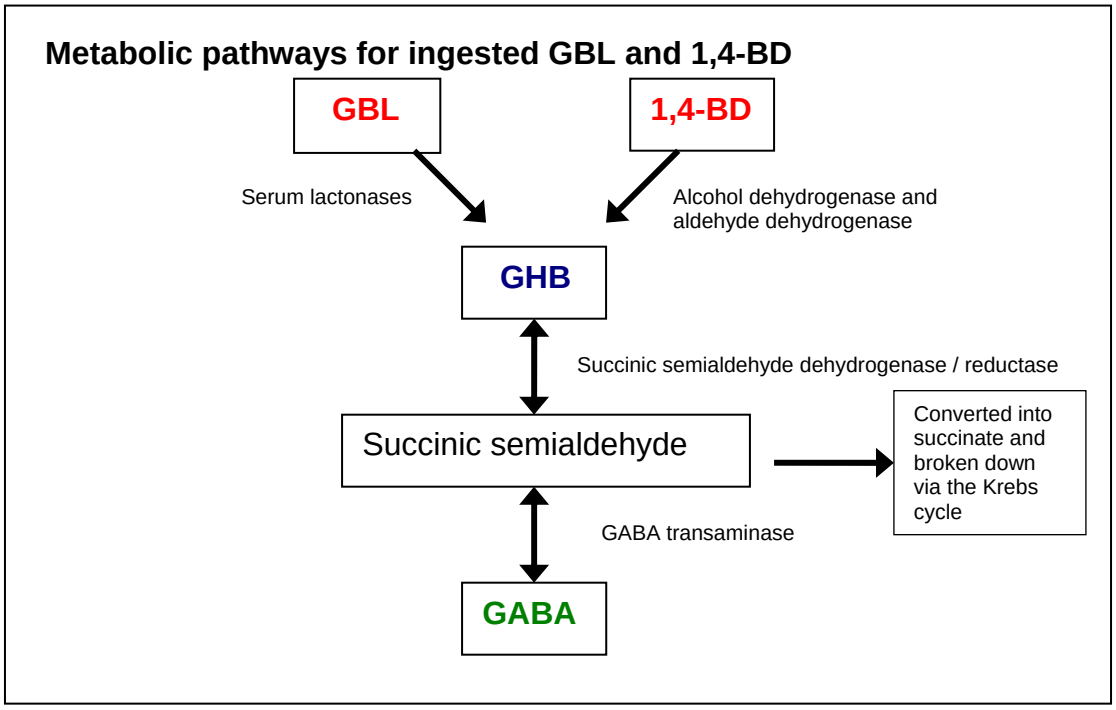
GBL

1,4-BD

3.3 GBL and 1,4-BD are converted into GHB as soon as they are absorbed and in this respect should be treated as pro-drugs (see diagram below). GBL is converted by serum lactonases (or nonenzymic hydrolysis) whereas 1,4-BD is converted by alcohol dehydrogenase and aldehydedehydrogenase (Gonzalez and Nutt, 2005).

3.4 For a review of the effects of GHB in the brain see Gonzalez and Nutt, (2005). GHB has an effect on specific GHB receptors where it binds in a reversible manner. The receptor is a G-protein linked receptor and is widely distributed throughout the brain. It appears that GHB is an inhibitory neuromodulator and is associated with a range of brain functions such as control of glucose metabolism, oxygen consumption and temperature regulation.

3.5 It is also likely that GHB activates $GABA_B$ receptors directly at concentrations above physiological levels to produce inhibition by reducing Ca^{2+} and lowering intracellular levels of cyclic AMP (Carter *et al*, 2004;Sakaba and Neher, 2003). GHB can activate $GABA_B$ receptors indirectly when it is converted to GABA.



3.6 As with most drugs of abuse, GHB has an effect on the dopamine system. However its actions are not clear with low doses seemingly disinhibiting dopamine cells causing increase dopamine release and higher doses causing inhibition of dopamine cells and thus diminished dopamine release (Cruz *et al*, 2004).

3.7 There is some evidence that GHB has an effect on serotonergic and opioid receptor systems. However, these effects are likely to be subtle due to the wide range of functions affected by GHB.

Pharmacokinetics

3.8 GBL and 1,4-BD are rapidly converted to GHB on ingestion. The half-life of GBL is approximately 1 minute (Gonzalez and Nutt, 2005). GHB itself is rapidly absorbed within 30 minutes in a dose dependent manner, serum levels peak 35-45 minutes after oral ingestion (Palatini *et al*, 1993). GBL is thought to be more readily absorbed which may be responsible for users saying its effects are more rapid (Nicholson and Balster, 2001).

3.9 Once GBL and 1,4-BD are absorbed and converted, GHB circulates freely as it is not bound to plasma proteins. Distribution then follows a two compartment model. Initial blood levels decline rapidly, approximately 1 hour after ingestion, followed by a slower period of metabolism. Clinical effects of the drug last approximately 3-4 hours (Gonzalez and Nutt, 2005).

3.10 Elimination of GHB appears to be non-linear, the rate-determining step is the activity of succinic semialdedyhe reductase (Struys *et al*, 2006). Elimination half-life of GHB is approximately 20 minutes, repeated dosing does not appear to affect metabolism (Ferrara *et al*, 1992). GHB can be detected in urine samples up to 8-10 hours and in blood samples 4-5 hours after ingestion of GBL or 1,4-BD.

Intoxication

3.11 Effects for which users take GBL and 1,4-BD for include euphoria and disinhibition. Even at low doses, most users will also experience somnolence and confusion. As the dose response curve is very steep, many regular users have experienced toxicity, which is associated with many symptoms including nystagmus, aggression, urinary incontinence and nausea (Galloway *et al*, 1997; Miotto *et al*, 2001).

3.12 Users report that GBL and 1,4-BD produce the same effects to GHB. Rats trained to discriminate saline from GHB showed that GBL produced cross-generalisation and 1,4-BD also fully substituted for both GHB and GBL (Baker *et al*, 2005). However, the same animals did not substitute for benzodiazepines, alcohol and ketamine. These findings suggest GBL and 1,4-BD produce similar subjective effects and that these are different from other sedating drugs.

3.13 There are several published case series' of patients with GBL and GHB overdoses attending emergency departments. In a Swiss study 65 episodes of intoxication with GBL and GHB are detailed in 48 individuals (Liechti *et al*, 2006). Seven of the patients attended multiple times, two of whom presented 6 times. In the majority of episodes (42 occasions, 65%) another drug or alcohol was reportedly taken.

