



# COMMENTS ON THE REPORTED STATISTICS ON PSYCHOTROPIC SUBSTANCES

## **Summary**

The analysis contained in the present section of the technical publication on psychotropic substances is based on statistical data furnished by Governments. The quality of the analysis depends on the quality of the data provided.

Use of substances included in Schedule I of the 1971 Convention should be limited to scientific research and, in certain cases, for the manufacture of psychotropic substances in other schedules. The isolated use of some substances in Schedule I for the manufacture of other substances has declined in recent years.

Manufacture of methylphenidate and its use for the treatment of attention-deficit hyperactivity disorder (ADHD) continued to increase worldwide. Global manufacture reached a new record, of over 63 tons, in 2012. Although the number of countries reporting manufacture of methylphenidate has increased in recent years, the United States of America remained the leading manufacturer, accounting for almost 97 per cent of the total output. The United States also remained the leading user of methylphenidate in 2012. Outside the United States, the main users of methylphenidate in 2012 were, in descending order, Canada, Germany, Spain, Switzerland, the Netherlands, Brazil, Sweden, Israel, South Africa and Australia.

Manufacture of amphetamines, which are the other central nervous system stimulants in Schedule II of the 1971 Convention, increased further and attained a new record, of over 50 tons (3.4 billion defined daily doses for statistical purposes (S-DDD)), in 2012. This development is due mainly to a significant increase in the manufacture of amfetamine and dexamfetamine in the United States during the year. The United States remained the largest consumer of amphetamines in 2012 in absolute terms, as well as in terms of per capita consumption.

Buprenorphine, an opioid analgesic listed in Schedule III of the 1971 Convention, has been increasingly used since the late 1990s in the treatment of pain and in substitution treatment for opioid addicts. Global manufacture of buprenorphine attained a new record of over 7 tons (919 million S-DDD) in 2012. Global calculated consumption of the substance has also continued to grow. The United States remained the leading user of buprenorphine in 2012, followed by Germany, France, Switzerland, Italy and Spain (in descending order). As in previous years, over 60 countries reported imports of buprenorphine.

A total of 35 benzodiazepines are currently under international control. Of those, 22 are classified as anxiolytics, and 12 are classified as sedative-hypnotics and are used in medical practice for pre-medication and the induction of general anaesthesia. Clonazepam is the only benzodiazepine that is used mainly as an anti-epileptic. Flunitrazepam, a sedative-hypnotic, is the only benzodiazepine that is listed in Schedule III of the 1971 Convention, while the rest of the benzodiazepines are listed in Schedule IV. In 2012, 19 Governments reported manufacture of benzodiazepine-type anxiolytics and 15 Governments reported manufacture of benzodiazepines decreased in 2012. This decrease may be attributed to the fact that one major manufacturing country did not provide its data on manufacture of benzodiazepines for 2012 to the Board. Alprazolam and diazepam remained, in that order, the most manufactured psychotropic substances in terms of S-DDD. Italy continued to be the leading manufacturer of both groups of benzodiazepines in 2012. Total calculated consumption of benzodiazepines followed the overall trend in global manufacture, showing a gradual decrease over the past three years. The combined total calculated consumption of both categories of benzodiazepines stood at 27 billion S-DDD in 2012.

Of the 12 barbiturates listed in Schedules II, III and IV of the 1971 Convention, the manufacture of five substances—phenobarbital, pentobarbital, butalbital, barbital and amobarbital (in that order)—together accounted for 99 per cent (on average) of the total manufacture of these

barbiturates during the period 2008-2012. Phenobarbital remained the most widely manufactured barbiturate in 2012, accounting for 79 per cent of total manufacture of all 12 barbiturates. China continued to be the leading manufacturer. Other leading manufacturers in 2012 were Hungary, the United States, Denmark and Germany (in descending order). International trade in most barbiturates has been declining during the past five years.

The 14 central nervous system stimulants listed in Schedule IV of the 1971 Convention are used mainly as anorectics or for the treatment of ADHD. Total reported manufacture of this group of substances has been on the rise during the period 2003-2012, and attained 2.6 billion S-DDD in 2012, the United States accounting for over half of the global total, followed by Germany and Italy. The United States remained the leading user of this group of substances, accounting for 74 per cent of global calculated consumption in 2012. Calculated consumption of stimulants in Schedule IV in the Americas remained the highest in the world. In 2012, the highest consumption rates, expressed in S-DDD per 1,000 inhabitants per day, were reported by the United States, followed by Chile and Brazil. Phentermine continues to be the most used substance in this group, accounting for 83 per cent of calculated consumption.

Substances for which global manufacture or international trade in recent years amounted to less than 1 kg are not mentioned separately in the analysis below; however, the data on those substances are included in the relevant group totals, as applicable.

## **Substances in Schedule I of the 1971 Convention**

- 1. Twenty-eight substances are listed in Schedule I of the 1971 Convention. The use of those substances should be prohibited, pursuant to the provisions of article 7 of the Convention, except for scientific and very limited medical purposes by duly authorized persons in medical or scientific establishments that are directly under the control of or specifically approved by their Governments. This restriction results from the fact that all substances in Schedule I are hallucinogens and/or central nervous system stimulants with very limited or no medical use. In line with this restriction, manufacture and stocks of, as well as trade in, those substances have been extremely limited, with the exceptions noted in the following paragraphs.
- 2. The 1971 Convention does not foresee use of the psychotropic substances in Schedule I by industry for the manufacture of non-psychotropic substances or products. However, until 2002, 2,5-dimethoxyamphetamine (DMA) was manufactured in the United States of America, exclusively for use in the manufacture of a non-controlled film dye, in amounts of several tons per year. Manufacture of DMA started to decline in 2002, owing to a decrease in the demand for photographic film, and stopped entirely in 2007. Global stocks of DMA, which have been depleted since 2008, stood at 59 grams at the end of 2012.
- 3. Another substance in Schedule I that is used by industry for the manufacture of non-psychotropic substances is *para*-Methoxy-*alpha*-methylphenethylamine (PMA). During the past decade, Denmark reported intermittent manufacture of PMA, with quantities ranging from 24 to 71 kg, for use in the manufacture of tamsulosin, an active pharmaceutical ingredient that is not under international control. There continues to be limited manufacture of PMA in Denmark and the United States. In 2012, Denmark manufactured 57.5 kg and the United States manufactured 16 grams.
- 4. Use of the psychotropic substances included in Schedule I for the manufacture of psychotropic substances that are included in other schedules was reported only by the United States. In that country, isomers of tetrahydrocannabinol (THC) listed in Schedule I are used in the manufacture of *delta-9*-tetrahydrocannabinol (*delta-9-THC*), a psychotropic substance listed in Schedule II. *Delta-8-Tetrahydrocannabinol* is the main substance among the isomers in Schedule I manufactured in the United States. During the past decade, reported manufacture in the United States of isomers of THC listed in Schedule I fluctuated between 327 kg in 2005 and 53 kg in 2010. In 2012, the total amount of isomers of THC manufactured in the United States was 60 kg. At the end of 2012, global stocks of such isomers stood at 150 kg, the vast majority of which were held in the United States.

#### **Substances in Schedule II of the 1971 Convention**

5. Listed in Schedule II are 17 substances that have little to moderate therapeutic usefulness and whose liability to abuse constitutes a substantial risk to public health. The substances belong to the following groups: central nervous system stimulants, anti-emetics, hallucinogens, sedative-hypnotics, antitussives and antidepressants. In addition to their various applications in human and veterinary medicine, some of these substances are used in industry for the manufacture of other psychotropic substances or for conversion into non-psychotropic substances.

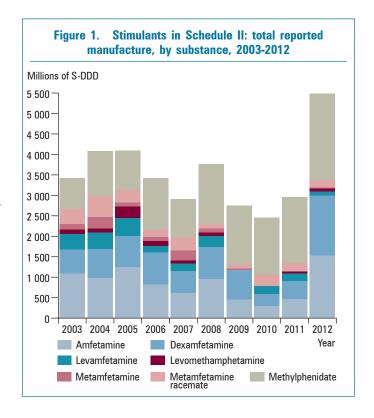
**Central nervous system stimulants** 

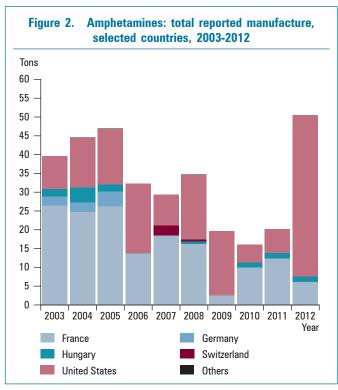
Total manufacture of central nervous system stimulants in Schedule II fluctuated in the period 2003-2012, as can be seen in figure 1. After decreasing for two consecutive years (2009 and 2010), total reported manufacture of this group of substances picked up again, first slightly in 2011 and then further in 2012, amounting to 5.5 billion S-DDD. This increase is mainly due to a significant increase in manufacture of amfetamine, dexamfetamine and methylphenidate<sup>1</sup> in the United States in 2012. That country accounted for 90 per cent of total output of stimulants in Schedule II during that year. In 2012, methylphenidate's share of total output of stimulants in Schedule II was 38 per cent. Amfetamine and dexamfetamine accounted for 28 and 27 per cent, respectively, of total output. Together with methylphenidate, these substances accounted for 93 per cent of total combined output in 2012.

#### **Amphetamines**

7. Both optical isomers of amfetamine (levamfetamine and dexamfetamine) and their racemic mixture (amfetamine), as well as both optical isomers of metamfetamine (levomethamphetamine and metamfetamine) and their racemic mixture (metamfetamine racemate), are listed in Schedule II. Statistical reports on amfetamine, dexamfetamine and metamfetamine have been received by the International Narcotics Control Board from Governments since the 1970s. Statistics for levamfetamine and levomethamphetamine have been available since 1986 and statistics for metamfetamine racemate have been available since 1988, reflecting the different dates on which those substances were brought under international control in the context of the 1971 Convention.

8. In 2012, as a result of a significant increase in the manufacture of amfetamine and dexamfetamine in the United States, the quantity of amphetamines listed in Schedule II that was manufactured worldwide rose to a record amount of 50.5 tons (3.4 billion S-DDD) (see figure 2). In 2012, amfetamine comprised 45 per cent and



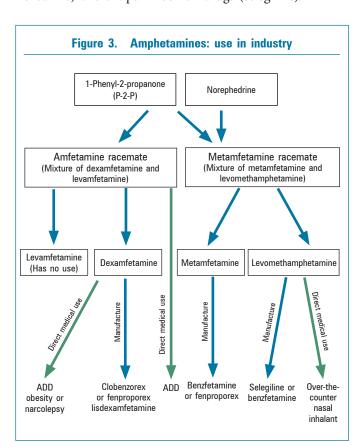


<sup>&</sup>lt;sup>1</sup>Of the other stimulants in Schedule II (4-bromo-2,5-dimethoxy-phenethylamine, fenetylline, methylphenidate, phencyclidine and phenmetrazine) only methylphenidate is manufactured and used in significant quantities.

dexamfetamine 43 per cent of the total output of amphetamines, while metamfetamine racemate and levamfetamine represented 6 and 3 per cent, respectively, with the United States accounting for nearly 85 per cent of the total manufacture of amphetamines, France accounting for 12 per cent and Hungary for most of the remainder. France continued to be the sole manufacturer of levamfetamine in 2012, where the substance was used for reconversion into amfetamine.

#### Use as intermediate substances

Amphetamines in Schedule II of the 1971 Convention are frequently used in industry as intermediary products for the manufacture of other substances (see figure 3). The new substances manufactured from amphetamines may be divided into two groups: other psychotropic substances, including those which are optical isomers of the original substance; and substances not controlled under the 1971 Convention. In France and the United States, amphetamines in Schedule II are widely used in industry for conversion into other amphetamines included in that Schedule. In the United States, amfetamine is also used in the synthesis of lisdexamfetamine (l-lysine-d-amfetamine), a prodrug of dexamfetamine, which is used in the treatment of ADHD. In 2012, about 11 tons of lisdexamfetamine were manufactured in the United States. In addition, amphetamines have mainly been converted into substances used as anorectics (benzfetamine, clobenzorex, fenproporex and levopropylhexedrine) and antiparkinsonian drugs (selegiline).



#### Direct medical use

10. For direct medical purposes, amphetamines are used mainly for the treatment of ADHD and narcolepsy. The extensive use of amphetamines for the treatment of obesity has been considerably reduced or discontinued in most countries. While the quantities of amphetamines used for direct medical purposes have been relatively small in most countries, the medical use of amfetamine and dexamfetamine in the United States has increased significantly since the 1990s. A significant increase in the use of amfetamine and dexamfetamine has also occurred in other countries, notably Australia and Canada. While France has traditionally been a major manufacturer of amphetamines, there is very limited medical use of amphetamines in that country, as almost all the amphetamines manufactured there are destined for export.

11. The countries with the highest levels of reported (i.e. furnished by Governments) consumption and calculated medical and industrial<sup>2</sup> uses of amphetamines, calculated on the basis of statistics provided for 2012<sup>3</sup> and expressed in S-DDD per 1,000 inhabitants per day,<sup>4</sup> are listed in tables 1 and 2 respectively, in order of their rate of use in 2012.

Table 1. Amphetamines: reported consumption rate, selected countries and territories, 2010-2012

	S-DDD per 1,000 inhabitants per day		
Country or territory	2010	2011	2012
United States	15.74	18.67	11.36
Australia	_	_	1.50
Canada	_	_	1.06
Netherlands	_	0.22	0.66
Christmas Island	_	_	0.43
Iceland	_	0.51	0.43
Sweden	0.29	0.31	0.41
United Kingdom	0.02	_	0.37
Chile	2.84	0.16	0.11
Finland	0.08	_	0.09
Denmark	0.06	0.07	0.03
Germany	0.04	0.13	0.03
Austria	0.02	0.01	0.01

<sup>&</sup>lt;sup>2</sup> Excluding use for the manufacture of other amphetamines and non-psychotropic substances.

