

COMMENTS ON THE REPORTED STATISTICS ON PSYCHOTROPIC SUBSTANCES

Summary

The analysis contained in the present section of the technical publication is based on statistical data furnished by Governments.

Substances included in Schedule I of the Convention on Psychotropic Substances of 1971 should only be used for scientific research and, in certain cases, for the manufacture of psychotropic substances in other schedules. The use of *delta*-8-tetrahydrocannabinol to obtain dronabinol, one of the stereochemical variants of *delta*-9-tetrahydrocannabinol listed in Schedule II, has remained high in recent years in the United States of America. Preparations containing dronabinol have been used as an anti-emetic mainly in the United Kingdom of Great Britain and Northern Ireland, the United States of America, Germany and Canada (in that order).

Methylphenidate is the main central nervous system stimulant listed in Schedule II. The United States remains by far the main manufacturer and user of the substance; however, manufacture and medical use of methylphenidate for the treatment of attention deficit disorder (ADD) continue to grow worldwide. In 2008, Canada, Germany, the Netherlands, South Africa, Spain and the United Kingdom were the other main users of methylphenidate apart from the United States. Amphetamines, the other central nervous system stimulants in Schedule II, are commonly used for the manufacture of other psychotropic substances and substances not under international control, as well as for direct medical purposes. The United States and France were the key manufacturers of amphetamines in 2008. The largest consumers of amphetamines in 2008 were the United States, Germany, Italy and Canada.

International trade in and consumption of buprenorphine, an opioid analgesic listed in Schedule III of the 1971 Convention, continued to expand due to the increasing use of the substance for detoxification and substitution treatment for heroin addicts. Despite the increasing number of countries reporting imports of buprenorphine, in 2008 the United States remained by far the largest importer, followed by Germany and France, whereas the highest consumption rates continued to be observed in countries in Europe.

Benzodiazepines are classified as anxiolytics and sedative-hypnotics and 35 are currently under international control. In medical practice, benzodiazepines are used for the short-term management of insomnia and for pre-medication and the induction of general anaesthesia. Consumption of benzodiazepine-type anxiolytics, notably alprazolam and diazepam, is higher in Europe than in any other region of the world. Total reported manufacture and consumption of benzodiazepine-type sedative-hypnotics, including flunitrazepam, have fluctuated significantly. Belgium had the highest and Japan the second-highest calculated rate of consumption of benzodiazepine-type sedative-hypnotics in 2008. In recent years, global consumption of flunitrazepam has shown a downward trend, while consumption of nitrazepam has been on the increase. International trade in flunitrazepam declined slightly in 2008, to below 1 ton. Japan continued to be the leading importer of flunitrazepam, accounting for 70 per cent of annual global imports.

Of the 12 barbiturates listed in the 1971 Convention, phenobarbital was the most widely used in 2008, in particular for the treatment of epilepsy. The substance accounted for 77 per cent of the combined manufacture of all barbiturates. Other important barbiturates were pentobarbital, butalbital and barbital accounting for 10, 9 and 3 per cent of total reported manufacture, respectively. China reported 56 per cent total manufacture of combined barbiturates, followed by Hungary (11 per cent) and Denmark, the Russian Federation and the United States (each 7 per cent). Although the use of individual barbiturates varies considerably among countries, in recent years the highest per capita combined consumption of barbiturates continues to be observed for countries in Europe.

The 14 stimulants listed in Schedule IV of the 1971 Convention are essentially used as anorectics or for the treatment of ADD. Total reported manufacture of this group of substances stabilized at an annual average of about 2 billion defined daily doses for statistical purposes (S-DDD) during the period 2004-2008. Phentermine continues to be the most used substance of this group. In 2008, the substance accounted for almost 67 per cent of global manufacture, followed by fenproporex (18 per cent). Consumption of stimulants listed in Schedule IV remained highest in the Americas (in particular, in the United States and Argentina). In both Africa and Oceania, consumption of Schedule IV stimulants increased in 2008, mainly due to the sharply increased use of phentermine in South Africa and Australia. In all other regions, the average rates of consumption of those stimulants declined.

Substances listed in Schedule I

1. Twenty-eight substances are listed in Schedule I of the Convention on Psychotropic Substances of 1971. 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. The manufacture and stocks of, as well as trade in, those substances have, therefore, been limited, with the exceptions noted in the following paragraphs.
2. Use of psychotropic substances in Schedule I in industry for the manufacture of non-psychotropic substances or products is not envisaged under the 1971 Convention. However, 2,5-dimethoxyamphetamine (DMA) has been used in the United States of America, the only manufacturer of the substance, in the manufacture of photographic film. The manufacture of DMA in the United States averaged 7 tons annually until 2001. In 2002, manufacture started to decline, fluctuating at around 1.5 tons until 2006. For 2007 and 2008, no manufacture was reported and consequently stocks of DMA held in the United States were depleted by the end of 2008. Although there is reportedly no substitute for DMA in the manufacturing process of a photographic film, the decrease in the production and usage of DMA in the United States reflect the decrease in its use as a non-controlled film dye.
3. Five countries reported the manufacture of 3,4-methylenedioxyamphetamine (MDMA) in the period 2004-2008. These are Australia, Ireland, Israel, Switzerland and the United States. Global stocks of MDMA at the end of 2008 amounted to about 530 grams, mainly held in the United States.
4. From 2005 to 2007, Denmark reported the manufacture of an average of 40 kg of p-methoxy-a-methylphenethylamine (PMA) annually, for use in the manufacture of a non-psychotropic substance. PMA was used in Denmark in 2006 and 2007 in the manufacture of tamsulosin, an active pharmaceutical ingredient.
5. Under the 1971 Convention, States parties may authorize limited use of substances listed in Schedule I for the manufacture of psychotropic substances in other schedules. The United States is the only country reporting the manufacture of isomers of tetrahydrocannabinol (THC) included in Schedule I for their use in the manufacture of *delta-9*-tetrahydrocannabinol (*delta-9*-THC), a psychotropic substance that has been listed in Schedule II since 1991. *delta-8*-Tetrahydrocannabinol is the main substance among the isomers in Schedule I manufactured in the United States. The manufacture of isomers of THC in Schedule I increased in the period 1998-2005, reaching a peak of 326 kg. Manufacture declined after that, totalling 94 kg in 2008. By the end of 2008, significant stocks were held only in the United States (584 kg). From 2002 to 2008, Denmark was virtually the only importer of those isomers, with an import of 838 grams effected in 2008.

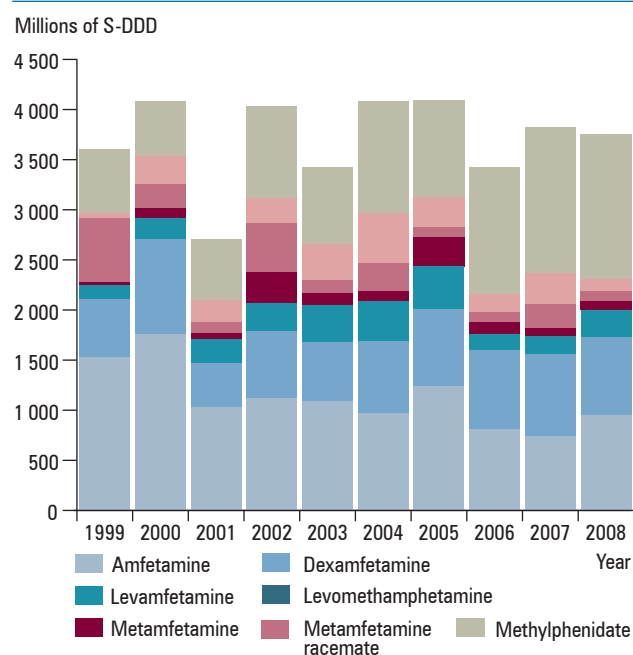
Substances listed in Schedule II

6. 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/or 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

7. Nine stimulants are listed in Schedule II: amphetamine, dexamfetamine, fenetylline, levamfetamine, levomethamphetamine, metamfetamine, metamfetamine racemate, methylphenidate and phenmetrazine. Total manufacture of central nervous system stimulants in Schedule II fluctuated in the period 1999-2008, as shown in figure 1. In 2008, total reported manufacture of this group of substances amounted to 3.8 billion defined daily doses for statistical purposes (S-DDD). Of the group, methylphenidate grew fastest, its share of total output of stimulants in Schedule II rising from 18 per cent in 1999 to 40 per cent in 2008. By contrast, manufacture of amphetamine decreased during that decade. In 2008, amphetamine and dexamfetamine accounted for 25 and 20 per cent of total output respectively. Together with methylphenidate, those two substances accounted for 85 per cent of the total combined output in 2008.

Figure 1. Schedule II stimulants: total reported manufacture, by substance, 1999-2008



Amphetamines

8. Both optical isomers of amphetamine (levamfetamine and dexamfetamine) and their racemic mixture (amphetamine), as well as both optical isomers of metamfetamine (levomethamphetamine and metamfetamine) and their racemic mixture (metamfetamine racemate), are listed in Schedule II.

9. In 2008, 34.5 tons (2.3 billion S-DDD) of amphetamines listed in Schedule II were manufactured worldwide. As in previous years, amphetamine, dexamfetamine and levamfetamine were the main amphetamines manufactured. In 2008, amphetamine had the highest share of total manufacture of amphetamines (41.5 per cent), followed by dexamfetamine (33.9 per cent), levamfetamine (11.6 per cent), metamfetamine racemate (5.2 per cent) and metamfetamine (4.2 per cent). During the period 1999-2008, the major manufacturers were the United States and France (see figure 2), accounting for 50 and 46 per cent respectively, while Hungary and Switzerland accounted for the remainder. Throughout that decade, France was virtually the only manufacturer of levamfetamine, which is solely used for reconversion into amphetamine.

Use as intermediate substances

10. Amphetamines in Schedule II are frequently used in industry as intermediary products for the manufacture of other substances (see figure 3). The new substances

Figure 2. Amphetamines: total reported manufacture, selected countries, 1999-2008

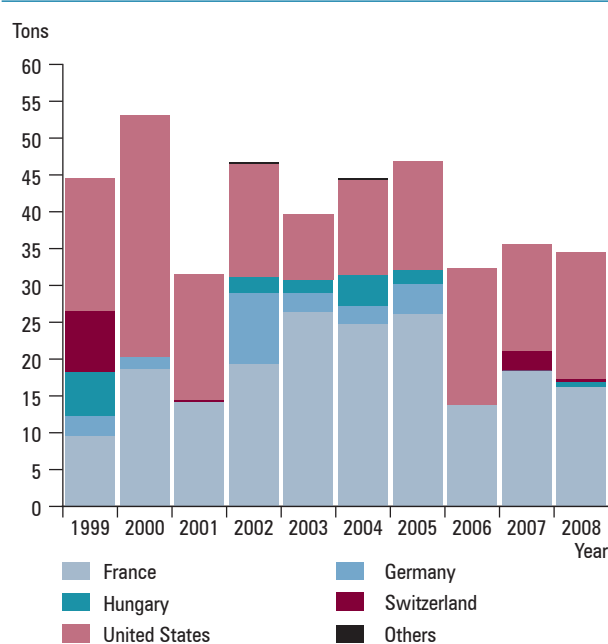
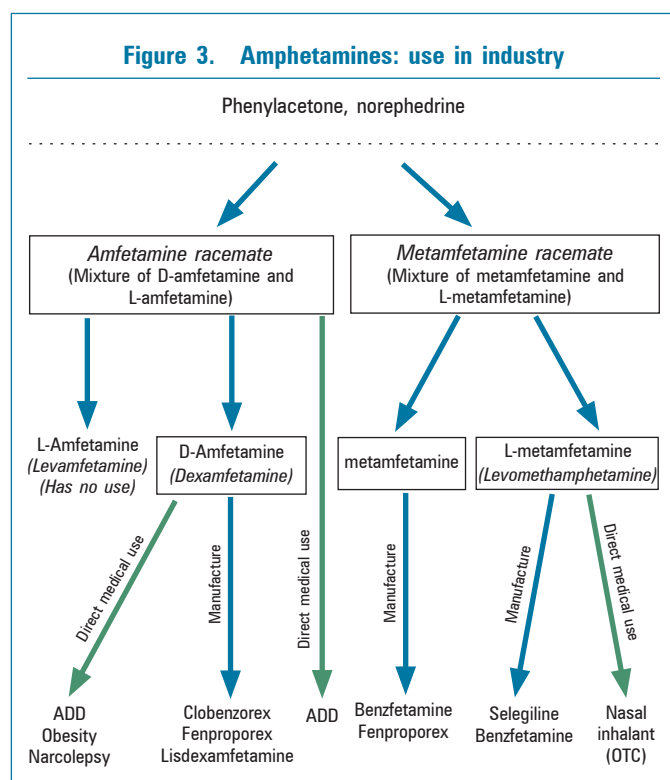


Figure 3. Amphetamines: use in industry



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 in the United States, amphetamines in Schedule II are widely used in industry for conversion into other amphetamines included in Schedule II of the 1971 Convention. In the United States, amphetamine is also used in the synthesis of lisdexamfetamine (L-lysine-d-amphetamine), a prodrug of dexamfetamine, which is used in the treatment of attention deficit disorder (ADD). In addition, amphetamines have mainly been converted to substances used as anorectics (benzfetamine, clobenzorex, fenproporex and levopropyl-hexedrine) and antiparkinsonian drugs (selegiline). Benzfetamine and fenproporex are included in Schedule IV of the 1971 Convention, whereas clobenzorex, levopropyl-hexedrine and selegiline are not under international control.

Medical use

11. For direct medical purposes, amphetamines are used mainly for the treatment of ADD in the United States. In addition, they are used to treat narcolepsy and obesity, although the widespread use of those substances for the treatment of obesity has been considerably reduced or discontinued in most countries. Although France is a traditional major manufacturer of amphetamines, there is very limited medical use of amphetamines in that country and almost all the amphetamines manufactured there are destined for export.

12. The countries with the highest levels of medical and industrial¹ use of amphetamines, calculated on the basis of statistics provided for 2004, 2006 and 2008² and expressed in S-DDD per 1,000 inhabitants per day,³ are listed in table 1.

Table 1. Calculated rate of use of amphetamines, selected countries, 2004, 2006 and 2008

Country ^a	(S-DDD per 1,000 inhabitants per day)		
	2004	2006	2008
United States	10.19	9.42	8.97
Germany	11.29	4.02	3.23
Italy	1.51	0.94	1.89
Canada	1.08	1.67	1.88
Czech Republic	7.00	3.60	1.52
Australia	2.17	1.50	1.25
United Kingdom	0.00	0.10	0.31
Norway	0.13	0.12	0.26
Sweden	0.16	0.17	0.20
Chile	0.20	0.28	0.21
Netherlands	0.12	0.12	0.15
Belgium	0.27	0.29	0.08
Finland	0.03	0.04	0.06
Denmark	0.04	0.05	0.06
Austria	0.01	0.01	0.01
Israel	0.05	0.01	0.01

^aCountries are listed in the order of their calculated rate of use in 2008 of amphetamines.