3.14 Typical signs and symptoms at presentation were coma, bradycardia and hypothermia. On 22 occasions (34%) coma was the initial presentation and was present in at total of 34 episodes (52%). Seizure-like movements were noted in 5 patients (8%). Interestingly, concomitant alcohol use was significantly associated with increased agitation and aggressive behaviour, whereas concomitant stimulant use was significantly associated with a deeper, more prolonged coma, and longer recovery times. Four patients were intubated and monitored in an intensive care unit. There was no significant difference between GBL and GHB toxicity and no fatalities were reported.

3.15 A case-series of 104 GHB overdoses presenting to an emergency department in Barcelona, Spain is reported (Miro *et al*, 2002). In this series, simultaneous alcohol consumption was reported in 73% and additional illicit drugs reported in 86% of cases. However, fewer cases presented in the Spanish study with coma than in the Swiss series (16% compared with 34% of cases) and mechanical ventilation was required less frequently.

3.16 An early case series reports on 88 patients presenting to an emergency department in San Francisco, USA between 1993 and 1996 (Chin *et al*, 1998). There was less concomitant use of alcohol (39%) and other illicit drugs (39%) than in the previous two series. However, rates of coma were high (28%) as were rates of bradycardia (36%) and hypothermia (31%). Twenty-six patients (30%) vomited and 21 (24%) had acidosis as measured by arterial blood gas sampling.

3.17 An Australian study surveying 76 GHB users found that half (53%) had experienced a ‘GHB overdose’ (Degenhardt *et al*, 2003). This was despite the fact that, although the sample had limited experience with GHB, they were experienced users of other drugs. Overdose was defined as becoming unrousably unconscious; furthermore 53% had experience vomiting after GHB use. Eight percent of the sample had experienced a seizure like episode.

3.18 Wood and Dargan report on a case series of 158 GHB/GBL patient presentations to the Emergency Department (ED) at St Thomas’ Hospital, London in 2006 (Wood and Dargan, oral presentation to the GBL Working Group). Of 1119 patient presentations with poisoning, 158 (14.1%) were for GHB/GBL intoxication. This represented 38% of all poisonings with drugs of abuse. Most had ingested GHB (95%) with only a minority reporting GBL ingestion (5%). Of the 8 patient presentations with reported GBL poisoning 7 were as a result of recreational use and 1 was a deliberate self-poisoning.

3.19 A significant number in the above study (25, 15.8%) had a Glasgow Coma Scale of 3 (range = 3-18) at presentation, the lowest score indicating severe coma. The majority (60.7%) were discharged home from the ED within 4 hours. However one patient died after accidental ingestion of a large volume of GHB. Most of the patients had other co-intoxicants, the most common being alcohol (34%), followed by Ecstasy (32%), and Ketamine (22%). For a significant number (35%) GHB/GBL was the only reported intoxicant.

3.20 In all of the above case series for those patients not requiring mechanical ventilation consciousness was typically regained within 5 hours of ingestion. No deaths were reported in all three published case series, although one death is reported from accidental overdose in the London series. Of concern is the high rate of concomitant drug and alcohol use. The higher rates reported in the Spanish study may be due to the availability of toxicological evidence as to concomitant drug and alcohol use which may have been under-reported by patients in the other two series. Worryingly, a high number of people overdose with GHB and this will only become a greater hazard if users switch to GBL and 1,4-BD with variation in strength and different absorption rates making the judgement of the correct dose problematic.

GHB related death

3.21 The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reported that GHB was associated with 11 deaths in the EU between 1995 and 2000 (Gonzalez and Nutt, 2005). All deaths were in the UK or Scandinavia. A more recent study from Sweden reports that there were 7 GHB-related deaths in 2004 (Knudsen *et al*, 2005). It was also noted that cases of GHB intoxication following GBL and 1,4-BD use have come to light.

3.22 A survey of the General Register Offices, cases referred to the Regional Laboratory for Toxicology, Birmingham and the National Programme on Substance Abuse Deaths (np-SAD) at St George's Hospital (London) was presented to the GBL Working group by John Corkery, Programme Manager np-SAD. Data from 1993 to 2005 were available, although there is likely to be some overlap with those reported on in the study above.

3.23 The np-SAD database identified 47 cases where GHB/GBL was found at post-mortem and/or implicated in death. Most cases identified were men (72%) and the mean age was 29.5years. The drugs reported at post mortem included GBL in 4 cases (9%) in all other cases GHB was the drug recorded. The coroner's verdict was most commonly accidental overdose/misadventure (43.9%) (Appendix 4).

3.24 Four GHB associated deaths in Sweden are reported in detail (Timby *et al*, 2000). In all cases the cause of death was reported as acute circulatory and respiratory failure and, with the exception of ethanol, all other drugs found were not considered to be clinically important. Urine concentration of GHB ranged from 260-620 mcg/g, urine levels were considered to be more reliable as GHB is a product of post-mortem decomposition.

3.25 For the decade from 1990 to 2000 the US Drug Enforcement Agency reported 68 GHB-related deaths (Miotto *et al,* 2001). It was only possible to identify information from one such case, a young adult female who took GHB in combination with alcohol (Nicholson and Balster, 2001). Another case report identifies a 35 year old male fatality who reportedly took GHB with some wine at a party (Mazarr-Proo and Kerrigan, 2005). GHB concentrations in the urine were 1665 mg/L, however no alcohol or other drugs of abuse were detected.

3.26 A retrospective search for GHB related deaths in Australasia over an 18 month period from January 2000 is reported (Caldicott *et al*, 2004). Ten cases of GHB-associated deaths were identified, with eight considered to be directly attributable to GHB. Only two of the eight cases were positive for ethanol toxicity.

3.27 In summary, it appears evident that GHB and related compounds cause profound unconsciousness and that the steep dose response curve places even experienced users at risk from death by intoxication. There is some evidence that concomitant alcohol use may be a risk factor, but it is clear that intoxication with GHB and related compounds can cause death in isolation.

Dependence

3.28 Dependence on GHB is a recognised clinical syndrome with similarities to alcohol dependence. Daily use of GBL and 1,4-BD is likely to produce the same clinical syndrome although, as yet, there are no published reports of dependence to these substances. There are reports on the internet of users becoming dependent on GBL and 1,4-BD with a clinical syndrome identical to that of GHB dependence (for example see www.erowid.org/experiences).

3.29 The GHB dependence syndrome is well characterised in a report that surveyed 42 regular GHB users in the US (Miotto *et al*, 2001). Twenty-one percent of this self-selected sample reported being physically dependent on GHB with three patients taking GHB two hourly to avoid withdrawal symptoms. The authors report that they treated one user as an inpatient who developed delirium similar to that which develops in alcohol dependence. Tolerance was also a feature in regular users.