<sup>&</sup>lt;sup>3</sup> The method used for calculating levels of consumption of psychotropic substances is explained in the explanatory note to table IV in part three of the present publication.

<sup>&</sup>lt;sup>4</sup>The list of S-DDD used in these calculations is presented in part one, table III, of the present publication.

Table 2. Amphetamines: calculated consumption rate, selected countries and territories, 2012

	(S-DDD per 1,000 inhabitants per day)	
Country or territory	2012	
Switzerland	6.09	
Cayman Islands	2.30	
Czech Republic	1.55	
Italy	0.46	
Norway	0.46	
France	0.27	
New Zealand	0.19	
Israel	0.11	
Belgium	0.07	
Belgium	0.0	

#### Comments on amphetamines, by substance

12. The manufacture of amfetamine gradually increased until it reached a peak of 30 tons in 1998, before falling gradually to 4.3 tons in 2010. In 2011, global manufacture of amfetamine started to rise again, reaching 23 tons in 2012, with the United States and France accounting for 88 and 11.7 per cent, respectively. Amfetamine is used mainly in combination with dexamfetamine in the United States. In 2012, around 2.4 tons of amfetamine were required for such use in the United States, which held about 83 per cent of global stocks of amfetamine in 2012 (9.7 tons). The United States and France, in that order, remained the main exporters of the substance. Total exports of amfetamine in 2012 amounted to 460 kg, the main importers of which were, in descending order, Canada (132 kg), Sweden (14.8 kg) and Switzerland (8.5 kg).

13. The trends in the manufacture of dexamfetamine reflect developments in the United States. During the 1980s, total output was fairly stable, at approximately 350 kg annually. It subsequently increased, although with many fluctuations, to reach a record level of 11 tons in 2009 and then decreased sharply to less than 5 tons in 2010 and 2011. In 2012, manufacture of dexamfetamine in the United States increased to a new record level of 21.4 tons. Stocks of dexamfetamine held in the United States amounted to 9.6 tons in 2012. The United States remained the main user of dexamfetamine for medical purposes, reporting consumption of 10.5 tons for 2012. Such use was also reported by a number of other countries, including Australia (176 kg), Canada (155 kg) and the Netherlands (60 kg). Global exports were 813 kg in 2012, of which France accounted for 670 kg and the United States for 91 kg. About 25 countries reported imports of dexamfetamine in 2012. Germany became the leading importer in that year, accounting for 41 per cent of the global total, followed by Canada, Australia and the Netherlands, in descending order, which together accounted for another 50 per cent of the total.

14. Global reported manufacture of metamfetamine, which amounted to 9.5 tons in 1999, has decreased since that year. The decline has been even more pronounced since 2008, after France and Switzerland ceased manufacturing the substance, with total output reaching less than 3 kg in 2010 and 2011. In 2012, global manufacture rose again and stood at 270 kg, almost all of which was manufactured in the United States (mainly for industrial purposes). Most other countries, which use metamfetamine for medical purposes, cover their needs through imports. The main importer of metamfetamine in 2012 was Spain (1.4 kg).

15. During the period 2003-2012, total reported manufacture of levomethamphetamine fluctuated between no output (in 2009 and 2010) and 4.6 tons (in 2002). The Czech Republic, France, Germany and the United States have traditionally been the main manufacturers of levomethamphetamine. In 2012, total output was about 1.1 tons, with the United States accounting for 980 kg and the Czech Republic for 89 kg. In recent years, on average about 470 kg of levomethamphetamine have been used annually in the United States for the manufacture of nasal inhalants for domestic use, which are exempted in that country from certain control measures in accordance with article 3 of the 1971 Convention. In 2012, 797 kg of levomethamphetamine were used for that purpose.

16. A total of 2.8 tons of metamfetamine racemate was manufactured in 2012. During the period 2008-2012, France and Hungary accounted on average for 63 and 37 per cent of global output, respectively. While in Hungary the substance is mainly used in the manufacture of nonpsychotropic substances, the output by other countries has mainly been exported to the United States, where it has either been converted into non-controlled substances or separated into levomethamphetamine and metamfetamine. Global stocks of metamfetamine racemate in 2012 stood at 2.5 tons. International trade in the substance averaged 1.4 tons during the period 2010-2012, with the United States accounting for all imports. Levomethamphetamine has been used mainly for export and has also been converted, in smaller quantities, into selegiline. Metamfetamine obtained during the process of separating it from levomethamphetamine has been added to stocks.

#### Methylphenidate

17. The use of methylphenidate for medical purposes increased significantly in the 1990s. Methylphenidate is used for the treatment of ADHD, primarily in children. It is also prescribed for the treatment of narcolepsy. The increase in the manufacture and use of methylphenidate is mainly the result of developments in the United States, where the substance is frequently prescribed for the treatment of ADHD and also heavily advertised, including directly to potential consumers. Since 2000, however, the use

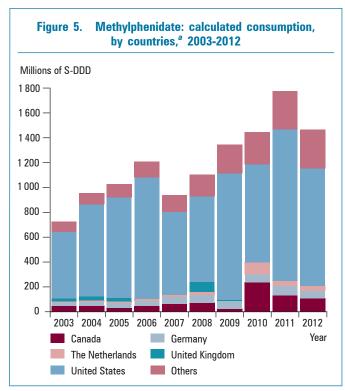
of methylphenidate for the treatment of ADHD has also been rising sharply in many other countries. In recent years, concerns have been raised about increasing misuse of preparations containing methylphenidate in some countries.

Global manufacture of methylphenidate started to rise rapidly in the 1990s, although with some fluctuations, reaching a record level of 63.2 tons in 2012, the highest amount ever reported (see figure 4). Since the 1990s, the United States has been the leading manufacturer of methylphenidate, increasing its output from 1.8 tons in 1990 to 10 tons in 1995 and then gradually increasing it further to a record level of 61 tons in 2012, which represents almost 97 per cent of global output for that year. Until 2009, the United Kingdom of Great Britain and Northern Ireland was the second largest manufacturer of methylphenidate. In 2010, however, manufacture of the substance in that country amounted to only a few grams. In 2011, the United Kingdom again became the second largest manufacturer, with an output of 3 tons of the substance, but that level dropped again in 2012 to some 6 kg. The other countries reporting manufacture of amounts of methylphenidate exceeding 1 ton in 2012 were Canada (1.2 tons) and Spain (1 ton); their combined output accounted for less than 4 per cent of global manufacture. Most of the methylphenidate manufactured in the United States continued to be used domestically, although exports from that country have increased in recent years. Global stocks of methylphenidate have increased in tandem with the rise in manufacture, increasing to more than 70 tons in 2012. The United States accounted for almost 79 per cent of global stocks at the end of 2012.

Figure 4. Methylphenidate: total reported manufacture. selected countries, 2003-2012 Tons 65 60 55 50 45 40 35 30 25 20 15 10 5 0 2003 2004 2005 2007 2008 2009 2010 2011 2012 Year Canada Switzerland United Kingdom Others United States

19. Despite the fact that manufacture of methylphenidate has spread to several other countries, the medical requirements for methylphenidate outside the United States continue to be met mainly by imports. International trade in methylphenidate increased during the period 1993-2012 from 980 kg to 25 tons. Switzerland was the main exporter of methylphenidate until 2006. Since 2007, however, the United States has been the leading exporter, accounting for 37 per cent of total exports in 2012. Other major exporting countries in 2012 were, in descending order, Switzerland, the United Kingdom, Spain and Germany. The number of countries and territories importing methylphenidate for domestic consumption has been growing. In 2012, 46 countries and territories reported imports of methylphenidate in amounts exceeding 10 kg.

20. The calculated global consumption of methylphenidate has followed an upward trend since 2007, reaching 52.3 tons (1.8 billion S-DDD) in 2011, but dropping to 44.2 tons (1.5 billion S-DDD) in 2012 (see figure 5). This decrease is mainly attributable to developments in the United States, which has traditionally been the leading user of methylphenidate for the treatment of ADHD and accounted for 64 per cent of calculated global consumption of methylphenidate in 2012. In that country, calculated consumption of methylphenidate decreased from 1.2 billion S-DDD in 2011 to 946 million S-DDD in 2012. The main users of methylphenidate in 2012 apart from the United States were, in that order, Canada, Germany, Spain, Switzerland, the Netherlands, Brazil, Sweden, Israel, South Africa and Australia.



<sup>a</sup> Statistical data submitted by Governments are used to calculate the approximate global consumption in a given year, expressed in S-DDD.

21. The countries and territories with the highest levels of reported (i.e. furnished by Governments) and calculated consumption of methylphenidate (calculated on the basis of statistics provided for 2011 and 2012) are listed in tables 3 and 4, respectively, in order of their level of consumption in 2012.

Table 3. Methylphenidate: reported consumption rate, 2010-2012

	S-DDD per 1,	S-DDD per 1,000 inhabitants per day		
Country or territory	2010	2011	2012	
Iceland	4.72	14.07	14.80	
United States	15.50	19.93	7.94	
Sweden	4.92	6.22	7.19	
Netherlands	_	6.63	6.69	
Denmark	5.09	5.88	6.37	
Canada	_	_	5.51	
Luxembourg	3.23	0.002	3.59	
Norfolk Island	_	0.96	2.37	
Australia	_	_	2.33	
Germany	1.98	1.97	2.08	
Chile	1.10	1.54	1.70	
Finland	_	_	1.47	
Sint Maarten	_	0.90	1.10	
Saint Helena	0.58	0.77	0.95	
Christmas Island	_	_	0.88	
United Kingdom	0.15	0.50	0.68	
Costa Rica	_	-	0.61	
Austria	0.44	0.30	0.51	
Turkey	_	-	0.48	
Brazil	_	0.38	0.39	
Singapore	0.26	0.27	0.28	
Estonia	0.06	0.15	0.22	
Lebanon	0.15	0.18	0.21	
Slovenia	0.04	-	0.17	
Qatar	_	-	0.16	
Ecuador	0.06	0.08	0.08	
Guatemala	_	0.09	0.06	

Table 4. Methylphenidate: calculated consumption rate, 2012

	S-DDD per 1,000 inhabitants per day		
Country or territory	2012		
Switzerland	14.72		
Israel	8.48		
Norway	6.94		
Dominica	5.53		
Cayman Islands	2.98		
Spain	2.82		
New Zealand	2.70		
Belgium	2.54		
Andorra	2.51		
Curaçao	1.32		
South Africa	1.02		

#### **Anti-emetics**

## delta-9-Tetrahydrocannabinol and its stereochemical variants

- 22. During the period 2008-2012, global manufacture of *delta*-9-THC gradually decreased from 233 kg (7.8 million S-DDD) in 2008 to 54 kg (1.8 million S-DDD) in 2012, led by a decrease in manufacture by the United States, the largest manufacturer of the substance worldwide. In 2012, the United States manufactured 49 kg of *delta*-9-THC, the majority of which was for domestic consumption. Germany remained the second largest manufacturer in 2012, reporting 4.5 kg of manufacture. Stocks held in the United States amounted to 965 kg, accounting for 85 per cent of the global total (1,338 kg) at the end of 2012, followed by Austria (12 per cent of global stocks) and Germany (2 per cent).
- 23. International trade in *delta-9-THC* grew slightly to 48 kg in 2012. Germany remained the largest exporter, with the United States and Austria being the main importers. The United States, Germany and Austria were the main users of the substance, reporting consumption of 103 kg, 4.8 kg and 2.8 kg, respectively.

## **Sedative-hypnotics**

24. Of the four substances from the group of sedativehypnotics in Schedule II, three of them, namely, gammahydroxybutyric acid (GHB), mecloqualone methaqualone, are neither barbiturates nor benzodiazepines. While mecloqualone has been listed in Schedule II since the adoption of the 1971 Convention, methaqualone, which was initially placed in Schedule IV, was moved to Schedule II in 1979 because of new information gathered over the years indicating its increased abuse potential and decreased medical usefulness. Both mecloqualone and methaqualone are nowadays no longer used in medical practice. The substance GHB, which was added to Schedule IV in 2001, was transferred to Schedule II in 2013. Secobarbital, the only barbiturate in Schedule II, was moved from Schedule III to Schedule II in 1988.

#### gamma-Hydroxybutyric acid

25. The substance GHB is used in the treatment of narcolepsy and, more rarely, alcoholism. Data for GHB may still be incomplete, as the substance was moved to Schedule II only in 2013. Reported manufacture of GHB increased steadily during the period 2006-2010, reaching a peak of 59 tons in 2010. After a significant drop in 2011, to 12.4 tons, global manufacture increased again, to 38.7 tons, in 2012,

the second-highest amount ever recorded for that substance. These fluctuations are mainly due to fluctuations in manufacture by the United States, a leading manufacturer of the substance. In 2012, reported manufacture of GHB in the United States amounted to 25.6 tons. Other manufacturers of GHB in 2012 were Germany (8.8 tons) and Ukraine (4.3 tons). Global stocks, which had attained 41 tons in 2011, declined to 24 tons in 2012. Italy and the United States remained the two largest holders of those stocks, together accounting for 76 per cent of global stocks in 2012.

26. International trade in GHB increased slightly from 2011 to 2012. In 2012, total reported imports amounted to nearly 16 tons, with Italy, the United Kingdom and France (in descending order) remaining the main importers. Germany, the United Kingdom, the United States and Ukraine (in descending order) were the leading exporters in 2012. Italy, the United States, Ukraine, France, the Russian Federation and Germany (in descending order) had the highest calculated consumption of GHB in 2012.

#### Secobarbital

27. Since 2000, Germany has been the major manufacturer of secobarbital. In 2012, its output amounted to 870 kg, accounting for over 93 per cent of total global

manufacture (931 kg), while the United States accounted for the remainder (61 kg). Global stocks of secobarbital stood at 833 kg in 2012, with the majority (88 per cent) held in Germany.

