



**Part two**

**Deuxième partie**

**Segunda parte**

# 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. The quality of the analysis depends on the data provided.

Use of substances included in Schedule I of the 1971 Convention should be limited to scientific research and, in certain cases, to 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 (*delta*-9-THC) listed in Schedule II, has declined in recent years, and so has the use of dronabinol. For 2010, use of *delta*-9-THC has been reported mainly by Germany, Austria and Switzerland (in descending order).

Methylphenidate is the main central nervous system stimulant listed in Schedule II. Its manufacture and medical use for the treatment of attention-deficit disorder (ADD) continue to increase worldwide. The United States of America remains the main manufacturer of the substance, although its share in global manufacture continued to decline, reaching 82 per cent in 2010. The calculated per capita consumption of methylphenidate in that year was highest in Canada, Iceland, the Netherlands and 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. France, traditionally the key manufacturer of amphetamines, continued to reduce its output of this group of substances in 2010, in response to decreasing demand. In absolute terms, the United States remained the largest consumer of amphetamines in 2010, followed by Canada and Australia.

Buprenorphine is an opioid analgesic listed in Schedule III of the 1971 Convention that is used in about 80 countries worldwide to treat pain and in detoxification and substitution treatment programmes for heroin addicts. International trade in and global consumption of buprenorphine increased markedly and steadily from the 1990s until 2009. For 2010, data from some major manufacturing and consumer countries are missing or incomplete.

A total of 35 benzodiazepines are currently under international control. Of them, 34 are classified as anxiolytics and sedative-hypnotics and are used in medical practice for pre-medication and the induction of general anaesthesia. Lack of data for 2010 from some major manufacturing countries, in particular India, affected the comprehensiveness of the information and the resulting analysis of the data on benzodiazepines. In 2010, the benzodiazepine-type anxiolytics diazepam and alprazolam remained the most manufactured psychotropic substances, in terms of defined daily doses for statistical purposes (S-DDD). Reported manufacture of benzodiazepine-type sedative-hypnotics in 2010 amounted to 5.5 billion S-DDD. In that year, Italy and China were the leading manufacturers of this group, accounting for 60 and 14 per cent of the total. Manufacture of and international trade in clonazepam, the only benzodiazepine classified as an anti-epileptic, increased during the last decade and, in 2010, the substance became one of the most widely used psychotropic substances.

Of the 12 barbiturates listed in the 1971 Convention, phenobarbital, an anti-epileptic, accounted for 78 per cent of the total manufacture, as in previous years, although total manufacture of that substance declined slightly compared with 2009 as a result of lower output reported by Hungary and the Russian Federation. A small increase in manufacture was reported for amobarbital, barbital, butobarbital and pentobarbital, the other main barbiturates, which accounted for 1, 4, 9 and 7 per cent of the total, respectively. The leading manufacturer of all combined barbiturates continued to be China (accounting for 70 per cent of global output), followed by Hungary (9 per cent), Denmark (8 per cent), the United States (5 per cent) and Germany (4 per cent).

The 14 stimulants listed in Schedule IV of the 1971 Convention are mainly used as anorectics or for the treatment of ADD. Total reported manufacture of this group of substances amounted to 1.8 billion S-DDD in 2010. Phentermine continues to be the most used substance in this group. In 2010, the substance accounted for 74 per cent of global manufacture; it was followed by mazindol (8 per cent) and phendimetrazine and amfepramone (6 per cent each). Calculated consumption of the stimulants listed in Schedule IV decreased in 2010 but continued to be highest in the Americas. In Africa, Asia and Oceania, consumption of stimulants in Schedule IV increased markedly in certain countries.