3.30 The users surveyed in the study above complained of frequent adverse events; loss of consciousness was reported by 66% and overdose by 28%. The survey participants emphasized the positive effects of GHB and showed limited concern about the adverse experiences. Interestingly, family members called the investigators with anecdotal complaints of increased aggression, irritability and memory problems in those who used GHB.

3.31 In Summary, regular GBL use and 1,4-BD use will produce a dependence syndrome. This diagnosis is based on a characteristic set of symptoms including; strong desire for a drug; poor control of drug usage; neglect of drug independent activities, persistence in drug use despite evidence of the harms caused; tolerance to the drug and a withdrawal syndrome.

Other

3.32 GBL is described as a mild skin irritant and a strong mucous membrane irritant in its technical data sheet (ABPI Compendium of data sheets and summaries of product characteristics). It can penetrate the epidermis and cause rash or eczema. However there is no current evidence of any harm caused to internal membranes.

3.33 A person intoxicated with GBL or 1,4-BD would be at risk of accidents if handling heavy machinery. Driving is likely to be hazardous in a similar way to being intoxicated with alcohol, with poor co-ordination and disinhibition producing greater risk taking.

3.34 Reports of increased aggression (Liechti *et al*, 2006; Miotto *et al*, 2001) especially with concomitant alcohol use, coupled with disinhibition could result in unprovoked violence to others. This has a bearing on the risks to society if GBL and 1,4-BD use were to become more widespread.

3.35 GBL has the potential to be used as an agent in drug facilitated sexual assault (also known as ‘date-rape’). GHB has been implicated in sexual assaults in the UK, other parts of Europe, and the US (Sturman, 1999). There is, at present, no evidence that GBL has been used in such assaults although detection of the substance and knowledge of the agent used by the victim is likely to be limited (see section 4).

4. Misuse

User groups

4.1 GBL and 1,4-BD abuse has only recently been recognised, although it has been previously recognised as a analogue of GHB. The history of abuse of these substances is related to the rise of GHB use. During the 1980s GHB was widely available in the US as a dietary supplement at health-food stores. Body-builders began using it to enhance muscle building and fat reduction. Reports of GHB use recreationally in night-clubs came to light in the early 1990s. By the end of this decade it had gained popularity as a 'club-drug' due to its purported euphoriant effects and sexual disinhibition. GHB use is common among a certain subset of gay men involved in 'circuit parties', sex clubs and at nightclubs (Halkitis and Palamar, 2006). There are no published case-series reports of GBL and 1,4-BD use in bodybuilders, as a club-drug, or in gay communities.

4.2 A study looked at patients presenting to the Accident and Emergency Department at St Thomas' Hospital, London in 2006 (Wood and Dargan, oral presentation to the GBL Working Group). The authors identified significant numbers of people presenting for treatment following GBL and GHB ingestion in Vauxhall's gay clubs. The majority of those presenting were in the 20-34 year old age group and almost all were male (94%). The authors report that people travel to Vauxhall from all over the UK and even Europe specifically for the gay clubbing scene in this area.

Dose and route of use

4.3 GBL and 1,4-BD are clear liquids. There are very few reports detailing the taste of these compounds but one internet user describes GBL as "a greasy feeling solvent with a characteristic unpleasant smell". This user goes on to say that the taste is unpleasant, like stale water. Some users have posted messages on user sites describing complicated techniques to turn liquid GBL into a powder form so as to produce capsules and to avoid the unpleasant taste. There are no reports of use by routes other than oral ingestion.

4.4 Users report that GBL has a faster onset of action than GHB. Recreational doses of GHB in a non-dependent user are usually above 2.5g (approximately 35mg/kg) and are often measured as one capful. There is very little consistency on recreational doses of GBL due to the variety of preparations available. A recreational dose of high purity GBL (99.9%) would be about 1ml. Users report that this would give a similar effect to 2.5g of GHB. GBL and 1,4-BD are approximately equipotent.

Source and price

4.5 GBL can be bought easily from traders on the internet. It can be purchased in sizes from 125ml to 10litres. A 250ml bottle of 99.9% pure GBL can be bought for £20, which equates to approximately 8p for a recreational dose (1ml).

4.6 Although less readily available than GBL, 1,4-BD can also be bought from internet traders. Direct sales from chemical distribution companies are not available.

Drug facilitated sexual assault

4.7 Reports of drug facilitated sexual assault (also known as 'date-rape') using GHB started to appear on the internet and in traditional media sources in the 1990s. Several properties of GHB and related compounds make them dangerous potential agents of drug facilitated sexual assault, these are: the low volume of dose required to elicit an effect; its ability to cause drowsiness or even unconsciousness, disinhibition, amnesia, and its fast elimination from body fluids therefore making it difficult to identify in samples taken from victims. GBL and 1,4-BD have an unpleasant taste but due to the small volumes necessary for assault this may not be noticed if added to a strongly flavoured drink. Both GBL and 1,4-BD are fully miscible with water.

4.8 A large toxicological study from the UK has reported on agents identified in 1014 cases of alleged drug facilitated sexual assault submitted to the Forensic Science Service over a two year period (Scott-Ham and Burton, 2005). It was not possible to distinguish between cases of GHB, GBL and 1,4-BD in the study and all were considered together. In only 2 cases could the presence of GHB or a related compound be confirmed out of 344 cases where a common drug of abuse (cannabis, cocaine, ecstasy, amphetamine, heroin and ketamine) was detected (0.6%). However, this may be an under-estimate of actual cases as these substances are undetectable in blood samples taken more than 6-8 hours, and urine samples taken more than 12-18 hours, after ingestion.

4.9 An earlier study from the US reports on the analysis of 1179 samples collected from victims of alleged drug facilitated sexual assault (Elsohly and Salamone, 1999). GHB or related compounds were found in 48 cases (4% of the total sample). The variation between this and the UK study may be due to different detection methods for assessing the presence of endogenous GHB in the body.

5. Seizures and Intelligence

5.1 Her Majesties Revenue and Customs (HMRC) cannot seize importations of GBL and 1,4-BD as they are not currently controlled in the UK. However, under European Union (EU) regulations imports and exports of GBL and 1,4-BD are monitored by EU customs authorities under the EU voluntary monitoring list.

5.2 HMRC have reported several instances of GBL being privately imported by individuals from legitimate suppliers and then being repackaged for export abroad (see HMRC report, Annex 2). GBL is ordered on internet sites from companies in the Netherlands, Israel and China. It has been imported in large amounts; in June 2006 a consignment of 1000kg was imported from China by sea container, purchased for £2,200 (see below). The chemicals are declared as various substances including video cleaner, wool cleaner, and magic stain remover.