28. Global trade volume of secobarbital dropped slightly, from 830 kg in 2011 to almost 750 kg (7.5 million S-DDD) in 2012. Germany remained the leading exporter of the substance, while the United Kingdom continued to be the main importer. The United Kingdom, Germany, Sweden, the United States, Belgium and the Netherlands (in descending order) were the main users in 2012.

#### **Antitussives**

#### **Zipeprol**

29. The Republic of Korea, which had stopped manufacturing zipeprol in 1999, resumed its manufacture in 2008 and 2009 mainly for domestic consumption. For 2012, no manufacture of the substance was reported. The Plurinational State of Bolivia, the main importer of the substance in previous years, reported consumption of 9.1 kg for 2011 and 9.6 kg for 2012.

## Substances in Schedule III of the 1971 Convention

30. Nine substances are listed in Schedule III of the 1971 Convention. According to the scheduling criteria adopted by the World Health Organization, substances in Schedule III are those whose liability to abuse constitutes a substantial risk to public health and which have moderate to great therapeutic usefulness. One substance, cathine, belongs to the group of central nervous system stimulants. Six substances belong to the group of sedative-hypnotics: four barbiturates (amobarbital, butalbital, cyclobarbital and pentobarbital), flunitrazepam and glutethimide. The two remaining substances, buprenorphine and pentazocine, belong to the group of analgesics.

## **Central nervous system stimulants**

#### Cathine

31. Cathine is used as a stimulant and for industrial purposes. Manufacture of cathine fluctuated considerably

during the period 2003-2012, varying between no output and a peak of 5.9 tons, which was reached in 2007. Until 2003, Germany was the only manufacturer of the substance. Other countries reporting manufacture of cathine in recent years were China and India. From 2007 to 2009, manufacture of cathine declined sharply to 55 kg, all of which was reported by China. In 2010, global output reached 800 kg, of which 500 kg was manufactured in India and 300 kg in China. No manufacture of the substance was reported in 2011 and only some grams were reported in 2012. Global stocks of cathine decreased to 263 kg in 2012; these were held mainly in Germany and Switzerland.

32. India and Germany were the main exporters of cathine in the period 2008-2012. Global exports of the substance averaged 1.5 tons during that time, with a maximum of 3.1 tons in 2008 and a minimum of 872 kg in 2011. In 2012, reported global exports amounted to 1.05 tons. The main importers of cathine during that year, in descending order, were South Africa, Germany and Switzerland.

## Sedative-hypnotics listed in Schedule III

33. Classified as sedative-hypnotics, barbiturates used to be prescribed for the treatment of anxiety and stress and, in some cases, as anaesthetics for short surgery interventions (ultra-short-acting substances). Nowadays, they are used mainly as anti-epileptics or for their selective anticonvulsant property. Barbiturates differ in speed of onset, duration of action and potency. Like benzodiazepines, barbiturates encountered on the illicit market have usually been diverted from licit circuits rather than synthesized in clandestine laboratories.

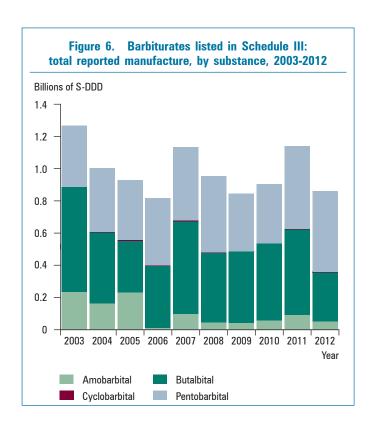
## Amobarbital, butalbital, cyclobarbital and pentobarbital

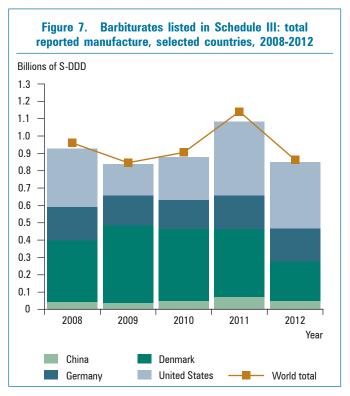
34. During the period 2003-2012, global manufacture of amobarbital, butalbital, cyclobarbital and pentobarbital fluctuated between 0.82 billion S-DDD and 1.27 billion S-DDD. For 2012, a global total of 862 million S-DDD was recorded, the lowest amount since 2006 as a result of decreased manufacture in Denmark. While manufacture of amobarbital has shown a downward trend in recent years, that of pentobarbital has increased (see figure 6). As in previous years, manufacture in China, Denmark, Germany and the United States accounted for almost 99 per cent of the total. Figure 7 shows the share of the main manufacturing countries, in total output, during the period 2008-2012.

35. After reaching a record high level in 2011 (51.4 tons or 514 million S-DDD), global manufacture of pentobarbital edged down slightly to 50.3 tons (503 million S-DDD) in 2012, owing to decreased manufacture in the United States. Total manufacture in the United States and Germany accounted for 91 per cent of the global total in 2012. Third came Denmark, followed by Canada and Japan. Total stocks of pentobarbital reached 38 tons (381 million S-DDD) in 2012, with about 41 per cent of them held in the United States, 28 per cent in Germany and 12 per cent in the United Kingdom. In 2012, the largest user of pentobarbital continued to be the United States, followed by Germany, France, Australia, Canada, Denmark and the Netherlands.

36. After increasing for two consecutive years in 2009 and 2010, the total volume of international trade in pentobarbital stabilized at 31 tons (309 million S-DDD) in 2012. Accounting for 41 per cent of global exports in 2012, Germany continued to be the top exporter, followed by the United States (15 per cent) and the Netherlands (11 per cent). France, Canada and the Netherlands, together, accounted for half of global imports in 2012.

37. Global manufacture of butalbital experienced a significant decrease in 2012, down from its record high of nearly 40 tons (532 million S-DDD) in 2011 to 23 tons (307 million S-DDD) in 2012, owing to decreased manufacture in Denmark and the United States. Despite a substantial drop in its manufacture, Denmark remained the





leading manufacturer (61 per cent of the global total), followed by the United States (37 per cent). Another significant manufacturer, Germany, did not report manufacture in 2011 and 2012. Manufacture in Denmark continued to be mainly for overseas markets, while that in the United States was predominately for domestic consumption. In that country, 3.5 tons (47 million S-DDD) were used in 2012 for the manufacture of preparations exempted from certain control measures, in accordance with article 3 of the 1971 Convention. Total volume of trade increased from 21.4 tons (286 million S-DDD) in 2011 to 31 tons (413 million S-DDD) in 2012, with Denmark remaining the largest exporter and Italy being the main importer. Global stocks of butalbital dropped to 22.3 tons (297 million S-DDD) in 2012, with around 63 per cent of that amount held in the United States and the remainder held mainly in Denmark and Italy.

38. Global manufacture of amobarbital fell from 9.4 tons (94 million S-DDD) in 2011 to 5 tons (50 million S-DDD) in 2012. This decrease can be attributed to a marked decrease in manufacture by China and no manufacture by Japan, the two main countries manufacturing and using amobarbital. As in previous years, the majority of the quantities manufactured in China was for domestic use. Global stocks stood at 950 kg (9.5 million S-DDD) in 2012, most of which were held in China and the remainder in the United Kingdom. Total international trade remained at about the same level, with China being the main exporter and the United Kingdom being the main importer. Total calculated consumption stood at 3.3 tons (32.8 million S-DDD) in 2012, almost all of it consumed in China.

39. Cyclobarbital was manufactured and used mainly in Europe. After Germany and Latvia stopped manufacturing the substance in 2003, Poland became the sole manufacturer of cyclobarbital. After recording a manufacture of 393 kg (2 million S-DDD) of cyclobarbital in 2011, manufacture in Poland rose to 484 kg (2.4 million S-DDD) in 2012. Of that amount, Poland exported 220 kg (1.1 million S-DDD), mainly to other countries in Europe. Amounting to almost 70 per cent of the global imports in 2012, the Russian Federation continued to be the main importer of cyclobarbital, with the remaining 13 per cent and 12 per cent imported by Georgia and Latvia, respectively.

#### Flunitrazepam

40. Flunitrazepam remains one of the most frequently abused benzodiazepines. The substance is diverted mainly from domestic distribution channels. Preparations containing flunitrazepam have often been diverted from the licit market and smuggled into countries where there is an illicit demand for such preparations. Because it had frequently been diverted and abused, flunitrazepam was transferred from Schedule IV to Schedule III in 1995. Several

countries, including major manufacturers and importers of the substance, have adopted strict control policies for flunitrazepam, in close cooperation with the pharmaceutical industry. Most of the preparations purportedly containing flunitrazepam that are sold on the illicit market are counterfeit products that do not contain that substance.

41. In medical practice, flunitrazepam, similarly to diazepam, has been used for pre-medication and for general anaesthesia. Prior to 1996, flunitrazepam was manufactured in several countries. After 1996, only Italy and Switzerland reported its manufacture; in 2010 and 2011, India also reported some manufacture of flunitrazepam. The manufacture of flunitrazepam in Switzerland, the main manufacturer of the substance, has fluctuated greatly; in some years, such as in 2005 and 2008 and during the period 2010-2011, no manufacture of the substance took place in that country. Those fluctuations are reflected in total global manufacture of flunitrazepam (see also paragraph 84 and figures 20 and 21 below), which in 2012 stood at 1.5 tons, with Switzerland accounting for 80 per cent of output (1.2 tons), followed by Italy (303 kg) and Germany (1.6 kg). Stocks of flunitrazepam held by manufacturers amounted to 1.3 tons in 2012, held mainly in Switzerland (82 per cent), Italy (11 per cent) and Brazil (3 per cent).

42. International trade in flunitrazepam averaged 1.1 tons per year during the five-year period 2008-2012, and stood at 1.2 tons in 2012. Italy and Switzerland were the leading exporters of flunitrazepam, together accounting on average for 91 per cent of global exports of the substance during the period 2008-2012. More than 50 countries reported imports or use of flunitrazepam during the period 2010-2012. Japan remained the leading importer of flunitrazepam in 2012, importing 702 kg or 67 per cent of global imports of the substance. Switzerland, Uruguay, Nigeria, Brazil and Germany (in descending order) reported imports ranging from 34 to 93 kg, accounting together for 26 per cent of global imports of the substance in 2012. Global calculated consumption of flunitrazepam increased by 2 per cent compared with 2011 and amounted to 909 kg (909 million S-DDD) in 2012, most of which was consumed in Japan (702 million S-DDD). Uruguay (36.7 S-DDD), Japan (15.2 S-DDD) and Austria (6.6 S-DDD) had the highest calculated rates of consumption measured in S-DDD per 1,000 inhabitants per day.

## **Analgesics listed in Schedule III**

#### Buprenorphine

43. Buprenorphine belongs to the family of opioids used mainly as analgesics. As shown in figure 8, global

manufacture of buprenorphine started to increase gradually beginning in the late 1990s, as the substance began to be used in higher doses for the treatment of pain and opioid addiction. After a significant drop in 2010, global manufacture increased again and attained a new record, with a total of 7,353 kg (919 million S-DDD) in 2012 reported by 13 countries, including the major manufacturing countries: the United Kingdom (4,608 kg), the Czech Republic (749 kg), Belgium (655 kg), Switzerland (453 kg), Australia (400 kg) and Germany (273 kg). Global stocks of the substance amounted to about 6.7 tons in 2012, an increase of almost 96 per cent from 2011. The majority of the stocks were held, in descending order, in the United Kingdom, the United States, Germany, the Czech Republic, Switzerland, Australia and France.

44. The volume of trade in buprenorphine has continued to increase since 1993, reaching a total of 7.2 tons in 2012, with over 60 countries reporting imports of the substance. Major importers in 2012 included the United States (4,749 kg), Germany (886 kg), France (510 kg), the United Kingdom (158 kg), Spain (119 kg) and Italy (104 kg). Among those countries, the United States reported a significant increase in imports over the 2011 level. The United Kingdom (3,233 kg), Belgium (731 kg), Germany (566 kg), the

<sup>a</sup> Statistical data submitted by Governments are used to calculate the approximate global consumption in a given year, expressed in S-DDD.

Czech Republic (526 kg), Australia (431 kg), Switzerland (239 kg) and France (100 kg) were the major exporters in 2012, together accounting for 97 per cent of total global exports.

45. Global calculated consumption of buprenorphine increased from 5.5 tons (681 million S-DDD) in 2011 to over 6 tons (756 million S-DDD) in 2012. With 524 million S-DDD, the United States accounted for 69 per cent of global calculated consumption in 2012, followed by Germany (9 per cent), France (5 per cent), Switzerland (4 per cent) and Spain and Italy (2 per cent each). The calculated consumption of buprenorphine in S-DDD per 1,000 inhabitants per day is shown in part three, table IV.5, of the present publication. Buprenorphine is used in several countries in detoxification and substitution treatment programmes for opioid dependence, including in Australia, Austria, Denmark, France, Germany, Hungary, Ireland, Malaysia, Switzerland and the United States. Diversions of preparations of buprenorphine, mainly from domestic distribution channels, have been reported by a few countries. Abuse of the substance, particularly among opioid addicts, has also been reported.

#### Pentazocine

46. Pentazocine is an opioid analgesic with properties and uses similar to those of morphine. Global total manufacture of the substance fluctuated during the period 2003-2011 between a low of 2.7 tons (13 million S-DDD) in 2003 and a high of 8.5 tons (42 million S-DDD) in 2009, mainly as a result of fluctuations in the total output of India and Italy, the two major manufacturing countries. In 2012, total manufacture of the substance amounted to 685 kg, of which 512 kg was manufactured in the United States. The pentazocine manufactured in the United States was mainly for domestic use. Italy and China, the two other major manufacturers in 2012, reported manufacture of 130 kg and 42 kg, respectively. India, which reported the manufacture of 6.7 tons of the substance for 2011, did not report manufacture of the substance in 2012. Global reported stocks of the substance decreased by 50 per cent from 2011, to 2,717 kg in 2012, as a result of absence of stock data from India and decreased stocks held in the United States. Major users of the substance in 2012 included, in descending order, the United States, Nigeria, Japan, Canada and Belgium.