Comments on amphetamines, by substance

13. The manufacture of amphetamine gradually increased until 1998, when it reached 30 tons. Since 1998, it fell steadily, to 14.3 tons in 2008. France and the United States were the main manufacturers, with France accounting on average for 45 per cent of global output during the period 2006-2008. For medical purposes, amphetamine is used mainly in combination with dexamfetamine in the United States, which is where around 61 per cent of global stocks were held in 2008 (10.7 tons). Total imports of amphetamine in 2008 amounted to 166 kg, the main importers being Canada (54 per cent), Germany (23.5 per cent) and Chile (13 per cent). In 2008, total imports of amphetamine amounted to 166 kg, the main importers being Canada (54 per cent) and Germany (24 per cent).

14. While the manufacture of dexamfetamine was stable during the 1980s, at a level of approximately 350 kg annually, it began to rise, with fluctuations, after 1991, reaching 11.6 tons in 2008. France and the United States

¹Excluding use for the manufacture of other amphetamines.

²The method used for calculating levels of consumption of psychotropic substances is explained in the explanatory note to table IV of the present publication.

³The list of defined daily doses for statistical purposes used in these calculations is presented in table III of the present publication.

were the main manufacturers. The United States was the main user of dexamfetamine for medical purposes. Medical use of dexamfetamine was also reported in a number of other countries, including Australia, Canada, Chile, Finland, Germany, New Zealand, Norway, Sweden, Switzerland and the United Kingdom of Great Britain and Northern Ireland. Global stocks of dexamfetamine increased from 1 ton in 1995 to 11 tons in 2008. Twenty-one countries reported imports of the substance, amounting to 481 kg, in 2008. Australia and Canada remained the main importers, accounting for 29 and 45 per cent of the total, respectively.

15. In 1999, the total reported manufacture of metamfetamine stood at 9.5 tons. After 1999, global output fluctuated but followed a decreasing trend until, in 2008, it amounted to 1.44 tons, with France and Switzerland contributing 71 and 29 per cent to the global total respectively. The United States was the main regular user of metamfetamine (mainly for industrial purposes). International trade in metamfetamine was limited in volume, fluctuating on average around 2 kg. Twelve countries reported imports of metamfetamine in 2008 in quantities ranging from 1 g to 84 g.

16. In the 10 years prior to 2008, the total reported manufacture of levometamphetamine fluctuated between 433 kg and 4.5 tons. In the period 2004-2008, Germany, France, the United States and the Czech Republic were the main manufacturers of the substance. Germany, the United States, France and the Czech Republic were also the main users of levomethamphetamine (for industrial purposes). In the United States, levomethamphetamine was mainly used for the manufacture of over-the-counter nasal inhalers, which were exempted in that country from certain control measures in accordance with article 3 of the 1971 Convention. Between 2003 and 2008, levomethamphetamine was also used in Italy, the main importer of the substance.

17. Metamfetamine racemate was mainly manufactured for export to the United States, for conversion into levomethamphetamine and metamfetamine. France and Hungary were the main manufacturers of metamfetamine racemate in the decade up to 2008. In 2008, global manufacture amounted to 1.8 tons, shared between France and Hungary (60 and 40 per cent respectively). Global stocks in 2008 stood at 4 tons. Global imports averaged 1.7 tons in the period 2004-2008, mainly accounted for by the United States.

Fenetylline

18. Manufacture of fenetylline was last reported in 1987. Worldwide stocks of fenetylline, which amounted to nearly 4 tons in 1987, were significantly reduced as a result of the voluntary destruction of all stocks of the substance in Switzerland in 1991 and of 50 per cent of

the stocks in Germany in 1992. By 2000, the remaining half of the German stocks had gradually been exported to the Netherlands, which became the only country holding significant stocks of fenetylline and the main exporter of the substance, accounting for over 92 per cent of global exports during the period 2006-2008. After 2004, Belgium became the main importer of the substance (72 kg in 2008), re-exporting a small part of its imports to Germany, Luxembourg and France. Belgium, France, Germany and Luxembourg were also the only countries to report the use of fenetylline for medical purposes after 2003.

Methylphenidate

19. The use of methylphenidate⁴ for medical purposes started increasing significantly since the 1990s. Methylphenidate is used for the treatment of ADD, primarily in children. It is also prescribed for the treatment of narcolepsy. The increase in the manufacture and use of methylphenidate is mainly a result of developments in the United States, where the substance is heavily advertised, including directly to potential consumers. However, during the decade up to 2008, the use of methylphenidate for the treatment of ADD rose sharply in many other countries as well. The calculated global consumption of the substance followed an increasing trend and more than doubled in 2008, reaching 52 tons compared to 25 tons in 2007 due to the sharp increase of consumption in the United States.

20. Global manufacture of methylphenidate started to rise rapidly in the first half of the 1990s; from 2.8 tons in 1990, it reached 19.1 tons in 1999. As a result of the increasing use of amphetamines for the treatment of ADD, methylphenidate manufacture dropped to 16 tons in 2000 (see figure 4). After 2000, total reported manufacture of the substance fluctuated, while following an overall increasing trend, and reached 43.5 tons in 2008. During the previous two decades, the United States has been the leading manufacturer of methylphenidate, increasing its output from 1.8 tons in 1990 to 38 tons in 2008. In the United Kingdom too, the manufacture of methylphenidate increased in 2008 compared with the quantities manufactured in 2006 and 2007. Most of the methylphenidate manufactured in the United States continued to be used domestically, although the volume of exports increased in previous years. Global stocks of methylphenidate continued to increase, reaching 40 tons in 2008 as a result of sharply increasing stocks held in the United States. In 2008, that country held 34 tons of methylphenidate, accounting for 85 per cent of global stocks.

21. The medical requirements for methylphenidate outside the United States are mainly met by imports.

⁴See table IV for details of the consumption levels of methylphenidate.

Figure 4. Methylphenidate: total reported manufacture, selected countries, 1999-2008

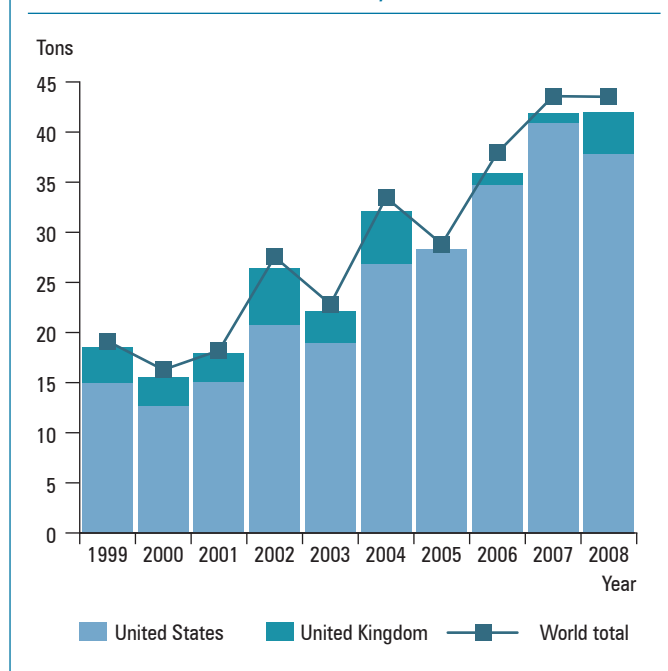
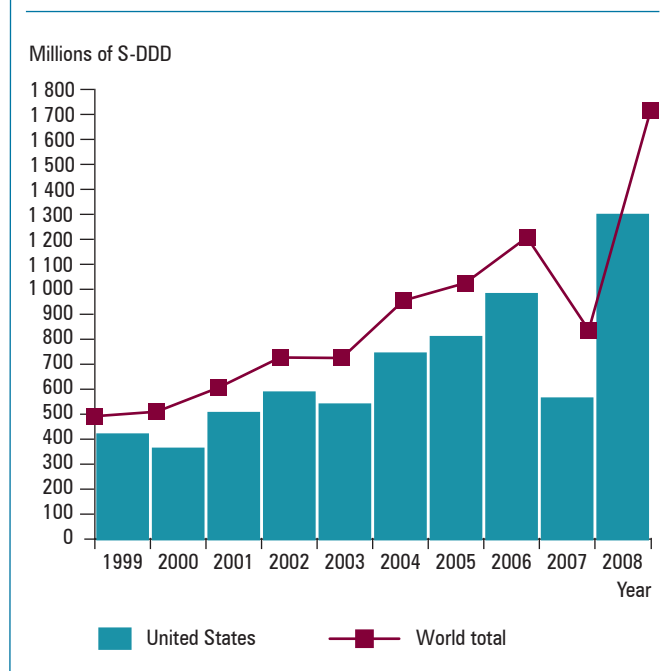


Figure 5. Methylphenidate: calculated medical consumption, 1999-2008



Note: 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)

International trade in methylphenidate increased during the period 1999-2008, from 5 tons to 14.7 tons. Canada, Germany, Spain and Switzerland remained the main importers of methylphenidate in 2008, mostly for re-export; together, they accounted for 60 per cent of global imports. Whereas Switzerland was the main exporter of methylphenidate until 2006, the United States took over that position in 2007 and held it in 2008. Other major exporting countries in 2008 were the United Kingdom and Spain (in decreasing order).

22. The number of countries and territories importing methylphenidate for domestic consumption continued to grow gradually during the decade prior to 2008; in that year, 87 countries and 9 territories reported such imports. For 2008, 37 Governments reported imports of methylphenidate in amounts exceeding 10 kg. Consumption of methylphenidate in the United States, by far the largest consumer of the substance, increased after the beginning of the 1990s to an average of 946 million S-DDD in the period 2006-2008 (see figure 5). In 2008, use in the United States reached almost 1.3 billion S-DDD. In the three-year period 2006-2008, the United States accounted for 75 per cent of the calculated worldwide use of the substance.

23. The level of methylphenidate use in the rest of the world averaged about 307 million S-DDD per year in the three years up to 2008. The major users of methylphenidate during the period 2004-2008 were the United Kingdom, Canada, the Netherlands, Germany and Israel, with sharply increasing use being reported by Canada, the United Kingdom, Iceland and the Netherlands.

24. The countries with the highest level of medical use of methylphenidate, calculated on the basis of statistics provided for 2004, 2006 and 2008 and expressed in defined daily doses for statistical purposes per 1,000 inhabitants per day, are listed in table 2.

Table 2. Methylphenidate: calculated medical consumption, 2004, 2006 and 2008

Country ^a	(S-DDD per 1,000 inhabitants per day)		
	2004	2006	2008
United States	7.14	9.18	12.03
Iceland	7.53	4.53	11.15
Canada	4.22	4.00	6.12
Israel	1.62	2.26	4.45
Norway	2.23	3.66	4.40
Netherlands	1.82	2.75	4.02
United Kingdom	1.38	-	3.67
Denmark	0.63	1.30	3.55
Switzerland	1.97	3.66	3.44
Sweden	0.58	1.59	2.51
Germany	1.11	1.39	2.19
Belgium	0.99	1.45	2.06
New Zealand	1.93	1.36	1.79
Australia	1.00	1.36	1.53
Andorra	0.25	0.51	1.50
Spain	0.49	1.26	1.18

^aCountries are listed according to their level of consumption of methylphenidate in 2008.

Phenmetrazine

25. Manufacture and medical use of phenmetrazine were discontinued in all countries. Small stocks of the substance were reported by Sweden (9 g) and the United States (7 g).

Anti-emetics

delta-9-Tetrahydrocannabinol and its stereochemical variants

26. During the 10-year period 1999-2008, the manufacture of *delta*-9-THC ranged between 120 kg and 315 kg. The manufacture of that substance was reported to have increased from 213 kg in 2007 to 233 kg (7.7 million S-DDD) in 2008. In 2007, the United States was the main manufacturer of *delta*-9-THC, accounting for 93 per cent of global manufacture of that substance. In 2008, however, when the United Kingdom (68.2 kg), Germany (35.4 kg) and Switzerland (592 g) also reported the manufacture of *delta*-9-THC, the share of the United States declined to 55 per cent.

27. After 2002, total reported stocks of *delta*-9-THC followed an increasing trend, reaching 556 kg in 2007 before dropping to 433 kg in 2008; almost all stocks were held by the United States, the United Kingdom and Germany. International trade in *delta*-9-THC increased steadily in the decade up to 2008, with total imports reaching 13.5 kg in 2008 (almost 30 per cent less than in 2007). Total calculated consumption of *delta*-9-THC, however, increased, from 284 kg in 2007 to 364 kg in 2008. The main users of *delta*-9-THC in 2008 were the United Kingdom (54 per cent), the United States (40 per cent), Germany and Canada.

Hallucinogens

Phencyclidine

28. Phencyclidine is primarily used as an anaesthetic agent in veterinary medicine. In the period 1996-2005, manufacture of small quantities of the substance was reported by several countries, with a peak in total manufacture in 2005 (2.1 kg). Since 2006, manufacture and international trade in phencyclidine amounted to less than 200 grams per year.

Sedative-hypnotics

Mecloqualone

29. Mecloqualone stopped being manufactured after 1980. The United States is the only country to have reported stocks of that substance (35 g in 2008).

Methaqualone

30. The last significant manufacture of the substance was reported in 1997 by Switzerland (340 kg) and the Czech Republic (43 kg). After that time, a further decrease in global manufacture was observed, as small quantities (amounts of just a few grams) were manufactured intermittently only in the United States. During the period 1999-2008, global stocks of methaqualone decreased from 1.6 tons in 1999 to 475 grams in 2008, held entirely by Switzerland, the United Kingdom and the United States. No medical use of the substance was reported for 2008.

Secobarbital

31. Prior to its rescheduling from Schedule III to Schedule II in 1988, secobarbital was frequently diverted from licit manufacturing and trading channels. After it was rescheduled, the manufacture of secobarbital declined substantially. In 2008, output of secobarbital amounted to 835 kg (8.4 million S-DDD), almost all of which was manufactured by Germany. The only other country reporting manufacture of secobarbital in 2008 was Japan (2 kg). Global stocks of secobarbital stood at 1,457 kg in 2008, held mainly by Germany (73 per cent), the United Kingdom (13 per cent) and the United States (10 per cent).

32. After 2002, global annual imports of secobarbital fluctuated at around 608 kg, with Germany being the main exporter (637 kg in 2008), accounting for about 90 per cent of global exports, and the United Kingdom being the main importer (553 kg in 2008). The United Kingdom, Sweden and Belgium had the highest calculated rates of usage of the substance in 2008.

Antitussives

Zipeprol

33. Zipeprol, an antitussive with bronchospasmolytic and mucolytic properties, was brought under international control in 1995. In 2001, France was the sole manufacturer of zipeprol, with a reported output of 666 kg (3.3 million S-DDD). No manufacture of the

substance was reported between 2001 and 2008, when the Republic of Korea manufactured 76 kg of zipeprol. In 2008, stocks of zipeprol were held only by Switzerland (277 kg). Switzerland, the Republic of Korea and Mexico reported imports of zipeprol in recent years; international trade in that substance decreased from 1.7 tons in 2004 to 17 grams in 2008.

Antidepressants

34. The only substance representative of the group of antidepressants is amineptine, which was included in Schedule II of the 1971 Convention in 2003. No information on manufacture or international trade was reported on the substance.