Five 200kg steel drums recently imported by a private individual from China (photo courtesy of Joe Onofrio, HMRC).

5.3 It is estimated that one company exported 3405 litres of repackaged GBL from the UK to the USA and Canada between 2001-2004 in approximately 800 separate parcels. Other importers have been thought to have packaged GBL for distribution within the UK and abroad.

5.4 The Forensic Science Service reported 2 seizures of GBL liquid totalling 500ml in the first three months of 2006. In the same period 23 seizures of GHB, totalling 2.7kg of powder and 1640ml of liquid, were recorded.

6. Commercial use

6.1 GBL and 1,4-BD have a wide variety of legitimate uses. Both chemicals are imported and used in large volumes by the manufacturing industry and distributed by the chemical distribution companies. Many of the companies that handle GBL and 1,4-BD in the UK are members of the Chemical Business Association (CBA). The CBA represents members' interests in the UK and Europe and promotes industry standards. The CBA co-ordinates 'Responsible Care', the industries voluntary code to safeguard health and safety within the industry, including diversion of potentially harmful chemicals.

6.2 The CBA reports that 1,000 tons of GBL and 5,000 tons of 1,4-BD are imported to the UK per annum. The chemicals are manufactured in Germany and shipped to the UK in sealed containers. The chemicals are not supplied without 'end-user' certificates i.e. documents describing how the compounds will be used. The majority of the imported GBL and 1,4-BD is used by a few large companies.

6.3 GBL can be used in consumptive industrial processes. This means that GBL will be consumed during manufacturing without being part of a new product. GBL is used in this way as a solvent in recrystallisation processes or as a solvent in the electronics industry. GBL is commonly used as a component in the manufacture of various cleaning agents and paints, where it remains as part of the finished product.

6.4 Much of the 1,4-BD imported is used as a raw material in the production of plastics and rubber, for example as polyurethane elastomers (e.g. Spandex). However it is also used as a solvent or binding agent in the manufacture of other products, for example paints and coatings.

6.5 Due to the large volumes of GBL and 1,4-BD handled by UK companies it would be impossible to rule out small scale diversion from legitimate supplies. However the voluntary code, to which all members of the CBA are signed up to includes measures to reduce the possibility of diversion. The code includes internal audit of supply and distribution, identification of suspicious orders and 'declaration of use' documentation for 1,4-BD and GBL that is sold on to other customers.

6.6 In summary both GBL and 1,4-BD are widely used chemicals in UK industry. They have a reputation as being safe and environmentally friendly and there are currently no clear alternatives that industry could easily switch to if the use of these chemicals became logistically difficult due to increased legislation. It appears that much more readily available

sources of GBL and 1,4-BD are overseas based internet sites selling pure GBL and 1,4-BD directly to the small scale consumer.

7. GBL & 1,4-BD control in other countries

The USA

7.1 In the US the Food and Drug Administration (FDA) banned over-the-counter sales of GHB in 1990. Since 2000 GHB has been under strict control when it was classified as a Schedule I substance (equivalent to heroin and cocaine) by the National Institute of Drug Abuse (USA). GBL and 1,4-BD are not scheduled but GBL is classified as a list 1 chemical and a controlled substance analogue, while 1,4-BD is listed as a controlled substance analogue.

7.2 A report from the US Substance Abuse and Mental Health Service Administration (SAMHS) found that the number of visits to Emergency Departments in which GHB and GBL were mentioned increased from 56 in 1994 to 4,969 in 2000 (Office of Applied Studies, 2002). There is no available epidemiological data investigating the impact of the change of legal status of GHB and the effect on use of GBL and 1,4-BD in the US.

Europe

7.3 GHB has a varied level of control across the European Union (EU) with some member states controlling it under misuse of drugs legislation whereas in others it is controlled by medicines acts. There is more widespread clinical use of GHB elsewhere in the EU where it is used for the treatment of Narcolepsy, as an anaesthetic agent, a hypnotic, and a treatment for alcohol dependence.

7.4 In Switzerland use of GHB was prohibited in December 2001. Prior to 1999, cases of GHB overdoses presenting to emergency departments were very rare, less than 5 cases a year (Liechti and Kupferschmidt, 2004). Cases of GBL overdoses became apparent in 1999, and in 2002 and 2003 reports of GBL intoxication began to replace GHB cases. This is the first evidence of a change to the legal status of GHB potentially impacting on the use of GBL.

7.5 There are published reports of GHB use in Scandinavia (Drasbek *et al*, 2006) and in Barcelona (Miro *et al*, 2002) where GHB intoxication represented 18% of all emergency department admissions by illicit drug consumption. However epidemiological data is not routinely collected and whether GBL or 1,4-BD was ingested is not reported.

7.6 The EU recently considered adding GBL and 1,4-BD to the UN list of pre-cursor chemicals, but this was rejected. It was agreed to place GBL and 1,4-BD on the EU voluntary watch list so that customs authorities had better information about the distribution of these chemicals.

Australasia

7.7 GHB, but not GBL and 1,4-BD, is a scheduled drug under the misuse of drugs legislation in New Zealand and Australia. There are GHB associated deaths reported in both these countries (Caldicott et al, 2004). A survey of GHB users in Australia found that experience of unconsciousness (52%) and vomiting (53%) following use was high (Degenhardt *et al*, 2002). Although authorities are aware of the potential of GBL and 1,4-BD use, there were no reported episodes from Australasia (Degenhardt *et al*, 2005).

8. Harm Reduction Strategies

8.1 Dr David Woods and Dr Paul Dargan (Guys and St Thomas Hospital) reported on a pilot project to improve the referral of 'poisoned' clubbers (presentation to the GBL and 1.4 Butanediol Working Group: March 2007). Strategies were targeted at specific areas working with clubs in the Vauxhall area of London, the Metropolitan Police Service, the Emergency Department (ED) at St Thomas' Hospital, and the Clinical Toxicology Service at the Guy's and St Thomas' Poisons Unit.

8.2 In the clubs, efforts have been made to improve awareness of door staff in recognising GHB/GBL disguised in containers purporting to be legitimate liquids. Training of door staff was undertaken and supervised by the Metropolitan Police. A training programme was instigated for members of club staff to act as club 'medics'. Staff would then be better able to recognise the signs of GHB/GBL intoxication and facilitate appropriate referral to the Emergency Department. Guidelines have also been developed and distributed in clubs and bars.