47. Global trade in pentazocine has been declining since 2009. Total exports further decreased from 2,320 kg in 2011 to 1,072 kg in 2012. The largest exporter in 2012 was Italy (800 kg). Major importers in 2012 were the United States, Nigeria, Pakistan and Portugal, in descending order.

<sup>&</sup>lt;sup>b</sup>The data for 2012 are incomplete.

#### Substances in Schedule IV of the 1971 Convention

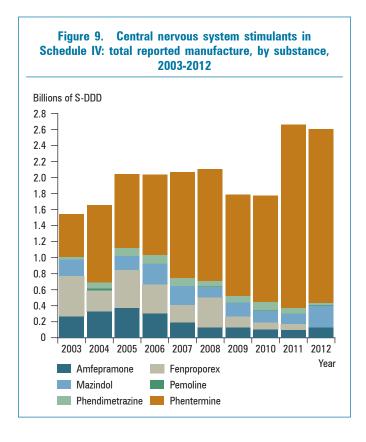
48. Sixty-two substances with various applications in medicine are listed in Schedule IV. They belong to the following groups: central nervous system stimulants (14 substances); benzodiazepine-type anxiolytics (22 substances); other anxiolytics (1 substance); benzodiazepine-type sedative-hypnotics (11 substances); benzodiazepine-type antiepileptics (1 substance); barbiturate-type sedative-hypnotics and anti-epileptics (7 substances); other sedative-hypnotics (5 substances); and analgesics (1 substance).

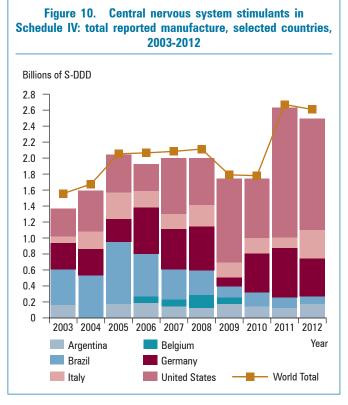
## **Central nervous system stimulants**

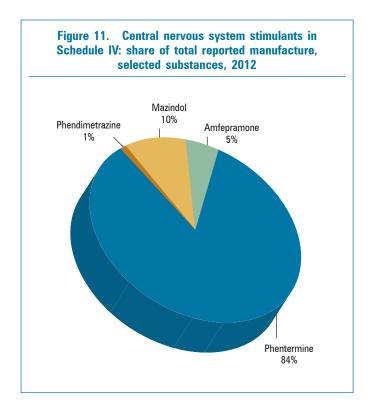
49. Fourteen central nervous system stimulants are listed in Schedule IV: amfepramone, aminorex, benzfetamine, etilamfetamine, fencamfamin, fenproporex, mazindol, mefenorex, mesocarb, pemoline, phendimetrazine, phentermine, pipradrol and pyrovalerone. The stimulants in Schedule IV are essentially used as anorectics or for the treatment of ADHD.

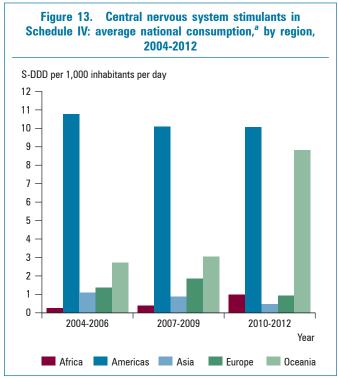
50. Reported manufacture of central nervous system stimulants in Schedule IV has been on the rise during the period 2003-2012, in spite of many fluctuations (see figure 9). Those fluctuations were mainly the result of developments in Brazil, Germany and the United States, which have traditionally been the main manufacturers. In 2012, global manufacture of this group of substances amounted to 2.6 billion S-DDD, the United States accounting for over half of the global total, followed by Germany and Italy (see figure 10).

51. In 2012, manufacture of phentermine (2.2 billion S-DDD) accounted for 84 per cent of total reported manufacture of all stimulants in Schedule IV, while the reported manufacture of mazindol (269 million S-DDD) accounted for 10 per cent, amfepramone (131 million S-DDD) accounted for 5 per cent and phendimetrazine (25 million S-DDD) accounted for 1 per cent (see figure 11). Reported manufacture of the other central nervous system stimulants in Schedule IV (benzfetamine, fenproporex and pemoline) accounted each for less than 1 per cent of total reported manufacture. No manufacture has been reported for the other stimulants in Schedule IV (aminorex, etilamfetamine, fencamfamine, mefenorex, mesocarb, pipradol and pyrovalerone).









<sup>a</sup>Statistical data submitted by Governments are used to calculate average annual consumption for a three-year period.

Figure 12. Central nervous system stimulants in Schedule IV: calculated global consumption, by substance, 2003-2012 Billions of S-DDD 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 <sup>'</sup>2007 <sup>'</sup>2008 <sup>'</sup>2009 <sup>'</sup>2010 <sup>'</sup>2011 <sup>'</sup>2012 2003 2004 2005 2006 Year Amfepramone Fenproporex Mazindol Pemoline Phendimetrazine Phentermine Others

<sup>a</sup>Statistical data submitted by Governments are used to calculate the approximate global consumption in a given year, expressed in S-DDD.

52. The fluctuations in total calculated global consumption of central nervous system stimulants listed in Schedule IV (see figure 12) mainly reflect changes in the use of phentermine in the United States and the use of amfepramone and fenproporex in Brazil. A total of 1.9 billion S-DDD of central nervous system stimulants listed in

Schedule IV were used in 2012. Of those, phentermine (1.58 billion S-DDD) accounted for 82.9 per cent, followed by mazindol (192 million S-DDD, or 10 per cent), fenproporex (59.5 million S-DDD, or 3.1 per cent), amfepramone (52 million S-DDD, or 2.7 per cent) and phendimetrazine (13.2 million S-DDD, or 0.7 per cent) (see figure 12). About 74 per cent of global calculated consumption of stimulants in Schedule IV in 2012 was accounted for by the United States (1.41 billion S-DDD), followed, in descending order, by Argentina, Australia and Brazil.

53. Calculated consumption of stimulants in Schedule IV in the Americas remained the highest in the world, at approximately the same levels as a decade ago (see figure 13). Decreases in the use of stimulants in Brazil achieved since 2006 have been almost offset by rising consumption levels observed in the United States. Levels of consumption decreased in Asia and Europe during the period 2010-2012 compared with the period 2006-2008, but increased markedly in Africa and, in particular, Oceania, where consumption of anorectics has increased significantly in some countries. In 2012, the highest consumption rates, expressed in S-DDD per 1,000 inhabitants per day, were reported by the United States (11.6 S-DDD), followed by Chile (1.2 S-DDD) and Brazil (0.5 S-DDD). Among the countries and territories that did not report consumption data, the highest calculated consumption rates, expressed in S-DDD per 1,000 inhabitants per day, were observed in Argentina (12.1 S-DDD), Australia (9.1 S-DDD) and China, Hong Kong Special Administrative Region, and Singapore (3.4 S-DDD each).

- 54. Phentermine has always been the most widely manufactured substance in the group of stimulants in Schedule IV. During the period 2003-2012, total reported manufacture of the substance gradually increased from 9 tons in 2003 to 34.4 tons in 2011, and stood at 32.6 tons in 2012, with the United States accounting for 20.7 tons, followed by Germany (7.22 tons) and Italy (4.7 tons).
- 55. International trade in phentermine also increased, reaching 17 tons in 2012. In recent years, the main exporter of the substance has been Germany (reporting exports of almost 7 tons in 2012), followed, in descending order, by Italy, the United States and Australia. The United States has been the main importer of phentermine in recent years, importing almost 8 tons in 2012. Imports of phentermine in quantities of more than 1 kg were reported in 2012 by 23 countries and territories.
- 56. Global manufacture of phendimetrazine decreased from 7.6 tons in 2010 to 1.8 tons in 2012. This decrease reflects developments in Italy, the main manufacturer of phendimetrazine in the period 2007-2011. Manufacture of phendimetrazine in that country declined gradually from 5.2 tons in 2009 to 733 kg in 2012. Phendimetrazine manufactured in Italy is mainly destined for export. Global exports decreased to 1.1 tons in 2012, of which Italy accounted for 58 per cent. Traditionally, the United States, followed by the Republic of Korea, have been the main importers and users of the substance. In 2012, Germany (43 kg), South Africa (26 kg) and Switzerland (4 kg) were the only countries reporting imports of phendimetrazine in quantities of more than 1 kg. No imports of phendimetrazine were reported by the Republic of Korea for 2011 and 2012.
- Total reported manufacture of amfepramone, which had averaged 22 tons per year during the period 2003-2007, decreased beginning in 2008 to about 9 tons per year on average. In 2012, total reported manufacture of amfepramone amounted to 10 tons. Only three countries reported having manufactured amfepramone in 2012: Switzerland (6.9 tons), Italy (2.4 tons) and the United States (570 kg). Brazil, which had reported the manufacture of 4.8 tons for 2011, submitted no report for 2012. Switzerland was the main exporter of amfepramone during the decade leading up to 2012, exporting 2.5 tons per year on average during the period 2008-2011. In 2012, Switzerland exported almost 7 tons, accounting for 83 per cent of global exports of the substance in that year. The largest imports of amfepramone were reported by the United States (5.3 tons), Germany (816 kg), the United Kingdom (402 kg) and Chile (289 kg). Nine other countries reported imports of amfepramone in quantities of more than 1 kg in 2012.
- 58. With the exception of 2005 and 2006, when manufacture of benzfetamine was reported by Ireland, Italy and Switzerland, the United States was the sole manufacturer of

- benzfetamine during the decade leading up to 2010. In 2011 and 2012, the United States and Italy together reported a total manufacture of 454 kg and 104 kg. International trade in benzfetamine remained limited in 2012, with only three countries reporting imports of the substance, including the United States and the United Kingdom. The United States was also the major consumer of benzfetamine in the period 2003-2012, reporting consumption of 137 kg for 2012.
- 59. Global reported manufacture of fenproporex has declined steadily since 2003, from 10 tons in that year to 1.4 tons in 2011, owing mainly to the decrease in manufacture reported by Belgium and Brazil, which were the major manufacturing countries in that period. In 2012, total output of fenproporex dropped to 6 kg, all of which was manufactured by Australia. Total reported imports of the substance, which had averaged 3.4 tons per year during the period 2006-2010, dropped to 313 kg in 2012, almost all of that amount imported by Brazil.
- 60. Argentina has been the main manufacturer of mazindol since 2003. It reported an annual average output of 160 kg of the substance during the period 2003-2012. In addition to Argentina, Brazil has intermittently manufactured mazindol, in amounts averaging 50 kg per annum. In 2012, Argentina manufactured 178 kg and Brazil manufactured 91 kg. Brazil held most of the global stocks of the substance at the end of 2012 (135 kg). Total exports of mazindol amounted to 39 kg, with Brazil accounting for 23 kg and Switzerland and the United Kingdom for the remainder.
- 61. No manufacture of pemoline was reported between 2005 and 2007. Since 2008, global manufacture of the substance has fluctuated between 392 kg in 2008 and 4 grams in 2009, reflecting developments in the Netherlands, which has been virtually the only country manufacturing pemoline since 2008. In 2012, total output of the substance amounted to 387 kg, all reported by the Netherlands, which has also been the main exporter. Stocks of pemoline have declined steadily, from 7.5 tons in 2004 to 188 kg at the end of 2012. During the decade ending in 2012, imports of pemoline averaged 338 kg a year. In 2012, total imports of pemoline stood at 360 kg, of which Japan accounted for 320 kg and the Netherlands for the remainder. In addition to being used as a stimulant, pemoline is used for the treatment of ADHD.

## **Benzodiazepines**

62. Thirty-three benzodiazepines were included in Schedule IV in 1984. Midazolam was added to Schedule IV in 1990 and brotizolam was added in 1995. Flunitrazepam was transferred from Schedule IV to Schedule III in 1995. During the decade ending in 2012, practically all countries and territories that reported to the Board manufactured or

traded in benzodiazepines in quantities of more than 1 kg at least once. Benzodiazepines are frequently diverted for subsequent smuggling and abuse.

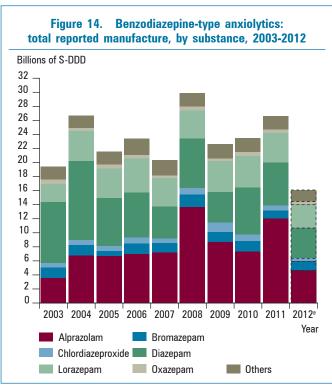
## Benzodiazepine-type anxiolytics

Twenty-two benzodiazepines are generally classified as anxiolytics. In the past decade, total reported manufacture of this group of substances fluctuated in the range of 19.4 billion and 29.9 billion S-DDD, averaging 23 billion S-DDD per year during the period 2003-2011 (see figure 14). Those fluctuations mainly reflect fluctuations in the manufacture of alprazolam and diazepam, the main substances in this group, which together accounted, on average, for almost 60 per cent of the total in the period 2008-2012. Global manufacture of this group of substances amounted to 16.1 billion S-DDD in 2012, which is 40 per cent lower than in 2011. The decline in 2012 is a result of the fact that data on manufacture of this group of substances from some countries, most importantly India, are missing. In 2011, manufacture in India accounted for 27 per cent of global manufacture of benzodiazepine-type anxiolytics.