Substances listed in Schedule III

35. Nine substances are listed in Schedule III. 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), glutethimide and flunitrazepam. The two remaining substances, buprenorphine and pentazocine, belong to the group of analgesics.

Central nervous system stimulants

Cathine

36. Cathine is used as a stimulant and for industrial purposes. Manufacture of cathine has fluctuated considerably during the decade up to 2008, reflecting the manufacturing levels of Germany, the only manufacturer of the substance until 2003. Global manufacture averaged 3.3 tons per year in the period 2004-2008. After a peak reached in 2007 (5.9 tons), only 324 kg were manufactured in 2008, by Italy.

37. Germany and Italy remained the leading exporters of cathine in the period 2004-2008, during which time global imports of the substance averaged 4.1 tons. The number of countries reporting imports of cathine remained relatively stable during the 10-year period 1999-2008; in the period 2004-2008, a total of 11 countries reported such imports. South Africa (average 1.8 tons) and Italy (average 1 ton) accounted respectively for 44 and 25 per cent of world imports during that period. Other regular importers of the substance were Egypt, France, Mexico and Switzerland.

Sedative-hypnotics

38. Barbiturates are a group of central nervous system depressants that are closely related in their chemical structure. Classified as sedative-hypnotics, they used to

be prescribed for the treatment of insomnia, anxiety and stress; in some cases, they have also been used as anaesthetics for short surgery interventions (ultra-short-acting substances). Nowadays, they are mainly used 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. The potential for abuse is great, and the long-term effects include the development of tolerance and strong physical and psychological dependence.

Amobarbital, butalbital, cyclobarbital and pentobarbital

39. Amobarbital, butalbital and cyclobarbital are mainly used as hypnotics (to induce sleep) in the treatment of intractable insomnia. Pentobarbital has also been used for pre-medication in anaesthesia. During the period 2004-2008, Denmark, the United States, Canada, New Zealand, Australia, Switzerland and Ireland (in descending order) had the highest calculated per capita use of the four substances. Total reported manufacture of those substances fluctuated during the decade ending in 2008. In 2008, it amounted to 952 million S-DDD (see figure 6). Figure 7 shows the distribution of total output by the main manufacturing countries during the period 2004-2008.

40. Global manufacture of butalbital decreased from 76 tons in 2002 to 24 tons in 2005 and, after gradually increasing to 43.2 tons in 2007, fell again in 2008, to 32.5 tons (433 million S-DDD) (see figure 8). During the decade prior to 2008, Denmark and the United States were the main manufacturers of butalbital, accounting for more than 95 per cent of the total output, followed by Germany (until 2005) and China. In 2008, Denmark and the United States accounted respectively for 71 and 28 per cent of global output. While Denmark and China manufactured this substance mainly for export, in the United States up to 30 per cent of the available butalbital was used for the manufacture of a number of preparations exempted from certain control measures in accordance with article 3 of the 1971 Convention.

Figure 6. Barbiturates listed in Schedule III: total reported manufacture, by substance, 1999-2008

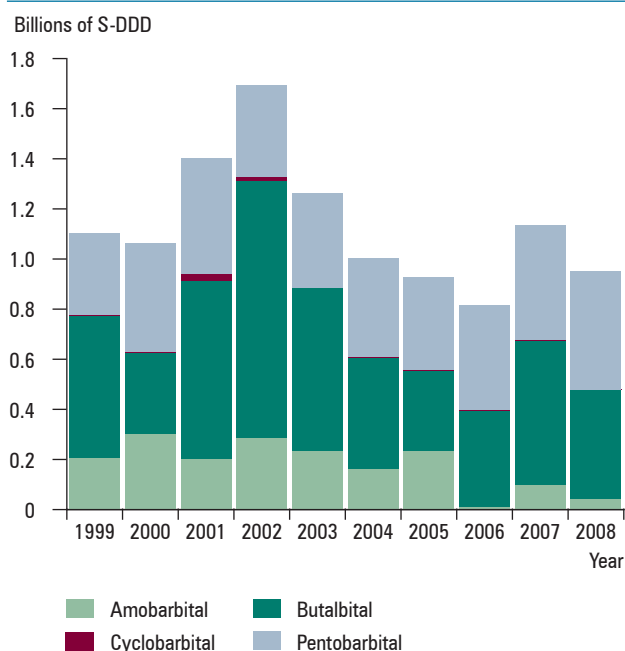


Figure 8. Butalbital: total reported manufacture, selected countries, 1999-2008

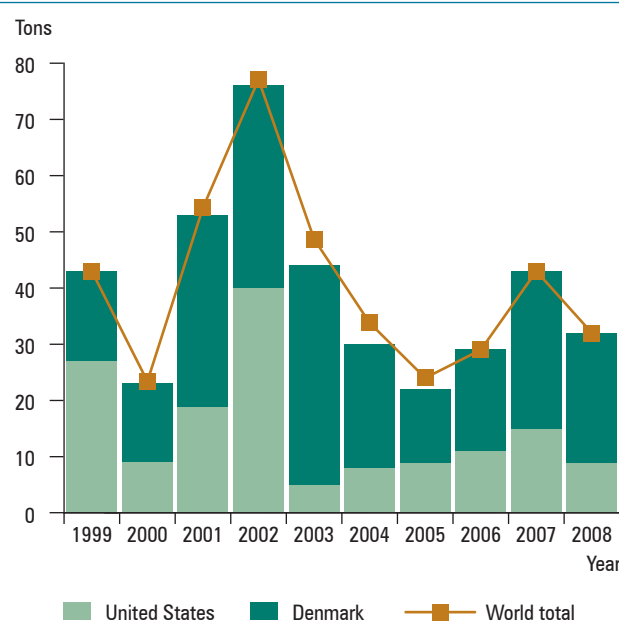


Figure 7. Barbiturates listed in Schedule III: total reported manufacture, selected countries, 2004-2008

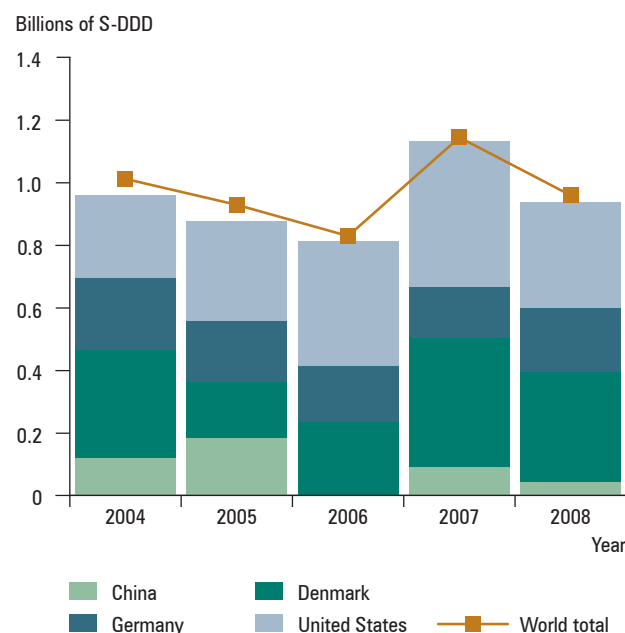
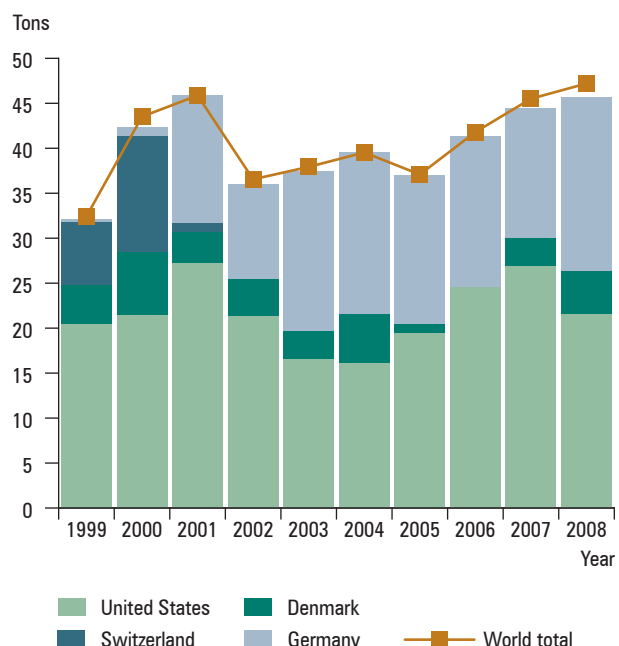


Figure 9. Pentobarbital: total reported manufacture, selected countries, 1999-2008



41. In the period 2004-2008, 10 countries reported exports of butalbital, with Denmark accounting for almost 92 per cent of global exports. The United States, Italy and Canada (in descending order) remained the main importers of butalbital, with the highest rates of usage of the substance.

42. In the decade prior to 2008, the total reported manufacture of pentobarbital fluctuated around 41 tons (see figure 9). In 2008, total output amounted to 47.2 tons

(472 million S-DDD), with the United States and Germany, the leading manufacturers of the substance in the 10-year period 1999-2008, accounting for 46 and 41 per cent of global output respectively. Denmark, the United Kingdom and Japan were the only other countries reporting manufacture of pentobarbital in 2008. During the period 2006-2008, New Zealand, Switzerland, Australia and Canada (in descending order) had the highest relative use of the substance, with annual averages ranging between 2 and 4.5 S-DDD per 1,000 inhabitants per day.

43. During the five-year period 2004-2008, an annual average of about 25 tons of pentobarbital was traded internationally. In 2008, the biggest exporters of the substance were, listed in descending order, Germany, Canada, the United States, France and Denmark, which together accounted for 97 per cent of global exports. Forty-eight countries reported imports of pentobarbital in 2008, the main importers being Canada (5.4 tons), France (3.4 tons), the United Kingdom (3.3 tons), Australia (2.2 tons), Switzerland (1.6 tons), the Netherlands (1.5 tons) and the United States (1.4 tons); together, those countries accounted for 78 per cent of global imports.

44. China and Japan were the main countries manufacturing and using amobarbital during the decade up to 2008. Denmark, Germany and the United States also reported intermittent manufacture. Global manufacture of the substance fluctuated between 20 tons and 30 tons during 1999-2003, then dropped to 9.8 tons in 2007 and to 4.5 tons (45 million S-DDD) in 2008. Total reported stocks of amobarbital stood at 1.8 tons in 2008. Global calculated use of the substance fluctuated around an average of 23 tons during the period 2002-2005, then declined substantially, albeit with fluctuations, to 4.8 tons in 2008. International trade in amobarbital also decreased, from an average of 5 tons annually in the period 2001-2005 to 229 kg in 2008, with Thailand, the Netherlands and Belgium being the main importers.

45. Use of the barbiturate cyclobarbital decreased considerably during the decade up to 2008. The substance was mainly used in some Eastern European countries, Latvia, Georgia, Belarus and the Russian Federation having the highest per capita rate of usage during the period 2004-2008. In 2003, Poland became the sole manufacturer of cyclobarbital, while Germany and Latvia reported some output until 2002. In 2008, Poland manufactured 439 kg of cyclobarbital (2.2 million S-DDD). Poland remained the main exporter of the substance. Total imports of cyclobarbital in 2008 amounted to 630 kg, with the Russian Federation accounting for 77 per cent of the total. A total of 491 kg of the substance was held in stocks at the end of 2008.

Glutethimide

46. During the early 1980s, several dozen tons of that substance were manufactured annually, mainly for conversion into aminoglutethimide, a non-psychotropic substance used as an antineoplastic agent. Global manufacture declined steadily during the 1990s and was stopped in 1998. However, manufacture of that substance was reported by Hungary, which manufactured about 700 kg of glutethimide in 2001, and China, which manufactured 240 kg in 2005. No manufacture of glutethimide was reported to INCB after 2005.

47. Parallel to the decline in manufacture, the volume of international trade in glutethimide decreased, from a peak of about 15 tons per annum in the period 1997-1998 to several hundred kilograms in 2002. Since 2003, the only trade transactions reported to INCB in quantities above 1 kg concerned Hungary, which exported 300 kg to Romania in 2003 and imported 200 kg in both 2004 and 2005 from China. No trade in glutethimide was reported for the period 2006-2008. Hungary and the United States were the only countries holding stocks of the substance (98 kg and 1.4 kg respectively).

Flunitrazepam

48. Flunitrazepam continues to be one of the most frequently abused benzodiazepines. The illicit market for flunitrazepam appears to be supplied mainly through diversion of the substance from domestic distribution channels and not through diversion from international trade. Preparations of flunitrazepam have frequently been diverted in one country and smuggled into countries with an illicit market for such preparations. Due to frequent cases involving the diversion or abuse of flunitrazepam, the substance 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. As a result of those measures, the number of reported diversions has declined and the majority of preparations sold on illicit markets purportedly containing "flunitrazepam" are actually counterfeit products that do not contain flunitrazepam.

49. In medical practice, flunitrazepam, like diazepam, is used for the short-term management of insomnia and, in some countries, for pre-medication and for induction of general anaesthesia. Before 1996, manufacture of flunitrazepam was reported by a number of countries, including Argentina, Brazil, the Czech Republic, Denmark, Italy, Japan, Spain and Turkey. After 1996, only Italy and Switzerland, which had started manufacture in 1997, continued to manufacture flunitrazepam. In 2007, those two countries manufactured a total of 1.7 tons of flunitrazepam, the largest amount of that substance ever reported to have been manufactured. In 2008, however, Switzerland did not manufacture flunitrazepam and Italy manufactured 247 kg (see figures 22 and 23, and para. 93 below).

50. International trade in flunitrazepam decreased from about 1 ton in 2007 to approximately 900 kg in 2008. Drawing from stocks, Switzerland, the leading exporter of the substance, exported 564 kg and Italy exported 327 kg in 2008. Those two countries together accounted for 96 per cent of global exports in 2008. Japan continued to be the leading importer of flunitrazepam, accounting for 70 per cent (611 kg) of annual global

imports (870 kg) in 2008, followed by Brazil, which imported 53 kg during that year. In addition, 22 countries reported imports of flunitrazepam in quantities exceeding 1 kg in 2008; those countries included Argentina, Austria, France, Germany, Greece and the Republic of Korea, which imported between 10 and 50 kg of the substance.