8.3 Dr David Woods and Dr Paul Dargan reported to the GBL and 1.4 Butanediol Working Group (March 2007) that they have audited and revised their guidelines and implemented subsequent training sessions. However it is too early in the scheme for evidence to be gathered on whether these strategies have had an impact on the number and severity of cases seen at the ED at St Thomas' Hospital.

9. Conclusions

9.1 GBL and 1,4-BD are rapidly converted to GHB once ingested. It is established that GHB is associated with coma and death in overdose and, because of its level of harms, has already been considered and classified under the Misuse of Drugs Act 1971. Therefore there is an *a priori* case for considering control of GBL and 1,4-BD.

9.2 GBL and 1,4-BD are widely used by the chemical industry in the UK. Regulation is therefore more complex for these substances as it has the potential to have a detrimental impact upon these industries.

9.3 There is little evidence that GBL and 1,4-BD are being used recreationally in the UK. However seizure evidence suggests there is a market for these substances.

9.4 Voluntary control within the chemical industry is seemingly effective. However, supplies of GBL and 1,4-BD are readily available on the internet. There is some evidence of end-product use.

9.5 There is potential for GBL and 1,4-BD to be used as weapons in drug facilitated sexual assault. GHB has been implicated in sexual assault in the UK, other parts of Europe, and the US (Sturman, 1999). The law enforcement agencies have reported 233 seizures of GHB between 2001 and 2006.

10. Options

10.1 Options considered by GBL Working Group and presented to the Technical Committee:

Option 1
Classify GBL and 1,4-BD under the Misuse of Drugs Act 1971. This would bring these two substances into line with GHB thereby closing the loop-hole that currently exists. However, this step may have a detrimental effect on the chemical industry in the UK and may be perceived to be out of proportion to the level of reported use currently. Limitations to classification could be considered to reduce the impact on the chemical industry.

Option 2
Call for tightening of the existing voluntary codes within the chemical industry. However, it is likely that this would have little impact on the recreational misuse of GBL and 1,4-BD as it is readily available from internet suppliers outside the remit of the UK chemical industry. The option of adding unpleasant chemicals, for example the unpleasant tasting Bitrex, to GBL and 1,4-BD imported to the UK could also be considered. However, this could also be bypassed by internet sources outside the UK or EU.

Option 3
Lobby for the inclusion of GBL and 1,4-BD in the EU Precursor Chemical Legislation. The aim of this option is to affect the import and export of GBL and 1,4-BD, although may be bypassed by sources outside the EU. However, we have subsequently been advised that this option is not viable. The EU Precursor Chemical Legislation is designed to monitor the movement and supply of chemicals which can be used to manufacture drugs of misuse, rather than to restrict the supply of industrial products which in themselves can be misused. As such, the inclusion of GBL and 1,4-BD into European Precursor legislation does not reflect the purpose of the legislation and would not be operationally viable, or constitutionally proper.

Option 4
Include GBL and 1,4-BD into a Home Office licensing system. However, the working group was concerned that it might place an unnecessary and disproportionate burden on an industry which is already effectively policing itself. There is very little diversion from legitimate industrial uses, and as such a licensing system seems excessive for these companies. Furthermore, it may still be bypassed by internet sources, where the true problem stems from.

Option 5
Watch and wait. As there is only a small body of published evidence of the recreational misuse of GBL and 1,4-BD it may be unwarranted to introduce legislative change at this stage. This option would encourage greater reporting

and evidence gathering to enable a more informed decision to be reached in the future.

10.2 Having considered the above options the Working Group concluded that there are essentially only two available options: Option 1 to bring GBL and 1,4-BD under control of the Misuse of Drugs Act, 1971, with or without a combination of Option 4 to include GBL and 1,4-BD in a licensing system; or Option 5 watch and wait.

10.3 After consideration of the evidence presented in this report and the options outlined above, the ACMD recommends that GBL and 1,4-BD are brought under control of the Misuse of Drugs Act 1971 and licensing arrangements are made for their legitimate industrial use. The harms and misuse of GBL and 1,4-BD are considered commensurate with Class C of the Misuse of Drugs Act 1971; classified in Schedule 1 of the Misuse of Drugs Regulations (having no recognised medicinal use).
However, the ACMD is mindful of the potential impact of control upon the legitimate use of GBL and 1,4-BD and therefore also recommends that the Government consults specifically on this aspect, and that the ACMD comments further following the outcome of the consultation before finalising its recommendation.

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Annex 1. Terms of Reference of the Advisory Council on the Misuse of Drugs

" It shall be the duty of the Advisory Council to keep under review the situation in the United Kingdom with respect to drugs which are being or appear to them likely to be misused and of which the misuse is having or appears to them capable of having harmful effects sufficient to constitute a social problem, and to give to any one or more of the Ministers, where either Council consider it expedient to do so or they are consulted by the Minister or Ministers in question, advice on measures (whether or not involving alteration of the law) which in the opinion of the Council ought to be taken for preventing the misuse of such drugs or dealing with social problems connected with their misuse, and in particular on measures which in the opinion of the Council, ought to be taken:

a) for restricting the availability of such drugs or supervising the arrangements for their supply;

b) for enabling persons affected by the misuse of such drugs to obtain proper advice, and for securing the provision of proper facilities and services for the treatment, rehabilitation and after-care of such persons;

c) for promoting co-operation between the various professional and community services which in the opinion of the Council have a part to play in dealing with social problems connected with the misuse of drugs;

d) for educating the public (and in particular the young) in the dangers of misusing such drugs and for giving publicity to those dangers; and

e) for promoting research into, or otherwise obtaining information about, any matter which in the opinion of the Council is of relevance for the purpose of preventing the misuse of such drugs or dealing with any social problem connected with their misuse".

A further duty is placed on the Council by the Act to consider any matter relating to drug dependence or the misuse of drugs which may be referred to them by any one of the Ministers concerned, and in particular to consider and advise the Home Secretary on any communication which he refers to the Council which relates to the control of a dangerous or otherwise harmful drug and which is made to Her Majesty's Government by any organisation or authority established by treaty, convention or other agreement or arrangement to which Her Majesty's Government is a party.