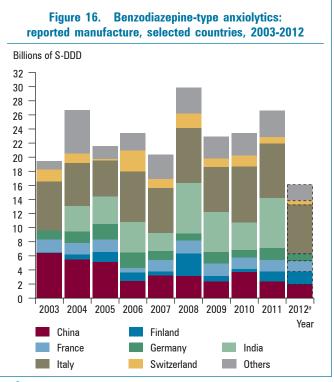
64. In 2012, alprazolam accounted for 29 per cent (4.6 billion S-DDD) of total reported manufacture of benzo-diazepine-type anxiolytics; diazepam for 26 per cent (4.3 billion S-DDD); lorazepam for 21 per cent (3.3 billion S-DDD); bromazepam for 8 per cent (1.3 billion S-DDD); chlordiazepoxide and oxazepam for 3 per cent each; clobazam for 2 per cent; and clorazepate and nordazepam for 1 per cent

each (see figure 15). The remaining substances in that group together accounted for 6 per cent of total reported manufacture. Up to 2007, fludiazepam had been intermittently manufactured in Japan; in the first reported manufacture since then, Switzerland reported manufacture of 7 grams of that substance in 2012. No manufacture of camazepam or pinazepam was reported for 2012, small quantities of which were last manufactured in 1991 and 2011, respectively. As shown

Figure 15. Benzodiazepine-type anxiolytics: share of total reported manufacture, by substance, 2012 **Others** 6% Nordazepam 0xazepam Alprazolam Lorazepam 29% 21% Diazepam Bromazepam 26% Chlordiazepoxide Clobazam Clorazepate



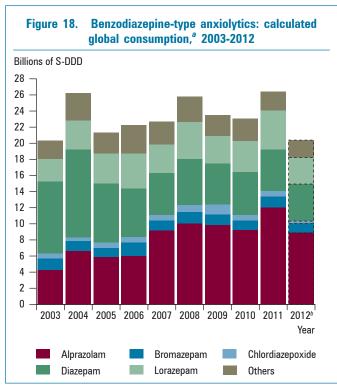
<sup>a</sup>The data for 2012 are incomplete.



<sup>a</sup>The data for 2012 are incomplete.

in figure 16, China, India and Italy were the leading manufacturers of benzodiazepine-type anxiolytics in the period 2003-2011. In 2012, owing to the absence of data from India for that year, Italy (7 billion S-DDD), China (1.9 billion S-DDD), Finland (1.8 billion S-DDD) and France (1.5 billion S-DDD) together accounted for 76 per cent of global manufacture of that group of substances (see figure 17).

Figure 17. Benzodiazepine-type anxiolytics: share of total reported manufacture, by country, 2012 Switzerland United States 2% Brazil Others 6% China 12% Finland 11% France 10% Italy 43% Germany 6%

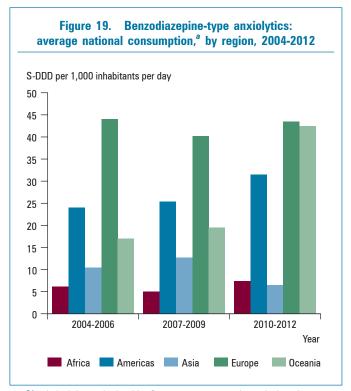


<sup>a</sup>Statistical data submitted by Governments are used to calculate the approximate global consumption in a given year. These consumption figures are expressed in defined daily doses for statistical purposes (S-DDD).

<sup>b</sup>The data for 2012 are incomplete.

65. Total approximate calculated consumption of benzodiazepine-type anxiolytics followed the overall trend in global manufacture. In 2012, the global calculated consumption for this group of substances amounted to 20.4 billion S-DDD (see figure 18). The United States, Brazil, Belgium, France, Spain, Japan and Italy (in descending order) were the largest consumers of this group of substances, in absolute terms, in 2012. The calculated consumption of benzodiazepine-type anxiolytics, expressed in S-DDD per 1,000 inhabitants per day, is shown in part three, table IV.3, of the present publication, with Slovenia (984 S-DDD), Belgium (360 S-DDD), Ireland (177 S-DDD), Finland (107 S-DDD) and Portugal (99 S-DDD) having the highest rates. Until 2010, Europe was consistently the region with the highest calculated average national consumption rates for benzodiazepine-type anxiolytics (see figure 19). The sharp increase in consumption levels in Oceania during the period 2010-2012 is the result of a marked increase in the imports and calculated consumption of alprazolam in Australia for 2011.

66. In 2012, total reported manufacture of alprazolam amounted to 4.6 tons, a decline of 62 per cent compared with 2011 due to significantly lower manufacture in the United States and because no data on manufacture were submitted by India, which had contributed 5.4 tons to global output in 2011. The main manufacturers of alprazolam in 2012 were Finland (1.7 tons), Italy (1.3 tons), France (989 kg) and China (251 kg), which together accounted for 92 per cent of global manufacture. They were



<sup>a</sup>Statistical data submitted by Governments are used to calculate the average annual consumption for a three-year period.

followed by Brazil (132 kg), Pakistan (90 kg), the United States (90 kg, down from almost 2 tons in 2011), Canada (41 kg), Argentina (30 kg) and the Russian Federation (5 kg). Global stocks of the substance have been relatively stable in the past five years, averaging 6.1 tons per year during the period 2008-2012. In 2012, the main stockholders, in descending order, were the United States, Finland, Canada, Italy and Brazil.

67. Alprazolam is available in many countries and all regions. Global exports have shown an upward trend during the past 10 years, rising from 4.9 tons in 2003 to 11.8 tons in 2011. In 2012, global reported exports fell to 10.8 tons. India, the United States, Italy, Finland, France and Belgium, in descending order, were the main countries reporting exports of the substance in 2012, their combined total accounting for 87 per cent of global exports. More than 100 countries reported imports of the substance during 2012. The main importers of alprazolam continued to be the United States (4.4 tons), Belgium (2 tons) and Italy (1.2 tons), mainly for re-export. Those countries were followed, in descending order, by Slovenia, Argentina, Brazil, Hungary and Switzerland. Global calculated consumption, which had averaged 10.3 billion S-DDD per year during the period 2008-2011, decreased to 8.9 billion S-DDD in 2012. The countries having the largest calculated consumption of alprazolam in absolute terms in 2012 were the United States (2.8 billion S-DDD), Belgium (1.2 billion S-DDD), Slovenia (727 million S-DDD) and Argentina (542 million S-DDD). Measured in S-DDD per 1,000 inhabitants per day, Slovenia (984 S-DDD), Belgium (309 S-DDD), Ireland (132 S-DDD), Hungary (57 S-DDD), Uruguay (44 S-DDD) and Argentina (37 S-DDD) had the highest rates of calculated consumption.

#### Diazepam

68. Diazepam continues to be the most traded substance in the group of benzodiazepine-type anxiolytics and is consumed in all regions of the world. Together with alprazolam, diazepam is among the benzodiazepines most often diverted and abused. Global reported manufacture of diazepam, which in the past decade had fluctuated between 43.5 tons in 2009 and 113 tons in 2004, fell to 43 tons in 2012, its lowest level in the past decade, mainly because no data on manufacture for 2012 were submitted by India, a major manufacturer and exporter of this substance, which in 2011 manufactured 7.1 tons of the substance. In 2012, Italy (17.7 tons), China (16.1 tons), Brazil (6.9 tons) and the United States (1.4 tons) accounted for 98 per cent of total reported manufacture. Global reported stocks of diazepam stood at 35.8 tons in 2012, held mainly in China, Italy, Brazil, Switzerland and the United Kingdom, in descending order.

69. International trade in diazepam, which averaged 57.2 tons annually during the 10-year period 2003-2012, amounted to 54.7 tons in 2012. Italy (19.4 tons) and China (9.5 tons) remained the leading exporters of the substance in 2012, followed by Switzerland and Denmark (5.6 tons each) and India (4 tons); together, those countries accounted for 81 per cent of global exports in 2012.

70. Practically all countries and territories imported diazepam at least once in the period 2008-2012. About 100 countries and territories reported imports of diazepam of more than 1 kg for 2012, the main importers being Ghana (5.8 tons), the United States (4.7 tons) and the Democratic Republic of the Congo (3.9 tons). Switzerland, Denmark and Spain imported 3.4 tons, 3.2 tons and 3 tons, respectively, mainly for re-export. Global calculated consumption of diazepam continued to decrease, standing at 4.6 billion S-DDD in 2012. Brazil (734 million S-DDD), the United States (648 million S-DDD), Ghana (579 million S-DDD), the Democratic Republic of the Congo (392 million S-DDD) and the United Kingdom (387 million S-DDD) had the highest calculated consumption of diazepam in 2012. Measured in S-DDD per 1,000 inhabitants per day, Ghana (65.1 S-DDD), Croatia (35.8 S-DDD), the former Yugoslav Republic of Macedonia (23.2 S-DDD) and Uruguay (18.9 S-DDD) had the highest calculated rates of consumption in 2012.

#### Lorazepam

71. Total reported manufacture of lorazepam was fairly stable during the period 2009-2011, averaging 10.9 tons per year. In the recent past, Italy, Germany and India were the three main manufacturers of the substance. In 2012, total reported output of the substance stood at 8.4 tons, of which Italy accounted for 64 per cent and Germany for 25 per cent. India had traditionally reported manufacture of lorazepam every year, with an output of 1.2 tons reported for 2011; however, no manufacture was reported by that country for 2012. Other countries reporting manufacture of lorazepam in 2011 were the United States (296 kg), Canada (276 kg), Poland (209 kg), Israel (68 kg), China (49 kg), Spain (34 kg) and Costa Rica (23 kg). Global reported stocks of lorazepam stood at 8.3 tons in 2012, mainly held, in descending order, in Germany, Italy, the United States and Ireland.

72. In 2012, total reported exports of lorazepam stood at 10.9 tons, 4 per cent lower than in 2011. The main exporters of lorazepam in 2012 were Italy, Germany, India, Ireland, Belgium and Hungary (in that order), which together accounted for approximately 94 per cent of total exports of the substance. About 60 countries and territories reported imports of lorazepam of more than 1 kg for 2012, the main importers being the United States (2.2 tons), Ireland

(1.2 tons), Belgium (1.1 tons, mainly for re-export), Spain (1 ton) and Italy (758 kg, for re-export), which together accounted for 60 per cent of all reported imports of the substance. During the period 2003-2012, global calculated consumption averaged 3.8 billion S-DDD per year. In 2012, it amounted to 3.3 billion S-DDD, with the highest levels being recorded for the United States (783 million S-DDD), Spain (382 million S-DDD), Italy (346 million S-DDD) and Canada (238 million S-DDD). Ireland (33.6 S-DDD), Belgium (27.7 S-DDD), Portugal (24.9 S-DDD), Spain (23.1 S-DDD), Austria (22.6 S-DDD) and Serbia (21.6 S-DDD) had the highest calculated rates of consumption, measured in S-DDD per 1,000 inhabitants per day.

#### **Bromazepam**

73. During the period 2003-2012, total reported manufacture of bromazepam fluctuated significantly within the range of 7.3 tons (2005) and 18.3 tons (2008), averaging 13.8 tons per year. In 2012, total reported manufacture of bromazepam stood at 12.7 tons, the main manufacturers remaining Italy (5.9 tons) and Switzerland (5.8 tons), followed by Brazil (931 kg) and Canada (108 kg). No other country reported manufacture of the substance in 2012, including India (the other manufacturer of bromazepam in the recent past), for which data on manufacture for 2012 are missing. Global reported stocks of bromazepam were fairly stable during the past five years, averaging 14.1 tons per year during the period 2008-2012. Most of the stocks in 2012 were held in Switzerland, Italy, France and Brazil, in that order.

74. International trade in bromazepam was stable during the period 2003-2012, with global exports averaging 16.8 tons annually. In 2012, as in previous years, the main manufacturing countries (Italy and Switzerland) were also the leading exporters of the substance, jointly accounting for 78 per cent of total exports. Ninety-four countries reported imports of bromazepam in 2012, with 23 of those countries reporting imports of more than 100 kg. France (3.2 tons, mainly for domestic consumption), Switzerland (2.1 tons, for re-export) and Italy (1.4 tons, for re-export) remained the main importers of bromazepam in 2012, jointly accounting for 43 per cent of total reported imports. Five further countries, namely Pakistan (951 kg), Germany (799 kg), Brazil (750 kg), Serbia (750 kg) and Japan (739 kg), accounted for 26 per cent of global imports during 2012. Global calculated consumption of bromazepam was fairly stable during the period 2003-2012, averaging 1.3 billion S-DDD. Total consumption decreased slightly, from 1.4 billion S-DDD in 2011 to 1.2 billion S-DDD in 2012, with France (251 million S-DDD), Brazil (153 million S-DDD), Italy (85 million S-DDD), Japan (74 million S-DDD) and Pakistan (73 million S-DDD) having the highest levels, in absolute terms.

#### Chlordiazepoxide

75. Since peaking in 2009 at 40.4 tons, total reported manufacture of chlordiazepoxide has decreased steadily, falling to 13.6 tons in 2012. Italy (11.3 tons) and China (1.8 tons), traditionally the main manufacturers of the substance, accounted for 97 per cent of the total reported output. Only three other countries reported significant manufacture of the substance in 2012: Canada (160 kg) and Poland and the United States (147 kg each). Data on manufacture in 2012 were missing from India, another major manufacturer of chlordiazepoxide, which had reported manufacture of 7.7 tons of the substance for 2011. Global reported stocks of this substance stood at 12.5 tons in 2012, held mainly in Italy, China, the United States, Brazil and Switzerland, in that order.

76. Global exports of chlordiazepoxide declined from 18 tons in 2011 to 16.9 tons in 2012. Italy (8.3 tons), China and India (2.5 tons each) and Switzerland (1.6 tons) were the largest exporters of chlordiazepoxide in 2012, jointly accounting for 88 per cent of global exports. More than 100 countries reported imports of chlordiazepoxide in the fiveyear period 2008-2012. Switzerland (2 tons), the Islamic Republic of Iran (1.4 tons), the United States (1.2 tons), Brazil (770 kg) and Ghana (645 kg) were the main importers of the substance in 2012, accounting together for 48 per cent of the global total. Calculated global consumption of the substance, after having peaked at 1.2 billion S-DDD in 2009, continued to decrease and fell from 660 million S-DDD in 2011 to 300 million S-DDD in 2012. The countries with the highest levels of consumption in 2012 were the Islamic Republic of Iran (45.2 million S-DDD), the United States (28.9 million S-DDD) and Italy (23.9 million S-DDD); while the highest rates of consumption measured in S-DDD per 1,000 inhabitants per day were recorded for Jordan (4.9 S-DDD), Iceland (2.5 S-DDD), Ghana (2.4 S-DDD) and the Islamic Republic of Iran (1.6 S-DDD).