Analgesics

Buprenorphine

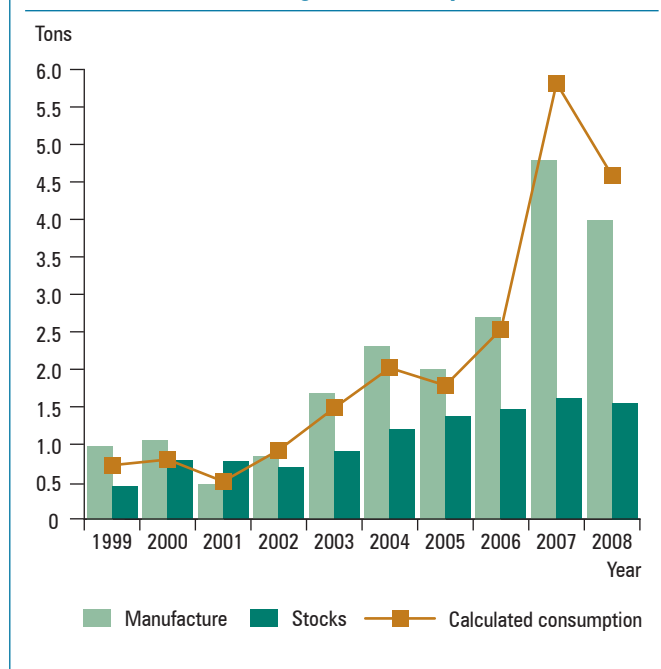
51. In several countries, buprenorphine,⁵ which belongs to the family of opioids used mainly as analgesics, is used in the detoxification and substitution treatment of opioid dependence. In the late 1990s, as the substance started to be used in higher doses for the treatment of opioid addiction, global manufacture of buprenorphine increased sharply, reaching 4.8 tons (4 billion S-DDD) in 2007 and then falling by 17 per cent to below 4 tons (3.3 billion S-DDD) in 2008 (see figure 10). In the decade ending in 2008, the United Kingdom was the main manufacturer, accounting for 73 per cent of the global total on average during the period 2004-2007 and increasing its share to 95 per cent in 2008. Buprenorphine manufacture was also reported by other countries, such as Australia, Belgium, China, the Czech Republic, Germany, India, Switzerland and the United States. Global stocks of the substance increased to 1.5 tons in 2008, the majority of which was held in the United Kingdom, Germany, France and the United States.

52. Total exports of buprenorphine increased from 100 kg in 1996 to over 1 ton in the period 2004-2007. In 2008, 2.8 tons of buprenorphine were exported, the United Kingdom (62 per cent), Australia (19 per cent) and Germany (11 per cent) being the main exporters of the substance. Belgium, the Czech Republic, Denmark, France, India and the Netherlands have also reported exports of buprenorphine in recent years.

53. In the period 2004-2008, 41 countries reported imports of buprenorphine in quantities exceeding 1 kg, the main importers of the substance being the United States, Germany, France and the United Kingdom; together, those countries accounted for 79 per cent of total imports. Other major importers of buprenorphine in 2008 were Italy (99 kg), Spain (73 kg), Australia (64 kg) and Belgium (39 kg). Calculated consumption of the substance continued to increase in many countries, in particular in the United States, France and Germany, as well as in several other countries in Europe. The increased use of buprenorphine for medical purposes has been accompanied by increased diversion and abuse of the substance. Currently, the illicit market for buprenorphine is entirely supplied by diversion, above all in the form of preparations used in the treatment of opioid addicts.

⁵See table IV for details of the consumption levels of buprenorphine.

Figure 10. Buprenorphine: total reported manufacture, stocks and calculated global consumption, 1999-2008



^aStatistical data submitted by Governments are used to calculate the approximate global consumption in a given year. Those consumption figures are expressed in defined daily doses for statistical purposes (S-DDD).

Pentazocine

54. Pentazocine, an opioid analgesic with properties and uses similar to those of morphine, was included in Schedule III in 1984. Total reported manufacture of pentazocine fluctuated between 2.9 tons and 6.7 tons during the decade 1999-2008, with total output reaching 4.3 tons (21.6 million S-DDD) in 2008. Italy (54 per cent) and India (45 per cent) continued to be the main manufacturing countries, with China producing the remainder in 2008. While most of the pentazocine manufactured by India was for domestic consumption, the pentazocine manufactured in Italy was destined for export. Other countries reporting manufacture of pentazocine were Hungary (136 kg in 2001), the United Kingdom (258 kg in 2002) and the United States (171 kg in 2001 and 316 kg in 2002). Total stocks of pentazocine averaged 2.9 tons in the period 2004-2008; the main countries holding those stocks were India, Italy and the United States.

55. International trade in pentazocine during the five years ending in 2008 averaged around 3.7 tons. Italy (58 per cent) and India (24 per cent) remained the main exporters of pentazocine in 2008. Of the 43 countries that reported imports of pentazocine in 2008, the United States (1.9 tons) and Pakistan (940 kg) together accounted for 64 per cent of total imports. The main consumers of pentazocine were India, Pakistan, the United States, Portugal and Japan.

Substances listed in Schedule IV

56. Substances included in Schedule IV have a therapeutic usefulness ranging from little to great. Sixty-two substances with various applications in medicine are listed in Schedule IV and 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 anti epileptics (1 substance); barbiturate-type sedative-hypnotics and anti-epileptics (7 substances); other sedative-hypnotics (5 substances); and analgesics (1 substance).

Central nervous system stimulants

57. Fourteen stimulants are listed in Schedule IV: amfepramone, aminorex, benzfetamine, etilamfetamine, fen-camfamin, fenproporex, mazindol, mefenorex, mesocarb, pemoline, phendimetrazine, phentermine, pipradrol and pyrovalerone. Both amfepramone and pipradrol were originally included in Schedule IV, while all the other stimulants were added later. The stimulants in Schedule IV are essentially used as anorectics or for the treatment of ADD.

58. Following its great drop in 1998, the total reported manufacture of central nervous system stimulants listed in Schedule IV subsequently recovered rapidly and stabilized in 2000. After 2005, it remained at an average of 2.07 billion S-DDD (see figure 11).

59. In 2008, the manufacture of phentermine (1.4 billion S-DDD) accounted for 66 per cent, fenproporex (376 million S-DDD) for 18 per cent and both amfepramone and mazindol (126 million and 128 million S-DDD respectively) for 6 per cent of total reported manufacture of the 14 stimulants in Schedule IV (see figure 12). Together, the manufacture of phendimetrazine, pemoline and benzfetamine accounted for less than 4 per cent. In 2008, no other central nervous system stimulants listed in Schedule IV were reported to have been manufactured.

60. After 2000, manufacture and consumption of phentermine increased steadily and the substance became the most used anorectic in the United States and in the world (see figure 13). A total of 2.1 billion S-DDD of central nervous system stimulants listed in Schedule IV were used globally in 2008. Phentermine accounted for 66 per cent (1.4 billion S-DDD) of that total; it was followed by fenproporex (243 million S-DDD), mazindol (200 million S-DDD) and amfepramone (149 million S-DDD).

61. Consumption of stimulants in Schedule IV in the Americas remained the highest worldwide. This was mainly due to high consumption levels in the United States, Argentina and Brazil. Overall, an average of 10.1 S-DDD per 1,000 inhabitants per day was

Figure 11. Central nervous system stimulants listed in Schedule IV: total reported manufacture, by substance, 1999-2008

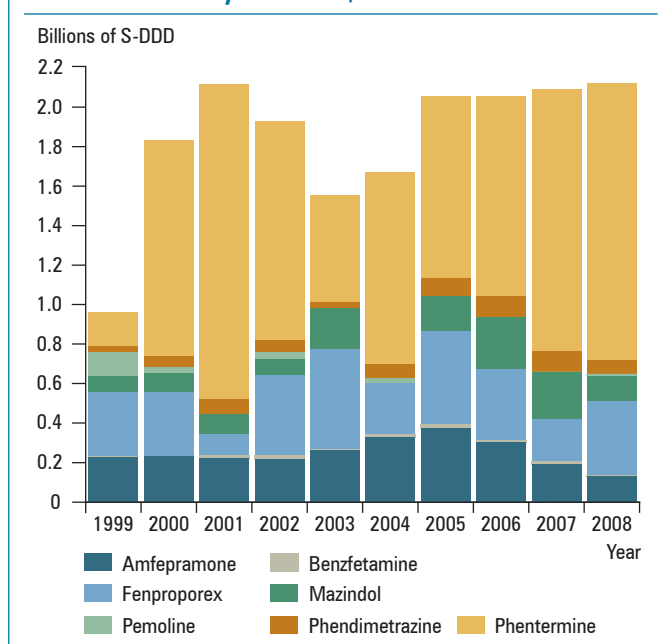
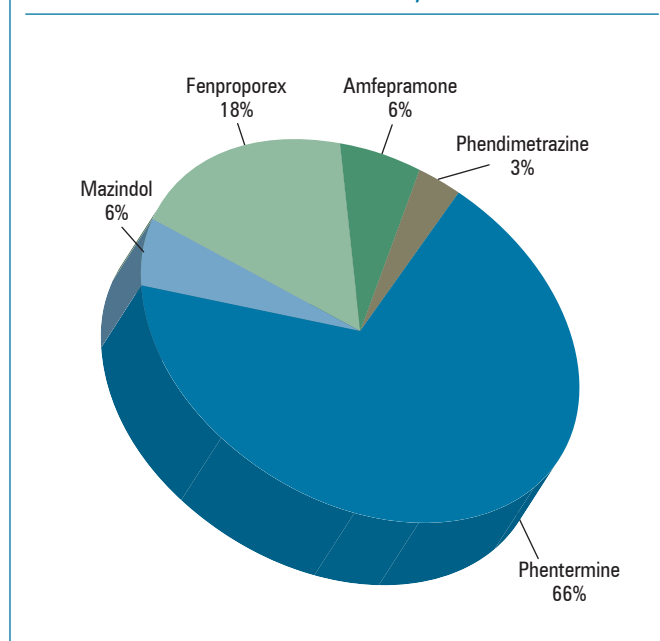
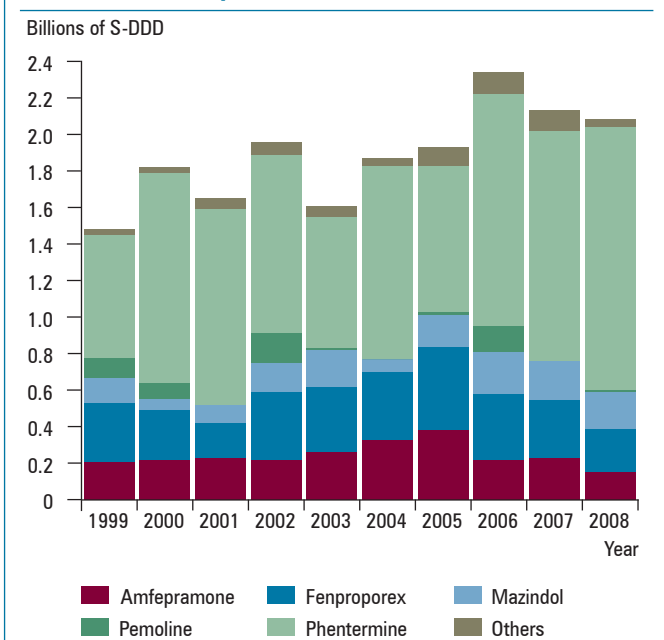


Figure 12. Central nervous system stimulants listed in Schedule IV: share of total reported manufacture, selected substances, 2008



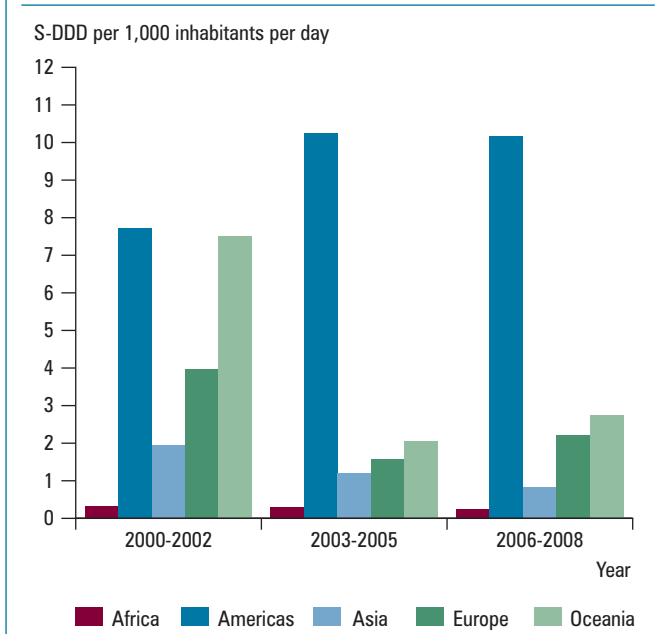
consumed in the Americas during the period 2006-2008 (see figure 14). In 2008, the United States (10.87 S-DDD per 1,000 inhabitants per day), Argentina (8.58 S-DDD), Switzerland (7.48 S-DDD) and Singapore (6.43 S-DDD) had the highest calculated rates of use of the central nervous system stimulants listed in Schedule IV.

Figure 13. Central nervous system stimulants listed in Schedule IV: calculated global consumption,^a by substance, 1999-2008



^aStatistical 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).

Figure 14. Central nervous system stimulants listed in Schedule IV: average national consumption,^a by region, 2000-2002, 2003-2005 and 2006-2008



^aStatistical data submitted by Governments are used to calculate average annual consumption for a three-year period.

62. In Africa, the average consumption of central nervous system stimulants increased in 2008 to 0.638 S-DDD per 1,000 inhabitants per day (from an average of 0.057 S-DDD per 1,000 inhabitants per day during the period 2006-2007), as a result of a sharp increase of phentermine use in South Africa. In Asia, the regional annual

average rate of consumption decreased during the decade ending in 2008, although very high consumption continued to be observed in selected countries. In Europe, the average consumption rate decreased compared with the rate for the previous decade, but picked up again; in some European countries, the consumption of stimulants increased considerably. Despite an overall decrease in the calculated rate of consumption observed in Oceania during the decade prior to 2008, calculated consumption increased 5-fold in 2008, as a result of the increased use of phentermine in Australia.

63. In terms of manufacture, phentermine has been the main substance in the group of stimulants in Schedule IV, although its share of total manufacture for all substances in this group has varied widely, between 0 and 76 per cent, in recent years. Total reported manufacture of the substance increased from an average of 9.5 tons annually during the period 1991-1995 to 50 tons in 1996, the highest level ever reported. Manufacture of the substance dropped in 1997 and completely stopped in 1998. After 1999, global reported manufacture of the substance fluctuated; it stood at 21 tons in 2008. In the period 2006-2008, the United States, Germany, Italy, India and Japan were the main manufacturers of phentermine.

64. During the three-year period 2006-2008, the volume of trade in phentermine averaged 11.8 tons. Germany and Italy, in that order, were the main exporters of phentermine, accounting together for 74 per cent of the global total in 2008, which was 13.2 tons. Other major exporters in 2008 were the United States, Australia and India. Forty-five countries reported importing phentermine at least once during the three-year period 2006-2008. The United States remained the main importer of the substance, accounting for 67 per cent of global imports in 2008. The only other main importer of phentermine in 2008 was Australia (1.2 tons).

65. Fenproporex is mainly used as an appetite suppressant. After growing steadily from 3 tons in 1998 to 10 tons in 2003, total reported manufacture of fenproporex fluctuated; it stood at 7.5 tons in 2008. Brazil has been the main manufacturer since 2003, accounting for about 50 per cent of global manufacture; in Brazil, fenproporex was mainly manufactured for domestic consumption. In 2008, Brazil and Belgium were the only manufacturers of the substance, with Brazil accounting for 57 per cent of the total. In 2006, Germany became the leading importer of the substance. In 2008, German imports accounted for nearly 70 per cent of global imports.