Annex 2. Membership of the Advisory Council on the Misuse of Drugs (November 2007)

Professor Sir Michael Rawlins	Professor of Clinical Pharmacology, University of Newcastle upon Tyne and Chair of the National Institute for Health and Clinical Excellence
Dr Dima Abdulrahim	Briefings Manager, National Treatment Agency
Lord Victor Adebowale	Chief Executive, Turning Point
Mr Martin Barnes	Chief Executive, DrugScope
Dr Margaret Birtwistle	Specialist General Practitioner, Senior Tutor – Education and Training Unit, St George's Hospital and Forensic Medical Examiner
Reverend Martin Blakebrough	Director, Kaleidoscope Drugs Project, Kingston upon Thames
Dr Cecilia Bottomley	Specialist Registrar in Obstetrics and Gynaecology,London
Ms Carmel Clancy	Principal Lecturer for Mental Health and Addictions, Middlesex University
Professor Ilana Crome	Professor of Addiction Psychiatry, Keele University Medical School, Harplands Hospital
Ms Robyn Doran	Registered Mental Health Nurse and Service Director Substance Misuse, Central and North-West London Mental Health Trust
Ms Dianne Draper	Public Health Policy Support Officer, Leeds
Mr Robert Eschle	School Teacher and Magistrate, Kent
Ms Vivienne Evans	Chief Executive, ADFAM
Professor C Robin Ganellin FRS	Emeritus Professor of Medicinal Chemistry, University College London

Dr Clare Gerada	General Practitioner, London and Primary Care Lead for Drug Misuse, Royal College of General Practitioners
Mr Patrick Hargreaves	Drugs and Alcohol Adviser, Durham County Council Education Department
Mr Paul Hayes	Chief Executive, National Treatment Agency
Mr Andrew Hayman	Assistant Commissioner, Metropolitan Police and Chair of the Association of Chief Police Officers Drugs Committee
Mr Russell Hayton	Clinical Nurse Specialist and Clinical and Services Governance Manager, Plymouth Drug and Alcohol Action Team
Ms Caroline Healy	Department of Health
Dr Matthew Hickman	Deputy Director, Centre for Research on Drugs & Health Behaviour, Senior Lecturer in Public Health, Bristol University
Mr Alan Hunter	Legal Mentor ABPI Calypso Temple Gardens Staines TW18 3NQ
Professor Leslie Iversen	Professor of Pharmacology, Oxford University
His Honour Judge Thomas Joseph	Resident Judge, Croydon Crown Court
Professor Michael Lewis	Professor of Oral Medicine, Cardiff University
Dr John Marsden	Research Psychologist, Institute of Psychiatry
Mr Peter Martin	Former Chief Executive, Addaction
Mrs Samantha Mortimer	Head of Personal, Social and Health Education and Citizenship, St Paul's Catholic High School, Manchester
Professor David Nutt	Professor of Psychopharmacology, University of Bristol

Mr Trevor Pearce	Acting Director General, National Crime Squad
DCC Howard Roberts	Deputy Chief Constable, Nottinghamshire Police
Mrs Kay Roberts	Pharmacist, Glasgow
Dr Mary Rowlands	Consultant Psychiatrist in Substance Misuse, Exeter
Dr Polly Taylor	Veterinary Surgeon, Cambridgeshire
Ms Monique Tomlinson	Freelance Consultant in Drug Misuse
Mr Arthur Wing	Assistant Chief Officer, Sussex Probation Area

Annex 3. HM Revenue and Customs

In bringing the report into the public domain, the ACMD has had to make a number of redactions to this Annex which have been made with careful consideration of the details of the specific information and sensitive data; in line with Home Office guidance.

GAMMA –BUTYROLACTONE (GBL) & 1,4 BUTANEDIOL (1,4-BD).

1. GBL: THE PRODUCT

Gamma-Butyrolactone (GBL).
CAS No 96-48-0
Harmonised Tariff Code 2932.29. 5010
Molecular Formulae C4 H6 O2.
Boiling Point 204 C (335 F).
Density 1.12.

- GBL is the only known precursor to gamma- hydroxy butyrate (GHB) which became a Schedule 1 drug in the USA on March 2000. (In 27 States).

- GBL is manufactured in the USA, Spain, Italy, Belgium, France and Switzerland. It is also manufactured in Japan, India and China.

HMRC Seizures.

- HMRC cannot seize importations of GBL/1,4-BD as they are not controlled in the UK.

- As long as the imports are properly declared and all UK import Duties and VAT are paid no Customs offence's have been committed.

Annex 4: GHB/GBL deaths in the UK - some initial findings

INTERNATIONAL CENTRE FOR DRUG POLICY NATIONAL PROGRAMME ON SUBSTANCE ABUSE DEATHS

Introduction

Presented are the results from a survey of the General Register Offices, cases referred to Dr Simon Elliott, The Regional Laboratory for Toxicology Dudley Road, Winson Green Birmingham, and the National Programme on Substance Abuse Deaths at St George's, University of London. Thanks to all concerned for supplying data.

The information given in this paper is being provided with the approval of Professor Hamid Ghodse, Director of the International Centre for Drug Policy, to enable as complete a picture from currently available information to be presented to the ACMD GBL/1,4BD Working Group for their consideration.

General Register Offices – GHB mentions on death certificate

Northern Ireland (to date) - 0
Scotland (1994 to 2005) - 5
England & Wales - ONS data (1993-2005 registrations) – 24
Combining these data gives the following frequencies by year

	England & Wales	Scotland
1996	1	
1999	3	1
2000	3	
2001	1	2
2002	5	2
2003	6	
2004	1	
2005	4	

National Programme on Substance Abuse Deaths (np-SAD), St George's University of London

At the time of writing, the np-SAD database has details of 47 named individuals where GHB/GBL was either found at post mortem and/or implicated in death. In addition, we are aware of a number of further cases where these substances have been found at post mortem and for whom we are currently seeking further information. The overall total of 47 cases includes the 5 Scottish cases referred to above - 3 of which are on the database.

There may be other cases yet to be notified to np-SAD but we are canvassing toxicologists to see if there are any other cases out there. Dr Elliott is assisting in this research as he often has cases from other areas referred to him for analysis; his PhD thesis was concerned with the application of special techniques to determine the presence of GHB/GBL.

Furthermore, some deaths involving GHB/GBL may not be identified as such because these substances have not been specifically tested for.

It is possible that closer examination of 2 of the cases may result in them being excluded as GHB/GBL cases due to he low levels found at post-mortem. Since GHB naturally occurs in the human body, it can sometimes be difficult to determine if it was produced by the body or ingested e.g. if there is no circumstantial evidence available.

In all of these instances it should be noted that the fact that a drug is recorded as being present post mortem or indeed recorded on the death certificate does not necessarily imply that it contributed to the death.

The following brief analyses are based on these 47 cases.