#### **Oxazepam**

77. During the period 2003-2012, total reported manufacture of oxazepam fluctuated within the range of 20.3 tons in 2007 and 34.4 tons in 2003, averaging 25.1 tons per year. Global reported manufacture of the substance declined to 22.7 tons in 2012, partly owing to the lack of data from India, which had reported output of 1.6 tons for 2011. Italy (20.1 tons), which manufactures the substance mainly for export, Canada (1.2 tons) and France (1.1 tons) remained the main manufacturers of oxazepam in 2012, jointly accounting for almost 99 per cent of global output. Global stocks were stable during the period 2011-2012, at an annual level of 18.4 tons. The volume of trade in oxazepam has gradually declined during the past decade, from 41 tons in 2003 to 17.3 tons in 2009, before increasing to 27.5 tons in 2012. Italy (21.7 tons), Germany and India (1.9

tons each) and Hungary (1.2 tons) remained the main exporters. A total of 47 countries reported imports of oxazepam in 2012. The main importers of oxazepam, together accounting for 66 per cent of total global imports, were France (10.3 tons), Germany (2.8 tons), Canada (1.7 tons) and the Netherlands and Australia (1.5 tons each). Those countries were also the countries with the highest calculated consumption in 2012, in absolute terms. Norway (7.6 S-DDD), Finland (7.3 S-DDD), Croatia (7.1 S-DDD), France (7 S-DDD) and Austria (5.8 S-DDD) were the countries with the highest rates of calculated consumption in 2012, measured in S-DDD per 1,000 inhabitants per day.

#### Clobazam

78. Total reported manufacture of clobazam fluctuated between 3.3 tons in 2009 and 6.8 tons in 2011 and stood at 5.8 tons in 2012. Germany (2.9 tons) and France (2.5 tons) remained the main manufacturers, and exporters, of the substance in 2012, while data on manufacture were missing from India, which had reported an output of 2 tons for 2011. Global reported stocks had increased over the past three years, reaching 4.7 tons in 2012, mainly held in France, Germany, Canada, Brazil and the United States, in that order. International trade in clobazam was fairly stable in the past 10 years, global reported exports averaging about 5.2 tons per year during the period 2003-2012. Seventy-six countries reported imports of the substance in 2012, including France (1.1 tons), Brazil (663 kg), Japan (300 kg), Pakistan (280 kg), Canada (260 kg), Spain (212 kg) and the United States (201 kg).

#### Clorazepate

79. Total reported manufacture of clorazepate declined from 8.4 tons in 2003 to 4.1 tons in 2011. In 2012, global manufacture recovered slightly and stood at 4.6 tons. France and Italy were the leading manufacturers of this substance during the period 2003-2012. In 2012, those two countries accounted for almost the entire output (except for 86 grams manufactured in Canada) and for 78 per cent of global exports. International trade in clorazepate has been stable in the past two years and averaged about 5.1 tons per year during the period 2011-2012. Spain (2.4 tons), the United States (548 kg), France (302 kg, for re-export), Switzerland (274 kg) and Thailand (223 kg) were the largest importers of clorazepate in 2012, while about 40 other countries reported import and use of the substance during that year.

## Other anxiolytics

80. Owing mainly to developments in Switzerland, traditionally the main manufacturer of nordazepam, total

reported manufacture of that substance varied during the period 2003-2011 between 1.3 tons in 2003 and a peak of 14.2 tons in 2006. In 2012, total global manufacture of nordazepam amounted to 2.5 tons (164 million S-DDD), with Finland (2 tons) and France (437 kg) being the largest manufacturers. Switzerland did not manufacture nordazepam in 2012. Use of nordazepam remained limited to a very few countries, namely, Finland, France, Morocco, Italy and Singapore, in descending order.

81. In 2012, global manufacture of tetrazepam stood at 21.8 tons (218 million S-DDD), manufactured mainly in France, Italy and Germany. In 2012, total reported manufacture of prazepam dropped to 1.4 tons (48 million S-DDD), as a result of no manufacture being reported by Switzerland. Total reported manufacture of ethyl loflazepate amounted to 417 kg (208 million S-DDD), Japan and France being the only manufacturers in the past decade. Since 2004, India has been the only country reporting manufacture of pinazepam; since no data on manufacture were submitted by India for 2012, global output for that year was recorded as zero. Similarly, there was no manufacture of camazepam and halazepam in 2012. The combined manufacture of clotiazepam, cloxazolam, delorazepam, fludiazepam, ketazolam, medazepam and oxazolam amounted to 511 million S-DDD in 2012.

#### Meprobamate

82. Meprobamate, the only non-benzodiazepine-type substance in Schedule IV used as an anxiolytic, has gradually been replaced by benzodiazepines, leading to a substantial decline in manufacture from 750 tons in the late 1970s to an annual average of 290 tons during the 1990s. During the period 2000-2009, total manufacture of meprobamate fluctuated around an annual average of 220 tons. Since then, total reported manufacture has declined continually, to 128 tons (107 million S-DDD) in 2012. China and Denmark were traditionally the main manufacturers of the substance, their combined output accounting for over 93 per cent of global manufacture in the past five years. India, which has also manufactured meprobamate in significant quantities, did not report such manufacture for 2012. The observed decline in global manufacture is primarily due to lower outputs in Denmark, which dropped from 40 tons in 2011 to 375 kg in 2012. China remained the leading manufacturer of meprobamate, reporting 127 tons of manufacture in 2012 (a 53 per cent increase over 2011). Global stocks have also continued to decrease since 2009. They stood at 47.1 tons (39.3 million S-DDD) in 2012, 93 per cent of which were held in South Africa (25 tons), France (9 tons), Hungary (4.8 tons), Denmark (2.9 tons) and the United States (2 tons).

83. International trade in meprobamate has also gradually declined, from 259 tons in 2007 to 134 tons in 2011,

before increasing to 172 tons in 2012. China (146 tons), India (13.3 tons) and Denmark (7.3 tons) were the main countries exporting meprobamate in 2012, jointly accounting for 97 per cent of global exports in that year. Other major exporters in 2012 included Switzerland (1.7 tons), France (959 kg), South Africa (910 kg) and Belgium (891 kg). A total of 34 countries reported imports of meprobamate in 2012, major importers being South Africa (114 tons), the Democratic Republic of the Congo (5.4 tons), Egypt (3 tons) and Turkey (2.4 tons). Belgium and Switzerland imported 1.8 tons and 1 ton, respectively, mainly for re-export. Global calculated consumption of meprobamate rose from 162 tons (135 million S-DDD) in 2011 to 196 tons (164 million S-DDD) in 2012, mainly due to increased consumption in South Africa. In that year, South Africa became the leading consumer of meprobamate, with 117.6 tons (98 million S-DDD), followed by Denmark (45.3 tons), Hungary (9.6 tons) and the United States (6.1 tons).

## Benzodiazepine-type sedative-hypnotics

84. Twelve benzodiazepines are generally used as sedative-hypnotics: brotizolam, estazolam, flunitrazepam, flurazepam, haloxazolam, loprazolam, lormetazepam, midazolam, nimetazepam, nitrazepam, temazepam and triazolam. Comments on flunitrazepam, a substance that was transferred from Schedule IV to Schedule III in 1995, are provided in paragraphs 40-42 above.

85. During the decade leading up to 2012, total reported manufacture of the 12 substances in the group of benzodiazepine-type sedative-hypnotics was 7.2 S-DDD per year, on average, fluctuating between 5.5 billion S-DDD in 2008 and 9.5 billion S-DDD in 2009, owing mainly to changes in output reported by Germany, Italy, Switzerland and the United States. In 2012, global reported manufacture of benzodiazepine-type sedative-hypnotics amounted to 6.5 billion S-DDD (see figure 20), 12 per cent lower than in 2011, mainly because of a decrease in global reported manufacture of lormetazepam and triazolam. In 2012, the major manufacturers of this group of substances remained Italy (40 per cent), Germany (20 per cent), Switzerland (19 per cent), Japan (9 per cent) and China (5 per cent). Global stocks held by manufacturers were stable in the past three years, at the level of 6.4 billion S-DDD in 2012, mainly held in Germany (33 per cent), Switzerland (17 per cent), Italy (15 per cent) and the United States (12 per cent). Calculated global consumption of this group of substances was less volatile than manufacture, fluctuating around an annual average of 8 billion S-DDD during the period 2003-2012. In 2012, calculated global consumption stood at 6.6 billion S-DDD (see figure 21).

Figure 20. Benzodiazepine-type sedative-hypnotics: total reported manufacture, by substance, 2003-2012 Billions of S-DDD 10 9 8 7 6 5 2 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 Brotizolam Estazolam Flunitrazepam Lormetazepam Nitrazepam Temazepam Triazolam Others

<sup>a</sup>The data for 2012 are incomplete.

Figure 21. **Benzodiazepine-type sedative-hypnotics:** calculated global consumption,<sup>a</sup> 2003-2012 Billions of S-DDD 10 9 8 7 5 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012<sup>t</sup> **Brotizolam** Estazolam Flunitrazepam Nitrazepam Lormetazepam Temazepam Triazolam Others

<sup>a</sup> Statistical data submitted by Governments are used to calculate the approximate global consumption in a given year. These consumption figures are expressed in defined daily doses for statistical purposes (S-DDD).
<sup>b</sup>The data for 2012 are incomplete.

86. Earlier in the decade, the calculated average annual consumption of benzodiazepine-type sedative-hypnotics, expressed in S-DDD per 1,000 inhabitants per day, was traditionally higher in Europe and in a few non-European

countries, such as Japan and Cuba, than in other regions. In recent years, however, there have been significant changes in average annual consumption rates across regions (see figure 22). While average consumption rates in Europe, the Americas and Oceania have been relatively stable in the past six years, standing at about 20, 9 and 10 S-DDD per 1,000 inhabitants per day, respectively, this indicator increased markedly in Asia, from 13.4 S-DDD to 18.7 S-DDD, mainly owing to a 29 per cent increase in the consumption rate of Japan, which stood at 63 S-DDD in 2012. It is also notable that the average annual rate of consumption of benzodiazepine-type sedative-hypnotics, although still low, almost doubled in Africa, and averaged 1.6 S-DDD per 1,000 inhabitants per day during the period 2010-2012. In 2012, South Africa and Nigeria had the highest rates of consumption in this region, with 1.8 and 1.5 S-DDD per 1,000 inhabitants per day, respectively. Calculated consumption levels of benzodiazepine-type sedativehypnotics in individual countries, expressed in S-DDD per 1,000 inhabitants per day, are shown in part three, table

this group has varied greatly over the years, since manufacturers tend to produce large quantities of a substance at a time in order to keep stocks on hand for future use. There have been significant fluctuations in total manufacture of brotizolam, flunitrazepam and lormetazepam, in particular, which has affected the total level for the group as a whole. In 2012, brotizolam was the most manufactured substance in the group of benzodiazepine-type

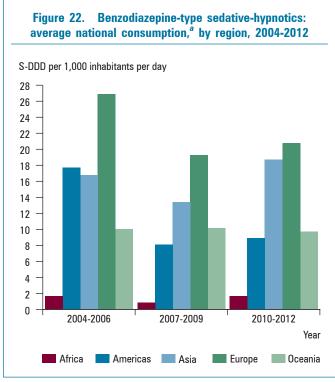
million S-DDD, or 10.9 per cent), lormetazepam (608 million S-DDD, or 9.4 per cent), estazolam (398 Benzodiazepine-type sedative-hypnotics: share Figure 23. of total reported manufacture, by substance, 2012 Estazolam Others Midazolam 4% Nitrazepam 11% Brotizolam 28% IV.2, of the present publication. The reported manufacture of individual substances in

Temazepam

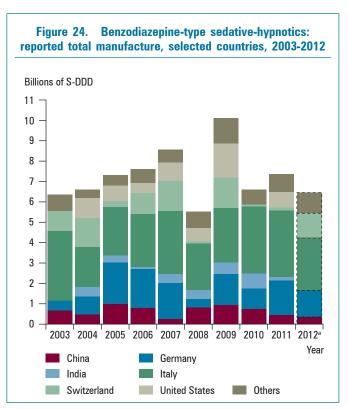
11%

Flunitrazepam

24%



<sup>a</sup>Statistical data submitted by Governments are used to calculate the average annual consumption for a three-year period.



Triazolam

3%

Lormetazepam

sedative-hypnotics, accounting for 1.8 billion S-DDD, or

28 per cent, of global manufacture of this group of sub-

stances (see figure 23). Flunitrazepam was second, with an

output of 1.5 billion S-DDD, or 24 per cent of global man-

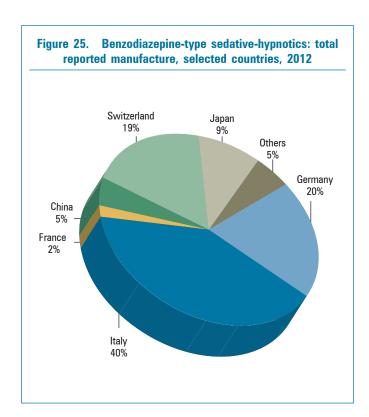
ufacture in 2012. Nitrazepam was third (716 million

S-DDD, or 11.1 per cent), followed by temazepam (702

<sup>&</sup>lt;sup>a</sup>The data for 2012 are incomplete.

million S-DDD, or 6.2 per cent), midazolam (231 million S-DDD, or 3.6 per cent) and triazolam (218 million S-DDD, or 3.4 per cent). The remaining substances in this group together accounted for about 4 per cent of total manufacture in 2012: flurazepam (141 million S-DDD, or 2.2 per cent), loprazolam (124 million S-DDD, or 1.9 per cent) and nimetazepam (16 million S-DDD); no manufacture of haloxazolam was reported.