66. The total reported manufacture of amfepramone, a substance mainly used as an anorectic, amounted to about 28 tons in 2005. The total figure decreased after 2005, amounting to 9.4 tons in 2008, as Brazil reported declining manufacture of the substance. Brazil, which manufactured amfepramone mainly for domestic

consumption, was the key manufacturer of the substance. In the decade prior to 2008, Brazil, Italy and Switzerland reported having manufactured the substance. Switzerland was the main exporter, exporting 2.6 tons in 2008 and accounting for 78 per cent of global exports; it was followed by Brazil, Italy and Germany. The largest imports of amfepramone in 2008 were reported by the United States (1.1 tons), Mexico (730 kg) and Germany (600 kg); together, those three countries accounted for nearly 66 per cent of global imports of the substance.

67. In 2008, the global manufacture of phendimetrazine, an anorectic, fell to 4.8 tons from 7.4 tons in 2007. Italy was traditionally the main manufacturer of the substance, which was mainly destined for export. In 2008, Italy manufactured 4.7 tons of the substance (98 per cent). Germany, which used to be an important manufacturer of the substance (2.6 tons in 2007) did not report any output in 2008. China, which had manufactured phendimetrazine in 2005 and 2006, reported no manufacture in 2007 and 2008. The United States used to be the main importer of phendimetrazine, accounting in 2007 for 71 per cent of global imports of the substance; however, that country's imports of the substance fell sharply, to only 4 kg, in 2008. The quantity of phendimetrazine imported by the Republic of Korea also fell sharply, from an average of 1.6 tons during the period 2005-2007 to 560 kg in 2008. The only other importers of phendimetrazine in 2008 were Germany and South Africa (17 kg and 14 kg respectively). The greatest consumer of the substance for the three-year period 2006-2008 was the Republic of Korea (1.08 S-DDD per 1,000 inhabitants per day), followed by Germany (1.00 S-DDD), Italy (0.45 S-DDD) and the United States (0.23 S-DDD).

68. Global manufacture of pemoline fluctuated widely during the decade prior to 2008, exceeding a few tons in some years. From 2005 to 2007 no manufacture of the substance was reported but in 2008, 393 kg were manufactured in the Netherlands. The Netherlands and Switzerland were the main exporters in the period 1999-2008. The main importers of pemoline during the three years up to 2008 were Japan (133.4 kg), followed by Chile (16.3 kg) and Switzerland (13 kg). In addition to being used as a stimulant, pemoline is used for the treatment of ADD.

69. Mazindol used to be manufactured almost exclusively in Brazil, where an average of 41 kg was produced during the period 2003-2007, both for domestic consumption and for export. In the three years up to 2008, Argentina replaced Brazil as the main manufacturer of mazindol and was the sole manufacturer of the substance in 2008, producing 128 kg. Global use of the substance fell steadily from 707 kg in 1998 to an annual average of 212 kg in the three years up to 2008. The biggest importers in the decade up to 2008 were Mexico (38.7 kg) and Switzerland (31 kg).

70. Until 2004, only the United States reported manufacture of benzfetamine, of which it reported manufacturing an average of 1.1 tons annually during the period 2000-2004. A large part of the substance manufactured in the United States has been utilized in that country for the manufacture of non-psychotropic substances. Between 2005 and 2007, smaller quantities of the substance were manufactured in Ireland (72 kg), Italy (58 kg) and Switzerland (308 kg), for export. In 2008, however, the United States was once more the sole manufacturer, reporting the manufacture of 388 kg of the substance. During the decade prior to 2008, international trade in benzfetamine was limited, with Peru importing 31 kg of the substance in 2003 and Latvia importing 22 kg in 2005. During the period 2006-2008, the United States was the main consumer of benzfetamine, consuming an average of 514 kg annually.

71. Manufacture of and trade in the other stimulants listed in Schedule IV has been reported sporadically. After 1995, only France reported the manufacture of pipradrol: 20 kg in 1999 and 8 kg in 2004. In 2004, France exported 2 kg of the substance to Canada and another 5.3 kg in 2007 to the same country. In the period 2003-2008, no manufacture of aminorex, etilamfetamine, fencamfamin, mefenorex, mesocarb or pyrovalerone was reported. Small quantities of fencamfamine, mefenorex and pipradrol were reported to have been traded, but not on a regular basis, and no international trade in aminorex, etilamfetamine, mesocarb or pyrovalerone was reported.

Benzodiazepines

72. 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.

73. The number of countries and territories reporting manufacture of and/or trade in benzodiazepine increased considerably. After 1990, about 200 countries and territories reported having manufactured or traded in benzodiazepines in quantities of more than 1 kg at least once.

Benzodiazepine-type anxiolytics

74. Twenty-two benzodiazepines are generally classified as anxiolytics. The total reported manufacture of this group of substances rose steadily from 1999 to 2001, when it reached a peak of 28.8 billion S-DDD. Global manufacture then fluctuated between 19 billion and 27 billion S-DDD between the years 2002 and 2007, and reached a new record of almost 30 billion S-DDD in 2008 (see figure 15). Fluctuations in the level of manufacture of benzodiazepine-type anxiolytics are usually a reflection of fluctuations in the manufacture of alprazolam and diazepam, the main substances in this group, which together accounted for 70 per cent (20.6 billion

Figure 15. Benzodiazepine-type anxiolytics: total reported manufacture 1999-2008

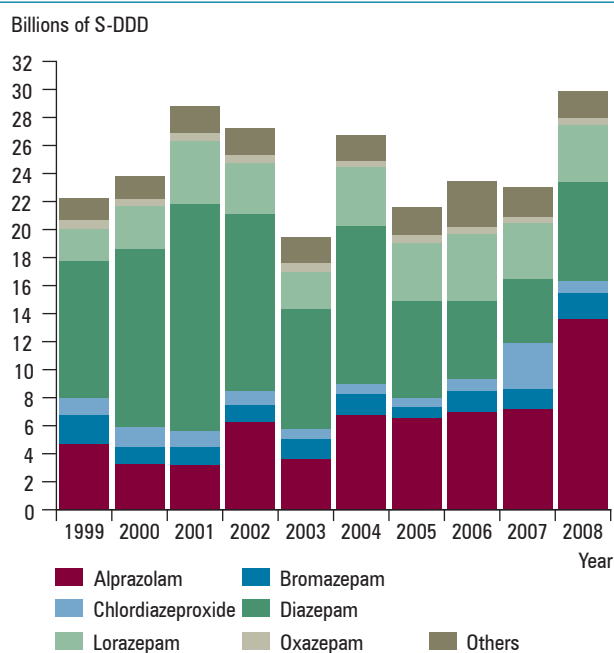


Figure 17. Benzodiazepine-type anxiolytics: share of total reported manufacture, selected countries, 2008

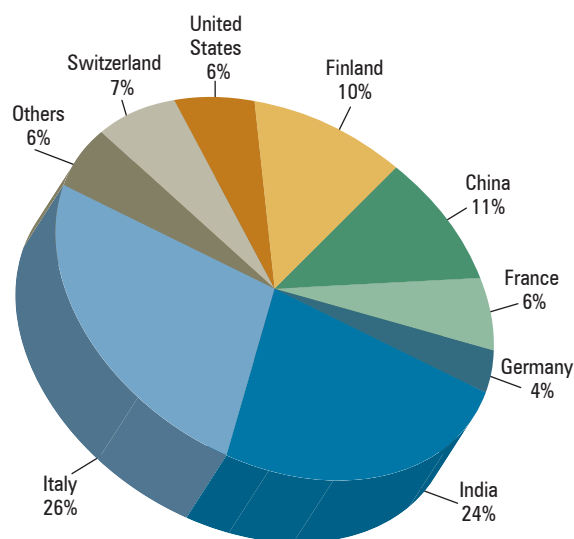


Figure 16. Benzodiazepine-type anxiolytics: share of total reported manufacture, by substance, 2008

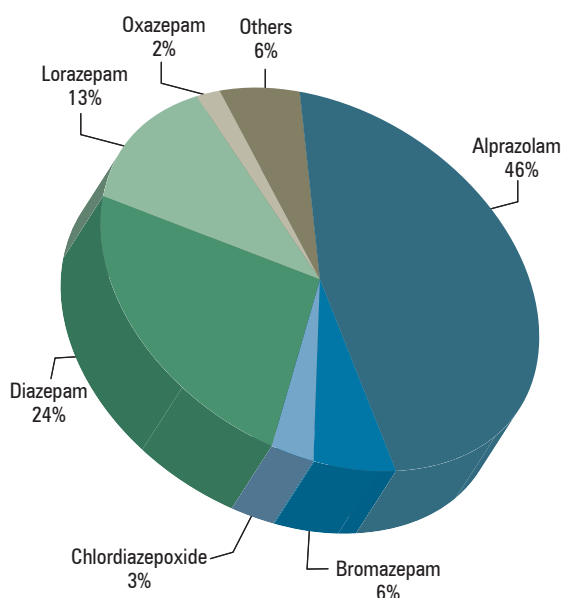
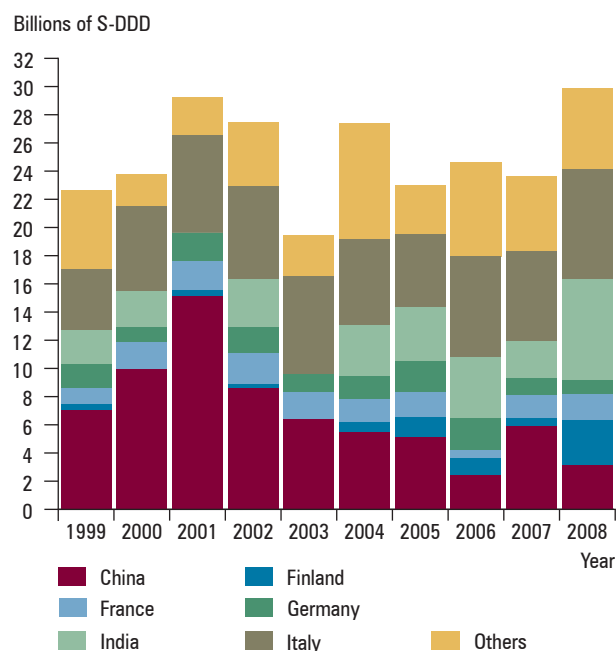


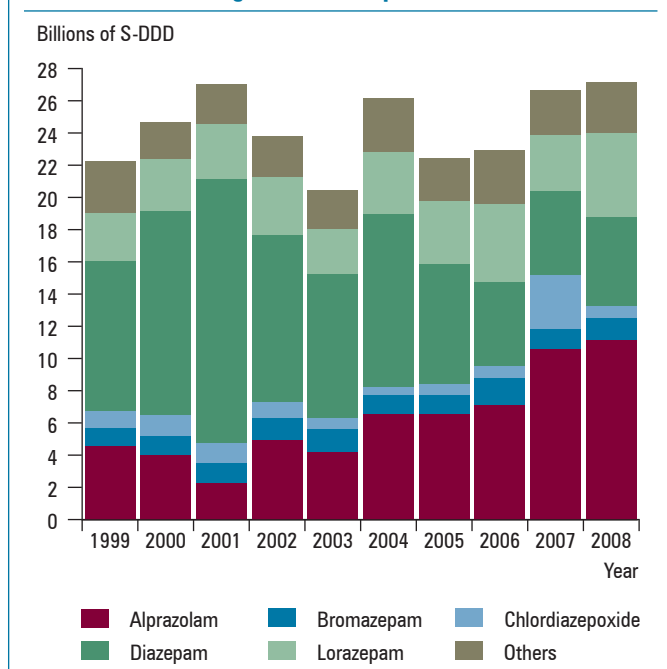
Figure 18. Benzodiazepine-type anxiolytics: reported manufacture, selected countries, 1999-2008



S-DDD) of the total in 2008. Compared with the previous year, in 2008 the share of alprazolam increased to 46 per cent (13.6 billion S-DDD) and the share of diazepam increased to 24 per cent (7 billion S-DDD). Third came lorazepam, accounting for 13 per cent (4 billion S-DDD) of total output. Chlordiazepoxide accounted for 3 per cent, bromazepam for 6 per cent and oxazepam for 2 per cent (see figure 16). Clobazam and nordazepam accounted for 1 per cent each of the total reported manufacture of benzodiazepine-type anxiolytics in 2008. The remaining 12 substances in that group (clorazepate,

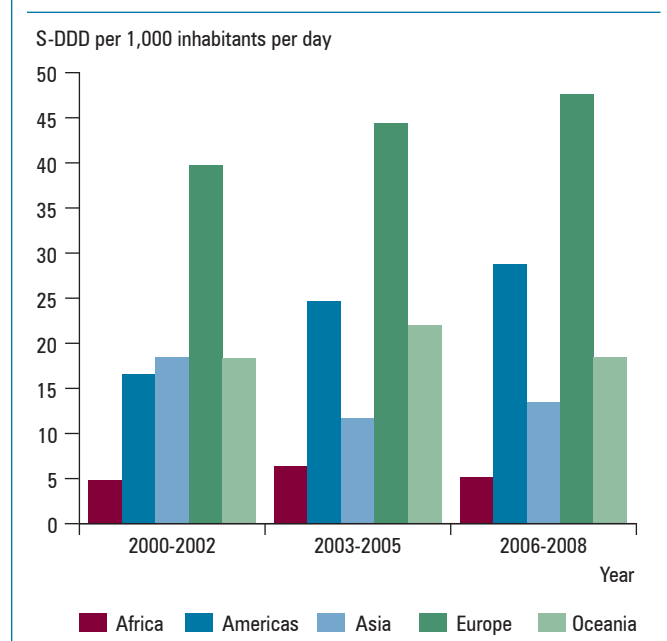
clotiazepam, cloxazolam, delorazepam, ethyl loflazepate, halazepam, ketazolam, medazepam, oxalozolam, pinazepam, prazepam and tetrazepam) each accounted for less than 1 per cent of the total reported manufacture calculated in defined daily doses for statistical purposes. No manufacture of camazepam or fludiazepam was reported in 2008. As shown in figures 17 and 18, China and Italy were the leading manufacturers of benzodiazepine-type anxiolytics in the 10-year period 1999-2008 and, together with India, accounted for 61 per cent of total manufacture in 2008.

Figure 19. Benzodiazepine-type anxiolytics: calculated global consumption, 1999-2008^a



^aStatistical 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).

Figure 20. Benzodiazepine-type anxiolytics: average national consumption,^a by region, 2000-2002, 2003-2005 and 2006-2008



^aStatistical data submitted by Governments are used to calculate the average annual consumption for a three-year period.

75. The approximate consumption levels calculated by INCB usually follow the trend in manufacture. In 2008, total consumption of this group of substances stood at 24.1 billion S-DDD (see figure 19), slightly higher than the quantity manufactured in 2007. The levels of consumption of benzodiazepine-type anxiolytics in defined

daily doses for statistical purposes per 1,000 inhabitants per day is shown in table IV.3 of the present publication. The calculated average national consumption of benzodiazepine-type anxiolytics is higher in Europe than in other regions (see figure 20).