Results

Year of death

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1995	1	2.1	2.1	2.1
	1997	1	2.1	2.1	4.3
	1998	2	4.3	4.3	8.5
	1999	3	6.4	6.4	14.9
	2000	3	6.4	6.4	21.3
	2001	7	14.9	14.9	36.2
	2002	7	14.9	14.9	51.1
	2003	3	6.4	6.4	57.4
	2004	3	6.4	6.4	63.8
	2005	6	12.8	12.8	76.6
	2006	11	23.4	23.4	100.0
	Total	47	100.0	100.0	

Age-group at death

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	15-24	14	29.8	30.4	30.4
	25-34	23	48.9	50.0	80.4
	35-44	8	17.0	17.4	97.8
	45-54	1	2.1	2.2	100.0
	Total	46	97.9	100.0	
Missing	System	1	2.1		
Total		47	100.0		

Age at death

N	Valid	46
	Missing	1
Mean		29.5621
Median		28.9979
Range		27.06
Minimum		19.95
Maximum		47.01

Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	34	72.3	72.3	72.3
	female	13	27.7	27.7	100.0
	Total	47	100.0	100.0	

Ethnicity

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NOT KNOWN	3	6.4	7.0	7.0
	WHITE	37	78.7	86.0	93.0
	BLACK CARRIBEAN	1	2.1	2.3	95.3
	BANGLADESHI	1	2.1	2.3	97.7
	OTHER	1	2.1	2.3	100.0
	Total	43	91.5	100.0	
Missing	System	4	8.5		
Total		47	100.0		

Occupation Status condensed

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not known	2	4.3	4.5	4.5
	unemployed	5	10.6	11.4	15.9
	employed	29	61.7	65.9	81.8
	childcare/houseperson	2	4.3	4.5	86.4
	student/pupil	4	8.5	9.1	95.5
	other	2	4.3	4.5	100.0
	Total	44	93.6	100.0	
Missing	System	3	6.4		
Total		47	100.0		

Living Arrangements condensed

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not known	1	2.1	2.3	2.3
	with others	25	53.2	56.8	59.1
	alone	18	38.3	40.9	100.0
	Total	44	93.6	100.0	
Missing	System	3	6.4		
Total		47	100.0		

Category of place of death

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Defined residential address	30	63.8	66.7	66.7
	Hospital/infirmary	11	23.4	24.4	91.1
	other	4	8.5	8.9	100.0
	Total	45	95.7	100.0	
Missing	System	2	4.3		
Total		47	100.0		

Accident Site

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	not known	1	2.1	2.5	2.5
	home	21	44.7	52.5	55.0
	street or highway	2	4.3	5.0	60.0
	place of recreation/sport	1	2.1	2.5	62.5
	other specified place	15	31.9	37.5	100.0
	Total	40	85.1	100.0	
Missing	System	7	14.9		
Total		47	100.0		

Drug Addict status

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NOT KNOWN	6	12.8	13.0	13.0
	YES	25	53.2	54.3	67.4
	NO	15	31.9	32.6	100.0
	Total	46	97.9	100.0	
Missing	System	1	2.1		
Total		47	100.0		

Coroner's Verdict

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	dependence on drugs	1	2.1	2.3	2.3
	non-dependent abuse of drugs	7	14.9	16.3	18.6
	accidental / misadventure	20	42.6	46.5	65.1
	open verdicts/unascertained	6	12.8	14.0	79.1
	all other verdicts	7	14.9	16.3	95.3
	abuse of drugs	2	4.3	4.7	100.0
	Total	43	91.5	100.0	
Missing	System	4	8.5		
Total		47	100.0		

Part of UK where death occurred

Country/Region	Frequency
Northern Ireland	0
Scotland	7
Wales	5
England	35
GOR area	
Greater London	10 (including 6 in Inner South)
Yorkshire	7
Greater Manchester	4
North West	4
Midlands	4
North East	2
Eastern	1
East Anglia	1
South West	1
Not known	1

Number of drugs at PM

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	6	12.8	13.0	13.0
	2	6	12.8	13.0	26.1
	3	13	27.7	28.3	54.3
	4	9	19.1	19.6	73.9
	5	6	12.8	13.0	87.0
	6	3	6.4	6.5	93.5
	7	2	4.3	4.3	97.8
	10	1	2.1	2.2	100.0
	Total	46	97.9	100.0	
Missing	System	1	2.1		
Total		47	100.0		

Combinations of PM drugs

Post mortem substances	Frequency
Alcohol	1
Alcohol, amphetamines, MDMA, MDA (no GHB pm)	1
GBL	1
GHB	4
Alcohol & GHB	4
Alcohol, GHB & hormones	1
Alcohol, GBL & cocaine	1
Alcohol, GHB & cocaine	3
Alcohol, GHB & chlordiazepoxide	1
Alcohol, GHB, MDMA	1
Alcohol, GHB, MDMA, MDA, cannabis	2
Alcohol, GBL, MDMA, cocaine & temazepam	1
Alcohol, GHB, MDMA, MDA, cocaine, diazepam & dextropropoxyphene	1
Alcohol, GHB, MDMA, MDA, cocaine, diazepam, diltiazem	1
Alcohol, GHB, methamphetamine, cocaine & benzodiazepines	1
Alcohol, GHB, MDMA, MDA, cocaine & olanzapine	1
Alcohol, GHB, amphetamine, diazepam, heroin, phenobarbitone	1
Alcohol, GHB, ecstasy, amphetamines, ketamine & cannabis	1
Alcohol, GHB & diazepam	1
Alcohol, GHB/GBL & diazepam	1
Alcohol, GHB, diazepam & dextropropoxyphene	2
Alcohol, GHB, diazepam & cocaine	1
Alcohol, GHB, codeine, paracetamol, zopliclone	1
Amphetamines & GHB	1
Amphetamines, GHB & alcohol	1
GHB, MDMA & MDA	1
GHB (GBL), MDMA, MDA, amphetamine, methamphetamine, temazepam	1
GHB, ecstasy & cocaine	1
GHB, MDMA, MDA, cocaine & ketamine	1
GHB, ecstasy, cannabis & lithium	1
GHB, cocaine, diazepam, atropine & lignocaine	1
GHB, diazepam & cannabis	1
GHB, diazepam, cannabis, morphine, codeine, temazepam, oxazepam	1
GHB, diazepam & codeine	1
GHB, desmethyldiazepam, morphine, chlordiazepoxide	1
GHB, benzodiazepines, codrydramol, paracetamol, diclofenac	1
NA	1

Levels of GHB/GBL (inc. Ante-Mortem)