88. The main countries reporting manufacture of benzo-diazepine-type sedative-hypnotics during the decade up to 2012 are shown in figure 24. Throughout that period, Italy was the leading manufacturer, accounting in 2003 for more than half of global manufacture of such substances. In 2012, Italy manufactured benzodiazepine-type sedative-hypnotics amounting to 2.6 billion S-DDD, which, although 30 per cent lower than in 2011, still accounted for 40 per cent of global manufacture of such substances (see figure 25).



#### **Brotizolam**

89. Brotizolam is a potent hypnotic. Together with triazolam, it has the lowest S-DDD of all psychotropic substances (0.25 mg). Germany was the first country to report manufacture of brotizolam, in 1997. Since that year, the substance has usually been manufactured by Germany in amounts of several hundred kilograms per year and, to a much lesser extent, by Italy and Japan. Global reported manufacture of brotizolam has increased by 20 per cent,

from 372 kg in 2011 to 446 kg in 2012. Germany (320 kg) and Japan (91 kg) remained the main manufacturers of the substance. Global stocks stood at 383 kg (1.5 billion S-DDD) in 2012, 79 per cent of which were held in Germany. Germany also remained the main exporter of brotizolam in 2012, accounting for 162 kg, or 80 per cent of total exports of the substance. Nine countries reported having imported more than 1 kg of brotizolam in 2012, Japan being the biggest importer (144 kg) and accounting for 71 per cent of total imports. Global calculated consumption of brotizolam stood at about 1.4 billion S-DDD in 2012, mainly in Japan (69 per cent) and Germany (23 per cent).

#### Nitrazepam

90. Italy, China and India, in descending order, were the main manufacturers of nitrazepam in the past decade. In the period 2003-2010, global reported manufacture of this substance ranged between 4 and 6.8 tons per year, with an annual average of 5.2 tons. In 2011, total manufacture of nitrazepam fell to 2.9 tons, owing to sharp decreases in the reported outputs of Italy and India. In 2012, global manufacture increased to 3.6 tons (716 million S-DDD), of which Italy accounted for 71 per cent. In the absence of data reported by India, which had been a major manufacturer of nitrazepam during the period 2003-2010, the only other countries reporting manufacture of nitrazepam in 2012 were China (850 kg), Canada (92 kg), Germany (50 kg), the Russian Federation (38 kg) and New Zealand (6 kg). Following the trend in manufacture, the global stocks of nitrazepam have been gradually decreasing in recent years, from 4.6 tons in 2009 to 1.4 tons in 2012. Exports of nitrazepam, which had averaged about 4.2 tons annually during the preceding nine years (2003-2011), increased from 3.2 tons in 2011 to 5.1 tons in 2012. Italy (3.6 tons), China (850 kg) and India (358 kg) continued to be the main exporters of the substance, together accounting for 94 per cent of all nitrazepam exports in 2012. Forty countries have imported nitrazepam in quantities exceeding 1 kg in the past five years (2008-2012). Japan (51 per cent), the United Kingdom (8 per cent), Nigeria (5 per cent), Germany (4.7 per cent) and Canada (4 per cent) were the main importers of nitrazepam in 2012. Global calculated consumption of nitrazepam, which amounted on average to almost 6 tons (1.2 billion S-DDD) annually during the period 2008-2010, has decreased significantly (by 44 per cent) in the past two years, with an average of 3.4 tons (684 million S-DDD) of the substance consumed annually during the period 2011-2012. Measured in S-DDD per 1,000 inhabitants per day, Japan (8.8 S-DDD), Bosnia and Herzegovina (4.4 S-DDD), Croatia (3.3 S-DDD), Australia (3.1 S-DDD) and Canada (3 S-DDD) had the highest rates of calculated consumption in 2012.

#### Temazepam

91. During the period 2003-2012, Italy was the leading manufacturer and exporter of temazepam and Canada, India, Poland, the United Kingdom and the United States reported intermittent manufacture of the substance for some of those years. In the past three years, global reported manufacture of temazepam gradually decreased from 21.6 tons in 2010 to 14 tons in 2012, with Italy accounting for about 93 per cent (13 tons) of the total. The only other manufacturers of the substance in 2012 were Canada (987 kg), the United States (23 kg) and Germany (6 grams). Global stocks of temazepam held by manufacturers stood at 10.4 tons in 2012 (a 28 per cent decrease compared with 2011), held mainly in Italy, the United States, the United Kingdom, Canada and Hungary, in descending order. Global exports of temazepam were stable in the past three years, averaging 19 tons per year during the period 2010-2012. Nineteen countries imported temazepam in quantities exceeding 1 kg in 2012, with the United States remaining the largest importer (10.9 tons) and consumer of the substance. The other major importers of temazepam in 2012 were Finland (1.2 tons), the Netherlands and Australia (about 1.1 tons each), and Canada and the United Kingdom (with about 1 ton each). Global calculated consumption of temazepam stood at 17.9 tons (897 million S-DDD) in 2012. The United States accounted for 51 per cent of the total, while Canada, Italy, Australia and the Netherlands, in that order, together accounted for 39 per cent. According to reported statistics, measured in S-DDD per 1,000 inhabitants per day, Finland (17.4 S-DDD), Canada (10.2 S-DDD) and the Netherlands (8.5 S-DDD) had the highest calculated rates of consumption in 2012.

#### Lormetazepam

92. In the period 2003-2011, total reported manufacture of lormetazepam was consistently above 1 ton, except in 2003 (380 kg) and in 2007 (809 kg). The fluctuations were the result of developments in Germany and Italy, the two main manufacturers and exporters of the substance. In 2012, global output of lormetazepam fell again, to 608 kg (608 million S-DDD), reflecting the output of Italy, which was the only country reporting manufacture of the substance that year. Global stocks held by manufacturers decreased to 1.3 tons (1.3 billion S-DDD) in 2012, mainly held in Germany (65 per cent), Italy (13 per cent) and Finland (10 per cent). The volume of reported international trade decreased from 1.9 tons in 2011 to 1.5 tons in 2012. Italy (582 kg), Germany (382 kg), Finland (197 kg) and Spain (158 kg) jointly accounted for 90 per cent of global exports in 2012. Twenty countries reported imports of lormetazepam in 2012, the main importers being Spain (456 kg), Finland (220 kg) and Belgium (195 kg). As in the past, some of those countries imported the substance mainly for re-export. The calculated global consumption, which had fluctuated in the past decade between 790 kg in 2003 and 2 tons in 2010, stood at 1.2 tons (1.2 billion S-DDD) in 2012. Rates of consumption continued to be particularly high in Europe, with the highest calculated rates of consumption, expressed in S-DDD per 1,000 inhabitants per day, recorded for Belgium (48), Spain (18), Italy (17) and Finland (10).

#### Estazolam

93. After staying fairly stable during the period 2008-2010 at an average annual level of 2.5 tons, global reported manufacture of estazolam gradually decreased in the following two years, to less than 1.2 tons (398 million S-DDD) in 2012, as a result of lower outputs reported by China, which was the major manufacturer of the substance during the period 2003-2011. In 2012, China reported manufacture of 501 kg of estazolam, which represents a 37 per cent reduction on the year before. Other countries reporting manufacture of estazolam in 2012 were, in descending order, Japan, Poland, Italy, the United States and Israel. The reported total stocks of the substance increased by more than five-fold in 2012 and amounted to 702 kg (234 million S-DDD), 81 per cent of which were held in China. Use of the substance outside the manufacturing countries has increased steadily since the 1980s, with international trade in 2011 reaching the highest level ever reported (405 kg). In 2012, global exports decreased slightly, to 384 kg. The leading exporters of estazolam have traditionally been Japan and Italy; in 2012, those two countries accounted for 63 and 29 per cent of global exports, respectively. About 15 countries reported imports of estazolam in quantities exceeding 1 kg during the period 2008-2012. In 2012, Italy (57 kg), the Netherlands (36 kg), Japan and Portugal (30 kg each), France (27 kg) and the United States (18 kg) jointly accounted for 87 per cent of total imports of the substance. Global calculated consumption of estazolam has continued its downward trend in the past three years, decreasing from over 2.5 tons (848 million S-DDD) in 2009 to 533 kg (178 million S-DDD) in 2012. Measured in S-DDD per 1,000 inhabitants per day, in 2012 Portugal (2.6 S-DDD), Japan (2.4 S-DDD) and Poland (1.4 S-DDD) had the highest rates of calculated consumption.

#### Midazolam

94. Global reported manufacture of midazolam, which had fluctuated significantly in the past decade within the range of 2.7 tons (2006) and 8.7 tons (2005) per year, dropped from 7.2 tons in 2011 to 4.6 tons in 2012. Brazil, India, Israel, Italy and Switzerland have been the main manufacturers of the substance. However, data on manufacture of midazolam for 2012 have not been received from

India and Switzerland did not manufacture the substance in 2012, which accounts for the drop in output. Israel was the largest manufacturer of midazolam in 2012, with 1.9 tons, followed by Brazil (1.4 tons), Italy (1 ton) and China (305 kg). In addition, Canada, Costa Rica, Ecuador and the United States reported manufacture of midazolam in 2012, their outputs ranging from 1 to 8 kg. In 2012, global reported exports of the substance stood at 7.6 tons, which represents a 20 per cent increase on the year before. As in previous years, Switzerland (3.1 tons), Israel (1.8 tons), India (654 kg), Italy (639 kg) and Germany (576 kg) continued to be the main exporters of midazolam, jointly accounting for 89 per cent of the global total. Midazolam is used in many countries; over 80 countries reported imports of midazolam in quantities above 1 kg in the period 2008-2012. The main importer in 2012 was Switzerland (1.2 tons, entirely for re-export), followed by the United States and Germany (949 kg each), France (496 kg) and Brazil (486 kg). Together, those countries accounted for 62 per cent of global imports of midazolam. Calculated global consumption of midazolam stood at 5.7 tons (285 million S-DDD) in 2012. Switzerland (2.7 S-DDD), Sint Maarten (2.6 S-DDD), Costa Rica (2.4 S-DDD), Curação (2.3 S-DDD), Portugal (1.8 S-DDD), Uruguay (1.6 S-DDD) and Hungary (1.5 S-DDD) were the countries with the highest rates of calculated consumption of midazolam for 2012, measured in S-DDD per 1,000 inhabitants per day.

#### Triazolam

95. Global reported manufacture of triazolam fluctuated significantly during the period 2008-2012, mainly reflecting the manufactured quantities reported by the United States, which had been the leading manufacturer of triazolam throughout the past decade. In 2012, the United States did not report manufacture of triazolam and, as a result, the global total dropped by 80 per cent, to 55 kg (218 million S-DDD), compared with 2011 (267 kg, or over 1 billion S-DDD). The only countries reporting manufacture of triazolam in 2012 were Italy (48 kg), Japan (6.5 kg) and Canada (6 grams). Total exports of triazolam in 2012 amounted to 288 kg. The United States (141 kg) continued to be the main exporter, followed by Italy (85 kg), Belgium (22 kg), Switzerland (15 kg), France (12 kg) and India (11 kg). More than 40 countries reported imports of triazolam in the period 2008-2012. Throughout the decade leading up to 2012, Japan was the largest importer of triazolam, accounting in 2012 for almost 60 per cent of global imports. Total calculated consumption of triazolam stood at 821 million S-DDD in 2012, with Japan (651 million S-DDD), Italy (96 million S-DDD) and Austria (27 million S-DDD) being the main consumers in absolute terms. In 2012, measured in S-DDD per 1,000 inhabitants per day, Japan (14 S-DDD), Austria (9 S-DDD) and Italy (4.4 S-DDD) had the highest calculated consumption rates of triazolam.

#### Flurazepam

96. Global reported manufacture of flurazepam stood at 4.2 tons in 2012, which is 21 per cent higher than in 2011. Italy continued to be the largest manufacturer, accounting for 80 per cent of total output, followed by Brazil and Canada. No other countries reported manufacture of the substance in 2012. Italy (2.8 tons) also remained the largest exporter of flurazepam in 2012, accounting for 73 per cent of global exports (3.8 tons). The main importers of flurazepam continued to be Spain (1.1 tons), Canada (378 kg), Germany (355 kg) and the United States (318 kg), which together accounted for 63 per cent of total imports of the substance in 2012. Rates of consumption continued to be higher in Europe, with the highest calculated rates of consumption in 2012, expressed in S-DDD per 1,000 inhabitants per day, recorded for Ireland (2.8 S-DDD), Belgium and Italy (1.7 S-DDD each) and Spain and Switzerland (1.2 S-DDD each).

#### Loprazolam

97. Total reported manufacture of loprazolam in 2012 amounted to 124 kg, all reported by France, which has traditionally been the main manufacturer and leading exporter of the substance and also held 92 per cent of global stocks (68 kg). In the past decade small quantities were occasionally manufactured by India, the United Kingdom and the United States. Global reported exports of loprazolam increased by 10 per cent over 2011 and stood at 189 kg in 2012. About 25 countries used loprazolam in the period 2008-2012, the main importing countries in 2012 being France (49 kg), Poland (43 kg), South Africa (17 kg) and Spain (15 kg).

#### Other benzodiazepine-type sedative-hypnotics

98. The remaining substances in this group, nimetazepam and haloxazolam, are manufactured and used almost solely in Japan. In 2012, that country reported manufacture of 80 kg of nimetazepam; no manufacture of or international trade in haloxazolam was reported.