Alprazolam

76. Total reported manufacture of alprazolam grew from about 1 ton per year in 1986 to 7.2 tons in 2007. In 2008, global manufacture increased to a new record level, at 13.6 tons, mainly due to increased output by Finland (2.9 tons), India (5.1 tons) and Italy (2 tons). The United States continued to be a major manufacturer of alprazolam (1.5 tons); it was followed by France (1.2 tons). Together, those countries accounted for 95 per cent of global manufacture of alprazolam in 2008.

77. In 2008, over 70 countries and territories in all regions of the world reported imports of alprazolam in quantities exceeding 1 kg. During that year, the main importers of alprazolam were the United States (2.3 tons), Canada (1.1 tons) and Belgium (1 ton); together, those countries accounted for 49 per cent of global imports of the substance. Global consumption, which had averaged 4.8 billion S-DDD during the period 2000-2005, started to grow in 2006 and attained a record of 8.9 billion S-DDD in 2008. The largest consumers of alprazolam during that year were India (2.5 billion S-DDD), the United States (1.3 billion S-DDD) and Finland (1.1 billion S-DDD).

Diazepam

78. Diazepam, the most traded substance in the group of benzodiazepine-type anxiolytics, is consumed in all regions of the world. During the period 2000-2004, global manufacture of diazepam averaged 123 tons. Subsequently, manufacture of that substance dropped, from 69 tons in 2005 to 45 tons in 2007. In 2008, however, global manufacture of that substance increased again, to 70.4 tons. As manufacture of diazepam by China, the leading manufacturer of the substance, remained stable at 26 tons, the increase was mainly due to Italy. That country more than doubled its manufacture of diazepam compared with the previous year (from 11 tons in 2007 to 24 tons in 2008). Increased manufacture of the substance was also recorded in 2008 for India (7.2 tons), Switzerland (6.7 tons) and Brazil (6.4 tons).

79. Export levels dropped from 60 tons in 2006 to 51 tons in 2007, but rose again, to 58.4 tons, in 2008. This was mainly due to increased exports by Italy and China, the world's leading exporters of diazepam, which exported 19.3 tons and 17 tons, respectively, in 2008. During that year, significant quantities (between 6.5 tons and 1 ton) were also exported by Switzerland, Denmark, Germany, United Kingdom and India, in that order.

80. About 120 countries and territories report imports in quantities of more than 1 kg of diazepam every year, indicating that use of that substance is widespread. In 2008, the largest importers of diazepam were Denmark and the United States (over 6 tons each), followed by Switzerland (4.6 tons), Germany (4 tons), Spain (2.3 tons) and Ghana (2.1 tons). Together, those countries accounted for 50 per cent of global imports. Global consumption of diazepam, which has decreased from 7.4 billion S-DDD in 2005 to 5.2 billion in 2007, stood at 5.6 billion S-DDD in 2008. According to calculated consumption figures, China remained the world's main consumer of the substance in 2008 (857 million S-DDD); it was followed by Brazil (697 million S-DDD) and the United States (684 million S-DDD).

Lorazepam

81. Total reported manufacture of lorazepam, which averaged 9.4 tons during the period 1998-2007, stood at 10 tons in 2008. Italy and Germany were the two main manufacturers of lorazepam (5.1 tons and 2.3 tons, respectively). Together with India (1.6 tons), they accounted for 90 per cent of total manufacture. Other countries that reported some manufacture of lorazepam in 2008 were Brazil, China, Poland, Spain, the United Kingdom and the United States.

82. Exports of lorazepam, which had decreased from 11.2 tons in 2006 to 9.6 tons in 2007, stood at 9.8 tons in 2008. The main exporters of the substance were Italy, Germany and India (in that order). Those countries together accounted for 90 per cent of total exports of the substance in 2008. Approximately 100 countries imported more than 1 kg of lorazepam at least once in the period 2003-2008. Of those countries, the United States, Spain and Germany imported the most, together accounting for 45 per cent of all imports of the substance during 2008. Global calculated consumption of lorazepam, which had averaged 3.7 billion S-DDD in the period 2001-2007, reached 4.7 billion S-DDD in 2008. The main consumers of lorazepam in 2008 were the United States (1.5 billion S-DDD), Spain (380 million S-DDD), Italy (365 million S-DDD), India (300 million S-DDD) and Germany (280 million S-DDD).

Bromazepam

83. Total reported manufacture of bromazepam fluctuated significantly in the period 1999-2005. After having increased sharply from an annual average of 6 tons during the period 1997-1998, global manufacture of the substance peaked at over 21 tons in 1999 and declined to an average of 14 tons in the following years. In 2008, global manufacture of the substance increased to 18.3 tons. Italy (4.8 tons) and Switzerland (9.4 tons) remained the leading manufacturers in 2008, followed by India (2 tons) and Brazil (1.8 tons).

84. Global exports of bromazepam increased slightly, from 16.5 tons in 2007 to 17.9 tons in 2008. As in previous years, the main exporters were Switzerland (7.1 tons) and Italy (5.7 tons), which together accounted for 71 per cent of global exports of the substance. Of the approximately 90 countries that reported imports of bromazepam in quantities of more than 1 kg in 2008, seven accounted for 60 per cent of global imports, namely, France, Switzerland, Italy, Brazil, Serbia, Germany and Japan, in that order. Calculated global consumption of bromazepam remained stable at 1.3 billion S-DDD in 2008.

Chlordiazepoxide

85. Total reported manufacture of chlordiazepoxide, which had decreased from 43 tons in 2000 to 25 tons in 2006, jumped to 100 tons in 2007, as a result of the record level of manufacture of the substance by China: over 91 tons in 2007. In 2008, however, global manufacture decreased again to 28 tons. Those fluctuations reflect changes in manufacture in the main manufacturing countries in 2008: India (10.3 tons), Italy (9.4 tons) and China (7.9 tons). Italy remained the main exporter, exporting 8.5 tons; China exported 7.1 tons and India exported 1.8 tons. Switzerland, which does not manufacture chlordiazepoxide, re-exported 1.7 tons of the substance in 2008.

86. Global imports of chlordiazepoxide, which had decreased from 24 tons in 2000 to 14.8 tons in 2006, stood at 15.8 tons in 2008. About 80 countries reported imports of the substance in quantities exceeding 1 kg. The main importers of chlordiazepoxide in 2008 were the Islamic Republic of Iran (2.2 tons), Switzerland (1.5 tons), Brazil (1.4 tons), Cuba (1.2 tons) and Iraq (1 ton). Calculated global consumption of the substance, which had decreased from 1.2 billion S-DDD in 2001 to 680 million S-DDD in 2006, stood at 763 million S-DDD in 2008.

Oxazepam

87. Global manufacture of oxazepam was fairly stable in the period 1998-2002, averaging nearly 30 tons per year. In 2003, it increased to 34 tons but decreased in subsequent years; it stood at 26.7 tons in 2008. As in previous years, Italy and France were the main manufacturers of oxazepam in 2008, reporting the manufacture of 16.4 tons and 8.2 tons of the substance respectively; they were followed by India, which reported manufacturing 1.3 tons. The volume of trade in oxazepam averaged about 40 tons annually during the period 2001-2003, but started to decline in 2004 and stood at 19 tons in 2008. Germany (3.7 tons) remained the main importer of oxazepam in 2008, followed by Canada, Australia and the Netherlands, in that order. France remained the largest consumer of oxazepam, accounting for 33 per cent of global calculated consumption in 2008.

Clorazepate

88. Total reported manufacture of clorazepate was stable, averaging 8.4 tons during the period 2001-2005. After that, it decreased to 5 tons in 2006 and 2007. Global manufacture of clorazepate stood at 6 tons in 2008, 73 per cent of which was manufactured by France, the main manufacturer of the substance. Italy came second, at 1.3 tons, accounting for 22 per cent of global manufacture of clorazepate in that year. About 60 countries imported a total of 7.9 tons of clorazepate. The main importers of clorazepate were Spain and France, together accounting for 61 per cent of global imports of the substance during 2008.

Clobazam

89. Total reported manufacture of clobazam, which fluctuated between 3 and 6 tons over several years, stood at 5.3 tons in 2008. The fluctuations reflect changes in the output by France and Germany, the main manufacturers of clobazam. In 2008, France manufactured 1.6 tons of clobazam and Germany 2.1 tons; those countries were followed by India, with 1.4 tons. International trade in clobazam remained stable at about 5 tons, with about 50 countries reporting imports of more than 1 kg of the substance.

Other anxiolytics

90. Total reported manufacture of nordazepam fell from 947 million S-DDD in 2006 to 419 million S-DDD in 2008, mainly as a result of decreased manufacture of the substance by Switzerland (246 million S-DDD in 2008). No manufacture of camazepam or fludiazepam was reported for 2008. The combined manufacture of the remaining 11 substances in that group (clotiazepam, cloxazolam, delorazepam, ethyl loflazepate, halazepam, ketazolam, medazepam, oxazolam, pinazepam, prazepam and tetrazepam) stood at 974 million S-DDD in 2008.

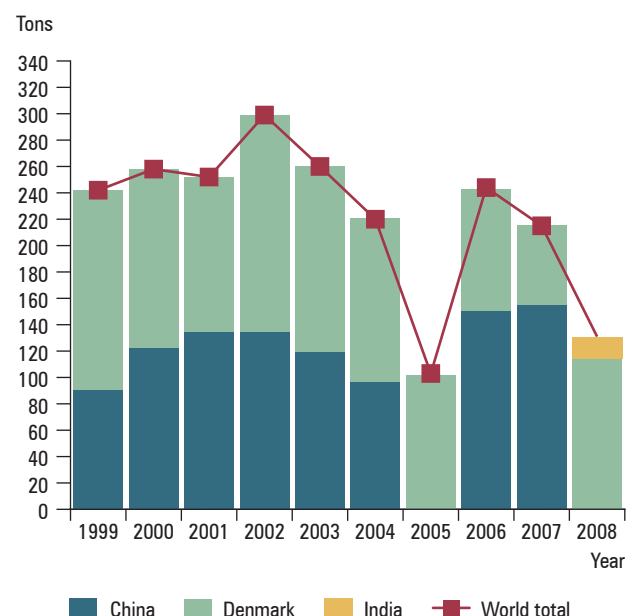
Meprobamate

91. Due to its gradual replacement by benzodiazepines, meprobamate, the only non-benzodiazepine-type substance in Schedule IV used as an anxiolytic, was manufactured in ever smaller quantities: from 750 tons in the late 1970s to an annual average of 560 tons during the 1980s and of 290 tons during the 1990s. After 2000, an annual average of 220 tons of meprobamate were manufactured. In 2005, global manufacture of the substance fell to a record low of 103 tons, rose once more in 2006 but dropped again, to 131 tons, in 2008 (109 million

S-DDD) (see figure 21). This represents the second lowest amount of meprobamate manufactured in the 20 years prior to 2008. The reported total manufacture of meprobamate reflects changes in the quantities manufactured by China, which did not manufacture the substance in 2005 and 2008. Denmark, the other major supplier of the substance, accounted for 114 tons (95 million S-DDD) in 2008. In addition, India manufactured 16 tons of the substance in 2008. Drawing from stocks, China exported 86 tons of the substance and Denmark exported 117 tons.

92. Imports of meprobamate averaged about 220 tons annually in the five-year period 2004-2008. France remained the largest importer of the substance. After purchasing an average of 97 tons of meprobamate annually during the period 2002-2007, almost all of it for domestic use, France imported 105 tons of the substance in 2008. Cuba was the second-largest importer of the substance in 2008: 41 tons. The other main importers of the substance in 2008 were South Africa (19 tons), Hungary (18 tons) and the United States (15 tons). About 50 countries reported imports of meprobamate every year. In 2008, France continued to be the leading consumer country, using 79 tons of meprobamate; it was followed by South Africa (77 tons) and Cuba (41 tons). After 1999, global consumption of meprobamate averaged 194 million S-DDD annually. In 2008, global consumption of the substance stood at 207 million S-DDD.

Figure 21. Meprobamate: reported manufacture, in selected countries, 1999-2008



Benzodiazepine-type sedative-hypnotics

93. 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 included in paragraphs 48-50 above.

94. Total reported manufacture of the 12 substances in the group gradually increased from 6.4 billion S-DDD in 1999 to over 8.5 billion S-DDD in 2007, but fell to 5.5 billion S-DDD in 2008. That decline was mainly attributed to markedly decreased manufacture of the substances by Germany and Switzerland. During the period 1998-2002, Belgium, Canada and Switzerland started reporting to INCB on their manufacture of benzodiazepines; those data brought the calculated levels of annual consumption closer to the levels of total manufacture (see figures 22 and 23).

95. The calculated average national consumption of benzodiazepine-type sedative-hypnotics, expressed in defined daily doses for statistical purposes per 1,000 inhabitants per day, has traditionally been highest in Europe (see figure 24). The levels of consumption of benzodiazepine-type sedative-hypnotics, in defined daily doses for statistical purposes per 1,000 inhabitants per day, is shown in table IV.2 of this publication.

Figure 22. Benzodiazepine-type sedative-hypnotics, total reported manufacture, by substance, 1999-2008

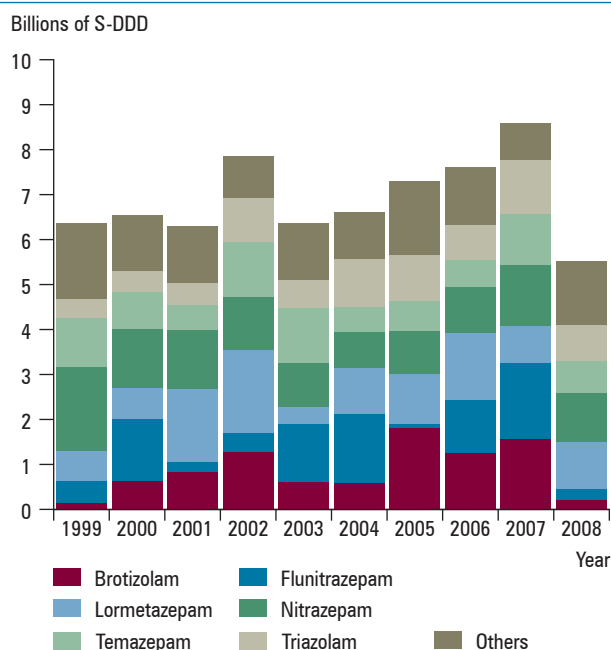
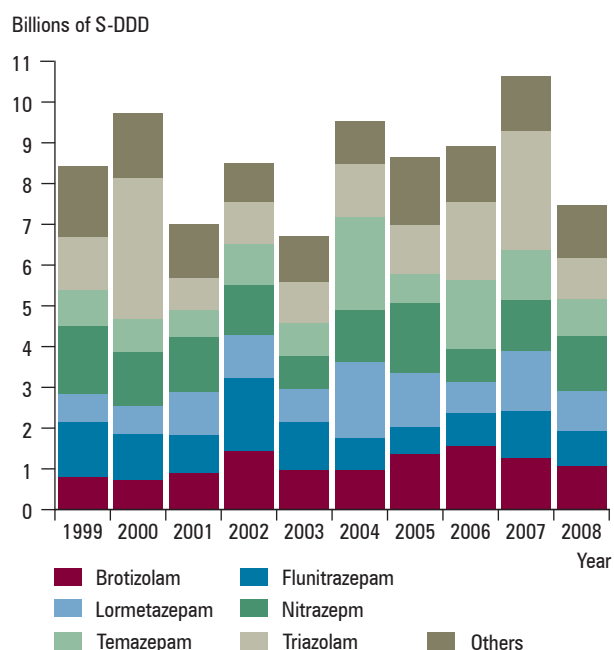
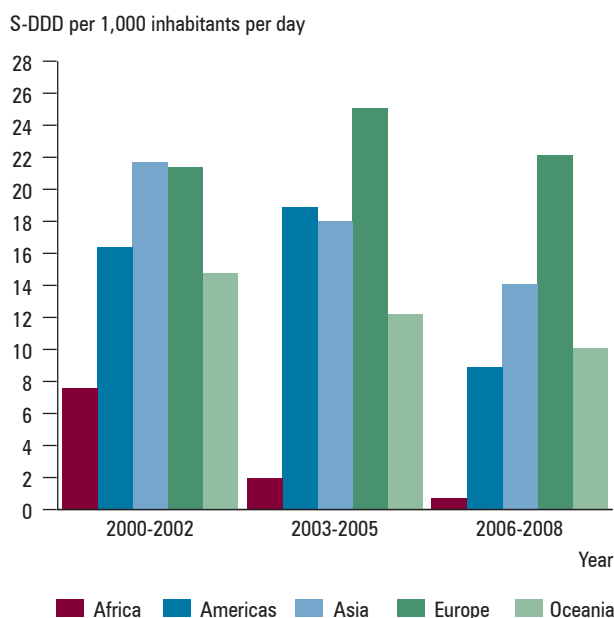


Figure 23. Benzodiazepine-type sedative-hypnotics: calculated global consumption,^a 1999-2008



^aStatistical 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).