Case no.	GHB		GBL		Alcohol		Stimulants present	Other drugs (inc. stimulants) present
	blood	urine	blood	urine	blood	urine		
1	340 mg/L				202			
2	1400mg/L						Y	Y
3	34.5mg/dL				116	136		
4	120mg/L	680mg/L			131	198	Y	Y
5	420mg/L						Y	Y
6					Y			
7	340ug/ml				Y		Y	Y
8	305ug/ml						Y	Y
9	120ug/ml	1mg/ml						Y
10	356mg/L				47			
11	110mg/L							Y
12	340ug/ml	1200ug/ml			265	370		Y
13	267mg/L	90mg/l			106	146		
14			189ug/ml	1mg/ml	200	261	Y	Y
15	360mg/L	796mg/L			196	297		Y
16	120mg/L				77	132	Y	Y
17	260mg/L						Y	
18	18ug/ml				240			Y
19	139mg/L				57		Y	
20	5ug/ml							Y
21			300ug/ml		195	264	Y	
22	129mg/L				29	18	Y	Y
23	0.17mg/ml	2.4mg/ml			79			
24	270mg/L	824mg/L			47		Y	Y
25	159mg/L	1464mg/L						
26	200mg/L						Y	Y
27	1575mg/L	1980mg/L						
28	220mg/L	2708mg/L			111	133	Y	Y
29	79.8ug/ml				217		Y	
30	>10mg/L							Y
31	30ug/ml				97	127		Y
32	45mg/L							Y
33	64mg/L	1150mg/L					Y	Y
34	100mg/L				97		Y	
35	430ug/ml AM		6500ug/ml (PM)					
36			800mg/L				Y	Y
37	96mg/dL				154			Y
38		3ug/ml			1		Y	Y
39	14mg/L				156		Y	
40	42mg/L							
41	NA							
42	22mg/l				15	10	Y	Y
43	NA						Y	Y
44	NA							
45	106mg/L	110mg/L	+	+	180	228		Y
46	403mg/L	0mg/L						
47	NA				190	264	Y	Y

Combinations of implicated drugs

Substances implicated	Frequency
Alcohol	1
MDMA	2
Methadone	1
GBL	1
GHB	6
Alcohol & cocaine	1
Alcohol & GHB	6
Alcohol, GBL & cocaine	1
Alcohol, GHB & cocaine	2
Alcohol, GHB, MDMA	2
Alcohol, GBL, ecstasy, cocaine & temazepam	1
GHB, amphetamines & ketamine	1
GHB, ecstasy & ketamine	1
Alcohol, GHB & diazepam	1
Alcohol, GHB, diazepam & dextropropoxyphene	2
Alcohol, GHB, diazepam & cocaine	1
Amphetamines & GHB	1
Amphetamines & GHB/GBL	1
GHB & cocaine	2
GHB, MDMA	2
GHB, ecstasy & cocaine	1
GHB, ecstasy, cannabis & lithium	1
GHB & diazepam	1
GHB, diazepam & codeine	1
GHB, benzodiazepines& paracetamol	1
None	2
NA	4

Circumstances of death/events leading up to death

Circumstances	Frequency
Following gym session, heavy meal & alcohol, took GHB to assist sleep & body building	1
Consumed after drinking to help sleep	1
Preceding recreational use of other substances	2
Experimentation following alcohol consumption	5
Recreational use following alcohol consumption	2
Recreational use with alcohol consumption	3
Recreational use with alcohol and stimulants	4
Recreational use after alcohol and other drugs	5
Following use of GHB and other recreational drugs	1
Following use of GHB and heroin	1
Following use of GHB and cocaine (injecting & snorting)	
Consumed after socialising	2
Found collapsed	3
Collapsed at club	1
Found dead at home	2
Administered by third party after use of recreational drugs	2
Found dead in car after taking analgesics & benzodiazepines	1
Rode bicycle into path of bus	1
Mistaken for water, anaphalactic shock	1
Found dead following fire	1
Drowned after taking drugs and drinking	1
Not known/not available	6

Underlying cause(s) of death

Cause	Frequency
Ingestion of GHB & alcohol	1
Ingestion of GHB, alcohol, MDMA	1
Fatal medical complications following combination of drugs (GHB, codeine, diazepam)	1
Effects of multiple drug ingestion (GHB, dextropropoxyphene, alcohol, diazepam)	1
Effects of GBL, alcohol, cocaine & ecstasy	1
GHB intoxication	4
GHB & amphetamine intoxication	1
GHB, ketamine, ecstasy intoxication	1
Alcohol toxicity	1
Alcohol & cocaine poisoning	1
MDMA poisoning	1
Methadone toxicity	1
GHB toxicity	4
GHB & alcohol toxicity	5
GHB, alcohol & cocaine toxicity	2
GBL alcohol & cocaine toxicity	1
GHB, alcohol & diazepam toxicity	1
GHB, alcohol, diazepam & dextropropoxyphene poisoning	1
GHB, alcohol & MDMA poisoning	1
GHB & amphetamine toxicity	1
GHB, amphetamine & ketamine toxicity	1
GHB & cocaine toxicity	2
GHB, cocaine & ecstasy toxicity	1
GHB & diazepam toxicity	1
GHB, ecstasy & cannabis overdose	1
GHB & MDMA toxicity	1
GBL & MDMA toxicity	1
GHB, MDMA, MDA, alcohol, diazepam & diltiazem toxicity	1
Combined drug and alcohol poisoning	1
Inhalation of products of combustion	1
Drowning, intoxication with MDMA and ecstasy	1
Pulmonary thromboembolism, suspected chronic drug use	1
Unascertained	1
Not available	2

Summary

Since the first known death in the UK associated with the ingestion of GHB/GBL in 1995, there have been at least 47 cases in which these substances were implicated. Of these 4 involved GBL, mostly in 2005-6, including one case on its own. The number of cases appears to have first peaked in 2001-2 and rising to higher levels in 2005-6.

Only 7/47 involved GHB/GBL on its/their own. The majority of cases involved the ingestion of at least two other substances, typically alcohol and/or stimulants. There was considerable variability in the range of GHB/GBL levels at post mortem. In many instances the effects on respiratory depression of GHB/GBL

were enhanced by the presence of alcohol and other CNS depressants such as benzodiazepines and opiates/opioids

Where the circumstances were known, the majority (232/41) of deaths followed recreational use, often by individuals with a history of substance use (63% of all deaths where addict status was known). A small number of cases involved the use of GHB to aid sleep and in one of these to assist body-building.

Most cases were male (72%), White (93%) where ethnicity was known, and aged less than 35 years of age (80%), and occurred in Metropolitan areas (74%), and were accidental in nature (80% where the circumstances are known).

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