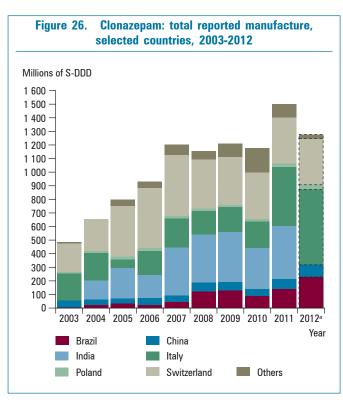
## Benzodiazepine-type anti-epileptics

#### Clonazepam

99. Clonazepam is a benzodiazepine that is used mainly as an anti-epileptic. In the past decade, global reported manufacture of clonazepam gradually increased, from 3.9 tons in 2003 to a record of 12 tons in 2011. In 2012, total output stood at 10.2 tons (1.3 billion S-DDD), owing to

the fact that data from India, which had reported output of over 3 tons for 2011, had not been received. Switzerland was the leading manufacturer of clonazepam in the world during the two decades leading up to 2010. In 2011, Italy became the largest manufacturer of the substance and, in 2012, its share of global output reached 43 per cent (4.4 tons). The other major manufacturers of clonazepam in 2012 were Switzerland (2.7 tons), Brazil (1.8 tons), China (720 kg) and Poland (284 kg) (see figure 26).

100. Total reported stocks of clonazepam almost doubled, increasing from 10.6 tons in 2011 to 20.5 tons in 2012, 76 per cent of which were held in Canada (10.8 tons) and Switzerland (4.9 tons). Global exports of clonazepam also followed an upward trend until 2011. After a record of 12.9 tons exported in 2011 however, total exports decreased to 11.7 tons in 2012. Switzerland, India and Italy remained the main exporters of clonazepam in 2012, together accounting for almost 80 per cent of the global total. More than 100 countries reported imports of clonazepam in 2012. Of those, eight countries imported more than 400 kg of the substance, both for domestic use and for re-export, namely, the United States (2.2 tons), Switzerland (1.2 tons), Brazil (904 kg), Spain (902 kg), Israel (901 kg), Argentina (838 kg), Canada (645 kg) and the Islamic Republic of Iran (475 kg). Use of clonazepam expanded from about 50 countries in 1995 to more than 140 countries in the period 2008-2012. Global calculated consumption of the substance remained stable in the past five years and averaged 1.2 billion S-DDD annually in the period 2008-2012. In



<sup>a</sup>The data for 2012 are incomplete.

2012, global calculated consumption stood at 1.3 billion S-DDD. The seven countries with the highest levels of calculated consumption of clonazepam were the United States (321 million S-DDD), Brazil (281 million S-DDD), Italy (137 million S-DDD), Argentina (97 million S-DDD), China (65 million S-DDD), the Islamic Republic of Iran (59 million S-DDD) and Israel (42 million S-DDD). The rates of calculated consumption of clonazepam, measured in S-DDD per 1,000 inhabitants per day, in individual countries are shown in part three, table IV.4, of the present publication.

# Barbiturate-type sedative-hypnotics and anti-epileptics listed in Schedule IV

Allobarbital, barbital, butobarbital, methylphenobarbital, phenobarbital, secbutabarbital and vinylbital

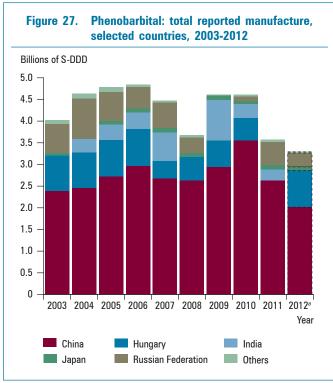
101. The seven barbiturates in Schedule IV are pharmacologically related to those in Schedule III. Five of the seven substances, namely allobarbital, barbital, butobarbital, secbutabarbital and vinylbital, are intermediate-acting barbiturates and are mainly used as hypnotics (to induce sleep). They are no longer used as daytime sedatives. The other two substances, methylphenobarbital and phenobarbital, have additional properties and are also used as anti-(long-acting barbiturates). epileptics Phenobarbital continued to be the most commonly used substance in this group in 2012, followed by barbital. More information on calculated consumption of phenobarbital is shown in part three, table IV, of the present publication.

Total reported manufacture of the seven barbiturates in Schedule IV (for both direct medical use and the manufacture of non-psychotropic substances) rose from 4 billion S-DDD in the period 1999-2000 to an average of 5.1 billion S-DDD in 2006. After that year, reported global manufacture started to decline, with fluctuations, to a total of 3.3 billion S-DDD in 2012. Changes in the quantities of phenobarbital manufactured, which continued to be the most widely manufactured substance in this group, accounted for the changes in output. In 2012, the share of phenobarbital in total manufacture (expressed in S-DDD) was 98.6 per cent. Barbital, butobarbital and secbutabarbital together accounted for the remainder. No manufacture of allobarbital or methylphenobarbital was recorded in 2012 and no manufacture of vinylbital has been reported since 1996.

103. In 2012, the countries with the highest calculated consumption rates of barbiturate-type sedative-hypnotics in Schedule IV were, in descending order, Italy, Georgia,

Thailand, Israel, France, Turkey, Lebanon, Albania, Denmark, Hungary and Lithuania, with consumption rates ranging between 0.13 and 0.03 S-DDD per 1,000 inhabitants per day. As for the barbiturate-type anti-epileptics listed in Schedule IV, the countries with the highest calculated consumption levels, in S-DDD per 1,000 inhabitants per day, were, in descending order, Bulgaria, Ukraine and Brazil. More information on calculated consumption is shown in part three, table IV, of the present publication.

104. Global manufacture of phenobarbital, which had fluctuated between 360 and 480 tons during the period 2003-2011, fell to 329 tons (3.3 billion S-DDD) in 2012. That decrease can be attributed to the decrease in manufacture in China and the Russian Federation, the leading manufacturers of that substance. Total manufacture decreased in China from 262 tons in 2011 to 201 tons in 2012 and in the Russian Federation from 53.7 tons in 2011 to 32 tons in 2012, while Hungary and Japan manufactured 84 tons and 9 tons, respectively, in 2012. India, which had manufactured 26 tons in 2011, did not report manufacture in 2012. For details on reported manufacture in selected countries, see figure 27. Global stocks of phenobarbital stayed at about the same level as in 2011 (163 tons), with around 78 per cent of them being held in China, Brazil, Switzerland, Hungary, France, the Philippines and Ukraine, in descending order. In terms of calculated consumption, major users of phenobarbital in 2012 included China, Brazil, the Russian Federation, Japan, the United States and Ukraine, in that order.



<sup>a</sup>The data for 2011 are incomplete.

105. Phenobarbital continues to be one of the most widely traded psychotropic substances, with an average of 140 countries trading the substance every year. Compared with 2011, the total volume of international trade in phenobarbital decreased to 242 tons in 2012. Hungary, India, China, Switzerland, the United States and Germany, in that order, together accounted for 91 per cent of total exports. More than 120 countries reported imports of phenobarbital in 2012. Major importers of the substance included the Russian Federation (18 per cent of total imports), Brazil (11 per cent), Switzerland (10 per cent), the United States (8 per cent), Ukraine (8 per cent), Germany (6 per cent), France (5 per cent) and Japan (4 per cent).

106. Global manufacture of barbital fell from 122 tons (245 million S-DDD) in 2011 to 23 tons (47 million S-DDD) in 2012, the lowest amount recorded since 1980. This decrease reflects a major decrease in manufacture by China, the leading manufacturer of barbital, which reported manufacture of only 21 tons in 2012 compared with 120 tons in 2011. Japan was the other major manufacturer; output in that country in recent years has remained at about 2 tons each year. The barbital manufactured in Japan was mainly for domestic consumption, including for use in the manufacture of non-psychotropic substances. Parallel to the decreased global manufacture, total calculated consumption of barbital decreased from 122 tons in 2011 to just 7 tons in 2012. China reported consumption of 58 tons of barbital in 2012. In terms of total calculated consumption, China, Italy, the United States and Thailand, in that order, continued to be the major users of the substance.

107. At almost 17 tons in 2012, the volume of international trade in barbital remained more or less at the same level as in 2011. China, the leading exporter of barbital, exported 8.3 tons in 2012 and Germany imported 8.3 tons and re-exported 7.2 tons during that year. A combined total of 4.1 tons was imported by Italy, the United States and Thailand. The United States used some of the amounts imported to manufacture preparations exempted from certain control measures in accordance with article 3 of the 1971 Convention. Japan, which had imported 4 tons in 2011, imported only 16 kg in 2012.

108. Manufacture of methylphenobarbital fluctuated considerably during the period 2003-2011, ranging between 10 kg and 22 tons, owing to significant changes in the output reported by the manufacturing countries, namely India, Switzerland and the United States. No manufacture of methylphenobarbital was reported in 2012. Global stocks of methylphenobarbital dropped from 5.6 tons in 2011 to 4.9 tons in 2012, with 94 per cent held in Switzerland. Based on total calculated consumption, Croatia, Switzerland and Italy, in that order, were the main users of the substance in 2012.

109. With 2.1 tons in 2012, the volume of international trade in methylphenobarbital remained at around the same level as in 2011 (1.8 tons). Croatia and Germany imported 900 kg of the substance each, together accounting for 86 per cent of total imports in 2012. Germany, which re-exported 900 kg during that year, India (500 kg) and Switzerland (250 kg) were the main exporters during 2012.

110. During the past 10 years, allobarbital has been manufactured intermittently by Germany and Belgium, in amounts of several tons per year. Since 2010, no manufacture of allobarbital has been reported. Global stocks of the substance continued to decrease steadily, from 1.3 tons in 2009 to 740 kg in 2012. Of these stocks, 59 per cent was held in Germany and the remainder, in descending order, in Ireland, Switzerland, Turkey and Israel. With only Switzerland reporting an export, of 200 kg of allobarbital to Turkey during 2012, global trade in that substance fell to 200 kg, just half of its volume in 2011.

111. Secbutabarbital has been manufactured intermittently during the past decade. After Germany stopped manufacturing the substance in 2003, the United States became the sole manufacturer. In 2012, the United States manufactured 94 kg of secbutabarbital. Global stocks of the substance went up from 56 kg in 2011 to 139 kg in 2012. Half of them were held in the United States, 34 per cent in Lebanon and 11 per cent in Germany. The United States and Lebanon were the main users in 2012. Lebanon was the only country that reported importing the substance (25 kg) in 2012.

112. No manufacture of butobarbital was reported between 2000 and 2011, with the exception of Germany reporting manufacture of 117 kg in 2008. In 2012, however, the United States manufactured 94 kg of that substance and consumed 25 kg of that amount. The other main consumer in 2012 remained Jordan, reporting total imports of 6 kg during that year. Global stocks of butobarbital increased to 106 kg in 2012, with 76 kg held by the United States and 26 kg by Germany.

#### Barbiturates in Schedules II, III and IV

113. Of the 12 barbiturates listed in Schedules II, III and IV of the 1971 Convention, five substances, phenobarbital, pentobarbital, butalbital, barbital and amobarbital, in that order, together accounted, on average, for 99 per cent of total reported manufacture of those barbiturates during the period 2008-2012. The shares of total manufacture of the 12 substances in 2012 are shown in figure 28. Phenobarbital remained the most widely manufactured barbiturate in 2012, accounting for 79 per cent of the total manufacture of the 12 barbiturates, followed by pentobarbital (12 per cent) and butalbital (7 per cent). China continued to be the leading manufacturer, accounting for 50 per cent of

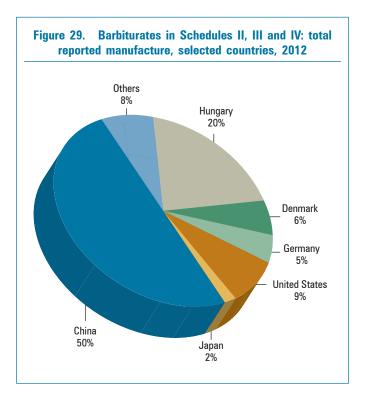
total manufacture of the entire group of barbiturates, followed by Hungary (20 per cent), the United States (9 per cent), Denmark (6 per cent), Germany (5 per cent) and Japan (2 per cent) (see figure 29).

Figure 28. Barbiturates in Schedules II, III and IV: share of total reported manufacture, by substance, 2012

Pentobarbital
12% Barbital
1%

Phenobarbital
79%

Phenobarbital
79%



## Other sedative-hypnotics listed in Schedule IV

114. Four substances from the group of sedative-hypnotics in Schedule IV are neither barbiturates nor benzodiazepines: ethchlorvynol, ethinamate, methyprylon and

zolpidem. Following a decision of the Commission on Narcotic Drugs in March 2013, GHB, which was initially added to Schedule IV in 2001, was rescheduled and moved to Schedule II of the 1971 Convention.

115. Zolpidem, which was brought under international control in 2001, is used mainly for the treatment of insomnia. During the period 2003-2012, global manufacture of the substance fluctuated widely, between 24 and 50 tons, around a 10-year average of 34 tons. Those fluctuations have reflected the changing outputs of the main manufacturing countries, France, India and Israel, which accounted for 83 per cent of global manufacture in the past five years. In the past two years, total reported manufacture of zolpidem was stable, with global output amounting to 32.3 tons (3.2 billion S-DDD) in 2012. France accounted for 12.6 tons and Israel for 12.3 tons; India, which manufactured 13.2 tons in 2011, did not report concerning

manufacture of zolpidem in 2012. Other countries, including the Czech Republic, Japan, Argentina, Canada, Italy and Brazil, in descending order, also manufactured significant quantities of zolpidem in 2012. Total stocks of zolpidem have increased steadily during the past five years and attained 29.1 tons (2.9 billion S-DDD) in 2012, 75 per cent of which were held in Israel, France and the United States, in descending order.

116. Zolpidem is one of the most widely traded and used psychotropic substances. Global reported exports amounted to 52 tons in 2012, with 34 countries reporting exports of the substance to about 100 countries. India (16.6 tons), France (9.9 tons), the Czech Republic (7.4 tons) and Israel (5.3 tons) were the main exporters in 2012, accounting for 76 per cent of global exports. The United States, France, Japan, Uruguay and the Czech Republic, in that order, had the highest levels of calculated consumption in 2012.