Figure 24. Benzodiazepine-type hypnotics: average national consumption,^a by region, 2000-2002, 2003-2005 and 2006-2008



^aStatistical data submitted by Governments are used to calculate the average annual consumption for a three-year period.

96. In 2008, 1.1 billion S-DDD of nitrazepam were manufactured, making nitrazepam the most manufactured substance in the group of benzodiazepine-type sedative-hypnotics (accounting for 20 per cent of the total). Lormetazepam was the second-most manufactured

substance in that group (accounting for 19 per cent of the total, or 1 billion S-DDD); it was followed by estazolam and triazolam (15 per cent each) and temazepam (13 per cent). In contrast, while 1.7 billion S-DDD of flunitrazepam were manufactured in 2007, that figure dropped to 246 million S-DDD (4 per cent) in 2008. That decline can be attributed to the fact that Switzerland, normally a major manufacturer of flunitrazepam, did not manufacture that substance in 2008 (see para. 49 above). Brotizolam held a share of 4 per cent (208 million S-DDD).

97. In 2008, Midazolam (305 million S-DDD), loprazolam (94 million S-DDD), flurazepam (82 million S-DDD) and haloxazolam (71 million S-DDD) together accounted for the remaining 10 per cent of the global manufacture of benzodiazepine-type sedative-hypnotics (see figure 25). No manufacture of nimetazepam took place.

98. Figure 26 shows the main manufacturers during the period 1999-2008. In 2008, Italy reported the manufacture of 2.3 billion S-DDD of benzodiazepine-type sedative-hypnotics (accounting for 41 per cent of global manufacture) and thus continued to be the main manufacturer of that group of substances (see figure 27).

Figure 26. Benzodiazepine-type sedative-hypnotics: reported total manufacture, selected countries, 1999-2008

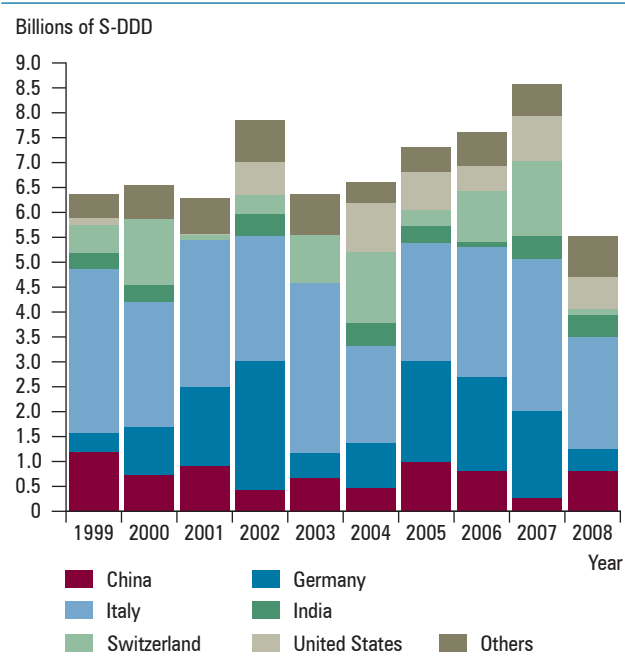


Figure 27. Benzodiazepine-type sedative-hypnotics: total reported manufacture, selected countries, 2008

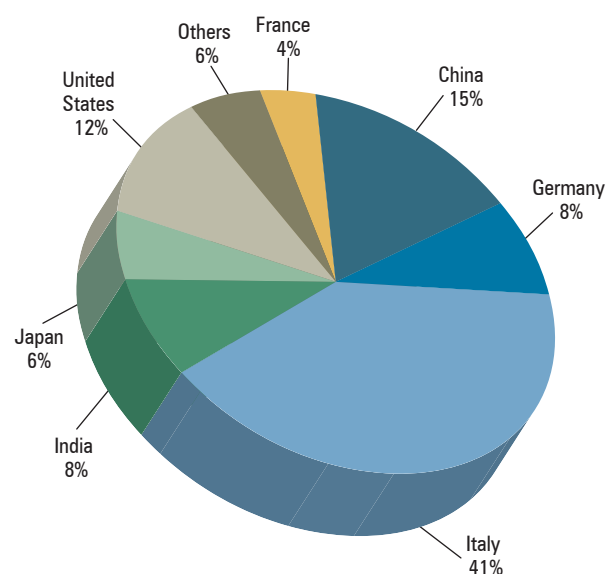
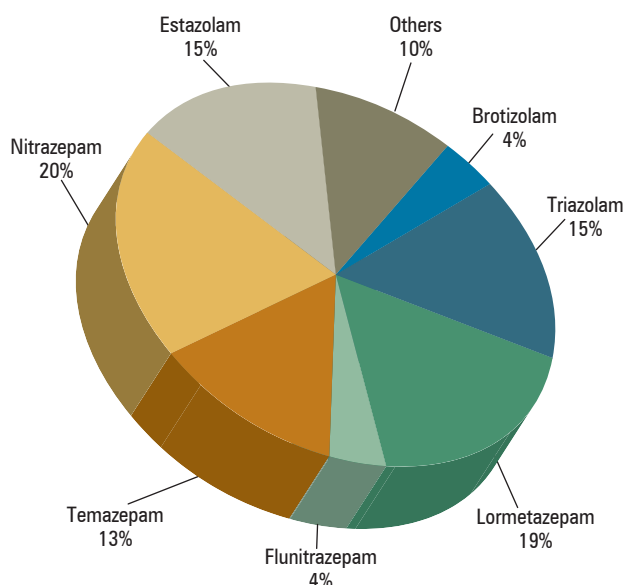


Figure 25. Benzodiazepine-type sedative-hypnotics: share of total reported manufacture, by substance, 2008



Triazolam

99. Triazolam is a potent hypnotic. Together with brotizolam, it has the lowest S-DDD of all psychotropic substances (0.25 mg). The substance is manufactured in amounts of several hundred kilograms per year. In 2008, it was reported that a total of 204 kg (816 million S-DDD) of triazolam had been manufactured. The United States, which remained the main manufacturer of the

substance (161 kg). France and Japan also reported having manufactured that substance during that year. Italy did not manufacture triazolam in 2008.

100. The major exporters of triazolam in 2008 were the United States and Italy, in that order. In addition, Australia, Belgium, France and Switzerland reported regularly importing and re-exporting triazolam. Japan continued to be the largest importer of triazolam, accounting for 36 per cent of global imports of the substance during 2008. Japan was also the largest user of that substance (108 kg or 431 million S-DDD); it was followed by Pakistan (50 kg or 200 million S-DDD).

Lormetazepam

101. The manufacture of lormetazepam reached a peak of 1.9 tons in 2002. After a sharp drop in 2003 to 380 kg, manufacture of that substance picked up again in 2004 and increased to 1 ton in 2008. Those totals reflect fluctuations in manufacturing by Germany and Italy, the two main manufacturers of lormetazepam. Germany and Italy are also the main exporters of that substance. France, the Netherlands and Spain are significant re-exporters of lormetazepam, importing and exporting quantities of up to several hundred kilograms per year. Calculated global consumption of lormetazepam increased from 415 kg in 1997 to 1.9 tons in 2004 but decreased in the following years; it stood at 986 kg in 2008. Italy, Belgium, Spain and France, in that order, were the largest users in that year.

Nitrazepam

102. Global manufacture of nitrazepam fluctuated between 4 and 9 tons per year after 1999. In 2008, a total of 5.5 tons of the substance were manufactured, by Italy (2.6 tons), India (2 tons) and China (800 kg). Exports of nitrazepam, which had averaged about 5.2 tons annually during the period 1999-2008, stood at 4.7 tons in 2008. As in previous years, Italy remained the main exporter of the substance, accounting for 73 per cent of total exports. Many countries import nitrazepam. After 1999, about 80 countries reported, at least once, nitrazepam imports of at least 1 kg. Japan remained the single largest importer of the substance (1.9 tons); it was followed by Poland (527 kg), Cuba (425 kg) and the United Kingdom (294 kg).

Temazepam

103. Temazepam is manufactured by Italy, Poland and the United States in amounts of 10-25 tons per year. In 2008, global manufacture of temazepam amounted to 13.9 tons, with Italy accounting for almost the entire amount. The United States, which intermittently manufactures 2-3 tons of temazepam per year, did not manufacture the substance in 2008.

104. The United States imported the largest quantity of temazepam (9.9 tons) in 2008; it was followed by the United Kingdom, Finland, Canada and Hungary, in that order. About 15 countries reported temazepam imports of over 1 kg in 2008. The United States was the major user, with 453 million S-DDD accounting for 51 per cent of global consumption of temazepam. It was followed by the United Kingdom, Canada, Australia and the Netherlands, in that order; together, those countries accounted for 36 per cent of global calculated consumption.

Brotizolam

105. Manufacture of brotizolam was reported for the first time in 1997, by Germany. Brotizolam is usually manufactured by Germany in amounts of several hundred kilograms per year and by Italy and Japan in amounts of several dozen kilograms per year. In 2008, only Japan reported manufacture (52 kg). That country was also the largest importer of brotizolam (130 kg). Switzerland and Germany also import significant quantities of brotizolam for re-export. In 2008, a dozen countries reported imports of more than 1 kg of brotizolam, totalling 415 kg. Global calculated consumption amounted to 1.1 billion S-DDD, with Japan (727 million S-DDD) and Germany (210 million S-DDD) accounting for 87 per cent of global consumption of the substance in 2008.

Estazolam

106. During the period 1998-2006, global manufacture of estazolam fluctuated between 1.5 tons and 3 tons per year, mainly as a result of fluctuations in manufacture by China, Japan and the United States. In 2007, global manufacture of the substance dropped to 790 kg but increased again in 2008, to 2.5 tons. Those fluctuations reflect changes in China, the leading manufacturer of estazolam. The United States stopped manufacturing estazolam after 2006. Of the 10 countries importing the substance in quantities of more than 1 kg, France, Italy, Mexico, Portugal and the United States accounted for 80 per cent of total imports in 2008.

Midazolam

107. Total reported manufacture of midazolam, which had been stable at an average of 2.6 tons per year during the period 2000-2004, fluctuated between 2.7 tons and 8.7 tons in the subsequent years; in 2008, global manufacture was 6.1 tons. Switzerland remained the largest manufacturer (2.4 tons), followed by Israel, Brazil, India and Italy, in that order. Global exports stood at 6.3 tons in 2008, drawing from global manufacturers' stocks. Midazolam is widely used, with about 80 countries regularly reporting imports of that substance of more than 1 kg. The major importers in 2008 were Brazil, France,

Germany and the United States, which together accounted for 44 per cent of global imports during that year.

Flurazepam

108. Having gradually declined from 10.6 tons in 1997 to 3.6 tons in 2004, global manufacture of flurazepam started to grow again in 2005; it stood at 5.5 tons in 2008. Italy was the single largest manufacturer and exporter of flurazepam, meeting 82 per cent of global demand for that substance. In 2008, 26 countries reported imports of flurazepam in quantities of over 1 kg. The major importer was Germany (504 kg). Significant quantities were also imported by the United States, Poland, Switzerland, the United Kingdom, Spain and Canada, in that order, each of which imported between 200 and 500 kg during that year.

Loprazolam

109. Total reported manufacture of loprazolam amounted to 94 kg in 2008, with France being the only manufacturer and the leading exporter of the substance. The United Kingdom (25 kg in 2000) and Spain (202 kg in 1993) are the only other countries that have ever reported manufacture of loprazolam. In 2008, imports of at least 1 kg of loprazolam were reported by 10 countries, each importing quantities of between 1 and 25 kg.

Benzodiazepine-type anti-epileptics

Clonazepam

110. Clonazepam is a benzodiazepine mainly used as an anti-epileptic. Total reported manufacture of clonazepam, which had remained at an annual average of about 4 tons during the period 1998-2003, started to rise in 2004 and reached 9.6 tons in 2007, the highest level ever recorded. In 2008, global manufacture of clonazepam decreased slightly, to 9.2 tons. Of that total, Switzerland, the world's leading manufacturer of clonazepam, accounted for 2.9 tons. India and Italy manufactured 2.8 tons and 1.4 tons, respectively; those countries were followed by Brazil, China, Israel, Poland and the United States, which manufactured quantities between 100 kg and 1 ton.

111. Global trade in clonazepam increased steadily from about 0.5 tons in 1995 to almost 9.9 tons in 2008. Clonazepam is widely traded, with some 80 countries reporting imports of the substance in amounts exceeding 1 kg. In 2008, Brazil, the Republic of Korea and the United States were the world's largest importers of

clonazepam (over 1 ton each). In addition, significant amounts of the substance were also imported by Canada, Switzerland, Argentina, Mexico and the Islamic Republic of Iran, in that order. Global calculated consumption also increased steadily, from 273 million S-DDD in 1996 to a new record of 1,200 million S-DDD in 2008. In that year, Brazil became the largest user of clonazepam (199 million S-DDD); it was followed by the United States (191 million S-DDD), the Republic of Korea (134 million S-DDD), India (89 million S-DDD) and Argentina (85 million S-DDD).

Barbiturate-type sedative-hypnotics and anti-epileptics

Allobarbital, barbital, butobarbitol, methylphenobarbital, phenobarbital, secbutabarbitol and vinylbital

112. The seven barbiturates listed in Schedule IV are pharmacologically related to those included in Schedule III. Five of the seven substances, namely, allobarbitol, barbital, butobarbitol, secbutabarbitol and vinylbital, are intermediate-acting barbiturates and are mainly used as hypnotics (to induce sleep) in the treatment of intractable insomnia. They are no longer used as daytime sedatives. The other two substances, methylphenobarbital and phenobarbital,⁶ have additional properties and are also used as anti-epileptics (long-acting barbiturates). Barbital, methylphenobarbital and phenobarbital were listed under Schedule IV when the 1971 Convention was adopted, while the other four substances were included in that Schedule in 1987. In 2008, the most widely used substance in the group of barbiturates remained phenobarbital.

113. Total reported manufacture of those barbiturates (for both direct medical use and the manufacture of non-psychoactive substances) gradually increased, reaching 5.4 billion S-DDD in 1998. Manufacture of those barbiturates briefly fell below 4 billion S-DDD in the period 1999-2000, then gradually rose to an annual average of 5.1 billion S-DDD in 2006 and decreased to 4 billion S-DDD in 2008. During the period 2004-2008, phenobarbital accounted on average for 94 per cent of total manufacture of the barbiturates included in Schedule IV (expressed in S-DDD). Barbital was second, accounting for 4 per cent of total manufacture; it was followed by methylphenobarbital, allobarbitol and secbutabarbitol. No manufacture of butobarbitol was reported between 1999 and 2008, when Germany reported the manufacture of 117 kg of the substance. No manufacture of vinylbital was reported after 1996.

⁶See table IV for details of the consumption levels of phenobarbital.

114. The countries with the highest calculated rates of use of barbiturate-type sedative-hypnotics during the period 2004-2008 were, in descending order, Yemen, Jordan, China, Denmark, Poland, Hungary and Japan, which averaged between 0.16 and 0.67 S-DDD per 1,000 inhabitants per day. With respect to the barbiturate-type anti-epileptics listed in Schedule IV, the countries with the highest per capita rates of use during the period 2006-2008, consuming on average between 5 and 16 S-DDD per 1,000 inhabitants per day, were, Bulgaria, Ukraine, Croatia, Latvia, Cuba, Benin, Brazil, the Russian Federation and Japan (in descending order).

115. Following a gradual rise after 1999, total reported manufacture of phenobarbital remained relatively stable during the period 2004-2007, averaging 468 tons annually. In 2008, the total output of phenobarbital fell by 21 per cent, to 368 tons (3.7 billion S-DDD). China was the leading manufacturer, accounting for 58 per cent of global output during the period 2004-2007 and for 71 per cent of global output in 2008 (see figure 28). The other main manufacturers of phenobarbital in 2008 were Hungary (54 tons), the Russian Federation (35 tons), Japan (10 tons) and Brazil (3 tons). In the period 2004-2008, phenobarbital was reported to have been manufactured also by Germany, India, Kazakhstan, the United Kingdom and the United States.

116. Phenobarbital continues to be one of the most widely traded psychotropic substances, with more than 160 countries importing the substance at least once during the period 2004-2008, with an average volume of trade of 312 tons per year (3.1 billion S-DDD). The

main importers in 2008 were Switzerland (64 tons), Ukraine (33 tons), the Russian Federation (28 tons), Brazil (25 tons), Germany (20 tons), Japan (20 tons) and Denmark (15 tons); together, those countries accounted for 62 per cent of the total. Of the 39 countries that reported exports of phenobarbital in 2008, China, Hungary, Switzerland, Denmark, France and the United Kingdom, in descending order, remained the main exporters; together, they accounted for 97 per cent of the total.

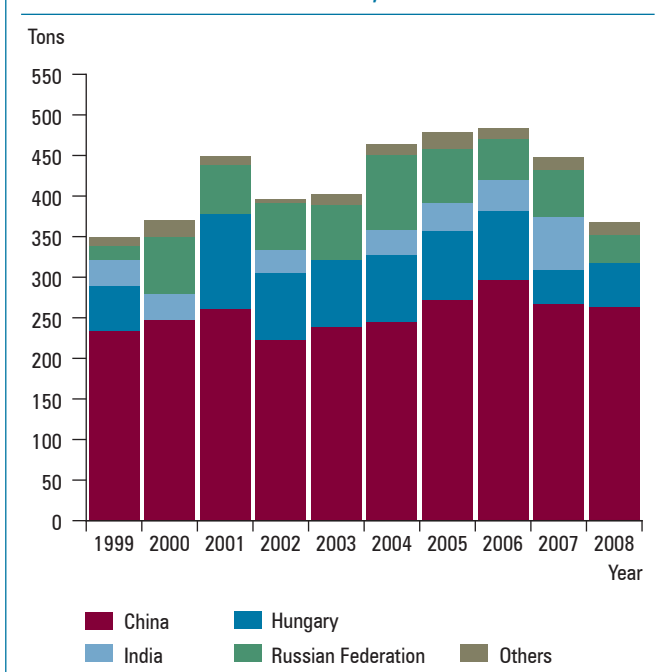
117. Total reported manufacture of barbital during the period 2004-2007 fluctuated around an annual average of 101 tons, but fell in 2008 by 21 per cent to 79 tons (158 million S-DDD). China remained the main manufacturer of the substance, accounting for 97 per cent of global manufacture during the period 2004-2008. Barbital is used in Japan and a few other countries in industry for the manufacture of non-psychotropic substances, as well as a number of preparations that are exempt from certain control measures in accordance with article 3 of the 1971 Convention. The industrial use of barbital in those countries decreased steadily, from 3.4 tons in 2004 to 250 kg in 2008, whereas total calculated consumption for direct medical purposes, which had remained fairly stable in the period 2004-2007 at an average of 104 tons, dropped to 81 tons in 2008.

118. The volume of trade in barbital declined sharply from 1998 to 2002, but stabilized during 2004-2007 at 15.6 tons annually, before falling to 10.2 tons (20.5 million S-DDD) in 2008. Of over 50 countries importing barbital at least once during the period 2004-2008, the main countries importing the substance were Germany (mainly for re-export), Japan and the United States. In 2008, as in previous years, 90 per cent of global exports of barbital were accounted for by China and Germany.

119. Manufacture of methylphenobarbital fluctuated in the decade prior to 2008 between 0.8 tons and 5.9 tons before increasing significantly to 22 tons (219 million S-DDD) in 2008. Throughout that period, the regular manufacturers of methylphenobarbital were India (21.7 tons in 2008), Switzerland (4.8 tons in 2006 but no manufacture reported in 2007 and 2008) and the United States (196 kg in 2008). Croatia had by far the highest rate of calculated use of methylphenobarbital (8.2 S-DDD per 1,000 inhabitants per day) in 2008; it was followed by Slovenia (1 S-DDD), India, Italy and the United States.

120. International trade in methylphenobarbital increased gradually between 2004 and 2008, from 1.8 to 3.8 tons. The main exporters continued to be, in descending order, Switzerland, Germany, India and Croatia. The main importers of methylphenobarbital in 2008 were Croatia, Germany (for re-export), the United States and Italy, which jointly accounted for 92 per cent of total imports.

Figure 28. Phenobarbital: total reported manufacture, selected countries, 1999-2008



121. From 1996 to 2005, only Germany reported having manufactured allobarbital, in quantities ranging between 393 kg and 4 tons. In 2006 and 2007, Belgium started manufacturing the substance, reporting an output of 2.5 tons in 2006 and 1.4 tons (14 million S-DDD) in 2007 (mainly for export); no manufacture was reported in 2008. Total stocks of the substance decreased until 2005 and then picked up, with 2 tons held on average during the period 2006-2008.

122. Total exports of allobarbital fell from 5.5 tons in 1998 to 1.6 tons in 2008. Germany, which had been the main exporter, was replaced by Belgium during the period 2006-2007. In 2008, the major importers of the substance were Jordan (400 kg), Switzerland (202 kg) and Hungary (95 kg), all of which used the substance for re-export.

123. Total manufacture of secbutabarbital decreased sharply, from 653 kg in 2002 (of which 78 per cent was manufactured in the United States) to 128 kg in 2003. Although no manufacture of the substance was reported in the period 2004-2005, the United States resumed manufacture of secbutabarbital in 2006, when it reported an output of 37 kg; that quantity increased to 48 kg annually in the years 2007-2008. In the period 2004-2008, only Germany, Lebanon, Switzerland, the United Kingdom and the United States reported trading in secbutabarbital.

124. In 2008, Germany reported having manufactured 117 kg of butobarbital. Prior to that, the last manufacture of butobarbital had been reported in 1998 by Denmark (1.3 tons). Consequently, global stocks of the substance, which decreased from 1.7 tons in 1998 to 34 kg in 2007, more than doubled in 2008, reaching the level of 71 kg. About 120 kg of the substance were traded in 2008, mainly between Germany and the United Kingdom.

Barbiturates in Schedules II, III and IV

125. Of the 12 barbiturates listed in Schedules II, III and IV of the 1971 Convention, the following five substances accounted on average for 98.3 per cent of total reported manufacture in the five-year period 2004-2008: phenobarbital (78 per cent), butalbital (7.5 per cent), pentobarbital (7.4 per cent), barbital (3.4 per cent) and amobarbital (1.9 per cent). The shares of total manufacture of those substances in 2008 are presented in figure 29. In 2008, China (56 per cent), Hungary (11 per cent), the Russian Federation (7 per cent), the United States (7 per cent), Denmark (7 per cent), Germany (5 per cent) and India (4 per cent) together accounted for 97 per cent of the total manufacture of the entire group of barbiturates (see figure 30).

Figure 29. Barbiturates listed in Schedules II, III and IV: share of total reported manufacture, by substance, 2008

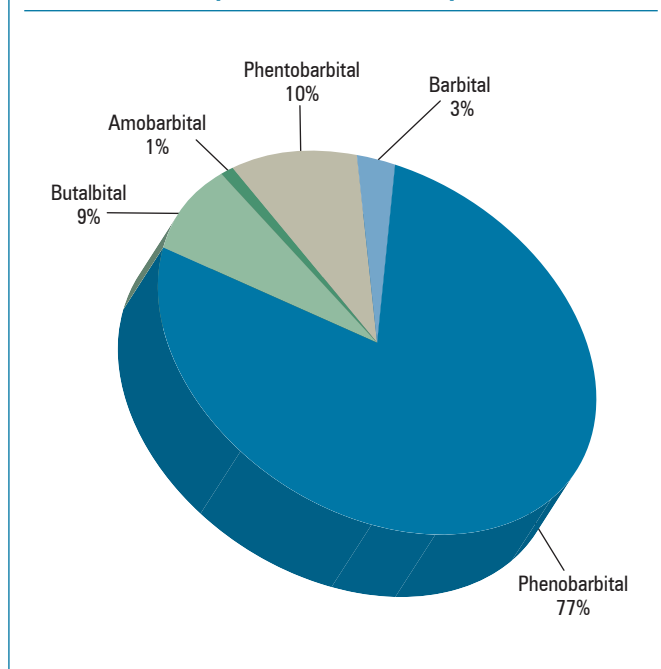
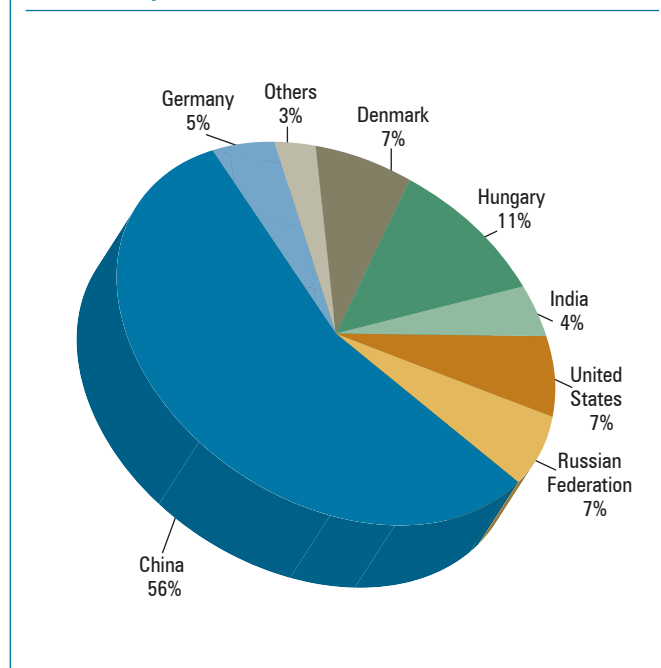


Figure 30. Barbiturates listed in Schedules II, III and IV: total reported manufacture, selected countries, 2008



Other sedative-hypnotics

126. Five substances from the group of sedative-hypnotics in Schedule IV are neither barbiturates nor benzodiazepines. While ethchlorvynol, ethinamate and methyprylon have been listed in Schedule IV since the adoption of the 1971 Convention, the other two substances, *gamma*-hydroxybutyric acid (GHB) and zolpidem, were added to the group of sedative-hypnotics in Schedule IV in 2001.

127. Data for GHB are still limited. After the substance was put under international control in 2001, and with the introduction of national control measures, the number of countries able to report on manufacture of and trade in GHB has been increasing. The substance is mainly used in the treatment of narcolepsy and, more rarely, alcoholism. GHB is manufactured mainly by Germany, Latvia and the United States; some GHB is also manufactured, albeit intermittently, by other countries, such as China, France, Ukraine and the United Kingdom. As in 2007, the United States was the main manufacturer (17.3 tons) in 2008, followed by Germany (6.7 tons), the United Kingdom (3 tons) and Ukraine (2.5 tons). As in previous years, Germany remained the main exporter (6 tons) in 2008 and the main importer was Italy (5.6 tons). In the period 2004-2008, about 30 countries reported importing more than 1 kg of GHB at least once.

128. Data on zolpidem are available for the period 2001-2008 for a number of countries. During that period, global manufacture fluctuated between 51 tons in 2002 and 24.2 tons in 2007. In 2008, global manufacture of zolpidem stood at 25.1 tons. France remained the main manufacturer during that year (almost 11 tons); it was followed by India (5.5 tons), Israel (3.5 tons), Argentina (2.6 tons) and the Czech Republic (1.1 tons). China, Germany, Slovakia, Spain and the United States also reported manufacture of zolpidem in previous years. The

main exporter of zolpidem was France, which accounted for 47 per cent of global exports (22 tons) in 2008. Zolpidem is a widely used substance, mainly for the short-term treatment of insomnia. In 2008, the United States was the main consumer, using 14.4 tons; it was followed by Japan, the Republic of Korea, Spain and Germany, in that order, each using between 1 and 2.5 tons. During the five-year period 2004-2008, more than 100 countries reported importing more than 1 kg of zolpidem at least once.

129. The manufacture of ethchlorvynol was last reported, by the United States, in 1999 (1.3 tons), and use of the substance was discontinued in 2001. The manufacture of ethinamate was last reported, by Germany, in 1988 (500 kg) and the manufacture of methyprylon was last reported, by the United States, in 1990 (2.1 tons). There were no reports of manufacture of or international trade in either ethinamate or methyprylon after 1991.

Analgesics

130. Lefetamine is the only analgesic included in Schedule IV. No manufacture of or trade in the substance was reported after 1996.