## Substances listed in Schedule I

1. Twenty-eight substances are listed in Schedule I. The use of those substances should be prohibited, pursuant to the provisions of article 7 of the 1971 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. The 1971 Convention does not foresee use of the psychotropic substances included in Schedule I by industry for the manufacture of non-psychotropic substances or products. However, in the United States of America, annual manufacture of 2,5-dimethoxyamphetamine (DMA) exceeded several tons in the years prior to 2002, exclusively for use in the manufacture of a non-controlled film dye. As of 2002, manufacture started to decline, owing to a decrease in the manufacture of photographic film. No manufacture has been reported after 2007 and, as a result, global stocks of DMA became depleted by the end of 2008. At the end of 2010 they stood at 141 g.

3. Israel, Switzerland and the United States reported the manufacture of 3,4-methylenedioxymetamphetamine

(MDMA) in the period 2006-2010. MDMA is used in those countries in research projects. Global stocks of MDMA at the end of 2010 amounted to 454 g; almost all of those stocks were held in Switzerland and the United States.

4. *para*-Methoxy-*alpha*-methylphenethylamine (PMA) has been used in Denmark for the manufacture of tamsulosin, an active pharmaceutical ingredient that is not under international control. In the period 2005-2007, Denmark manufactured an average of 40 kg of PMA annually for such use. In contrast to 2008 and 2009, when there was limited or no manufacture of PMA, in 2010 Denmark manufactured 27.5 kg of PMA.

5. The United States is the only country that has reported use of a substance in Schedule I for the manufacture of psychotropic substances in other schedules. In that country, isomers of tetrahydrocannabinol (THC) listed in Schedule I are used in the manufacture of *delta*-9-tetrahydrocannabinol (*delta*-9-THC), a psychotropic substance listed in Schedule II. *delta*-8-Tetrahydrocannabinol is the main substance among the isomers in Schedule I manufactured in the United States. After reaching a peak of 326 kg in 2005, manufacture of isomers of THC in Schedule I declined, reaching 53 kg in 2010. By the end of 2010, global stocks stood at 114 kg, all held in the United States.

## 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

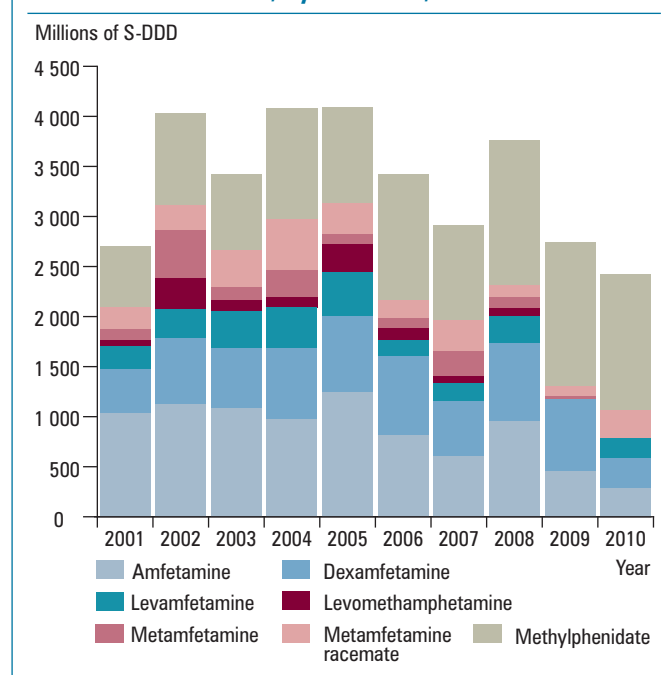
7. Total manufacture of central nervous system stimulants in Schedule II fluctuated in the period 2001-2010, as can be seen in figure 1. In 2010, total reported manufacture of this group of substances continued to decrease and amounted to 2.4 billion S-DDD. Of the group, methylphenidate grew fastest, its share of total output of stimulants in Schedule II rising from 22.5 per cent in 2001 to 56 per cent in 2010. By contrast, manufacture of amphetamines decreased over the decade. In 2010, dexamfetamine and amfetamine each accounted for 12 per cent of total output. Together with methylphenidate, these substances accounted for 80 per cent of the total combined output in 2010.

### Amphetamines

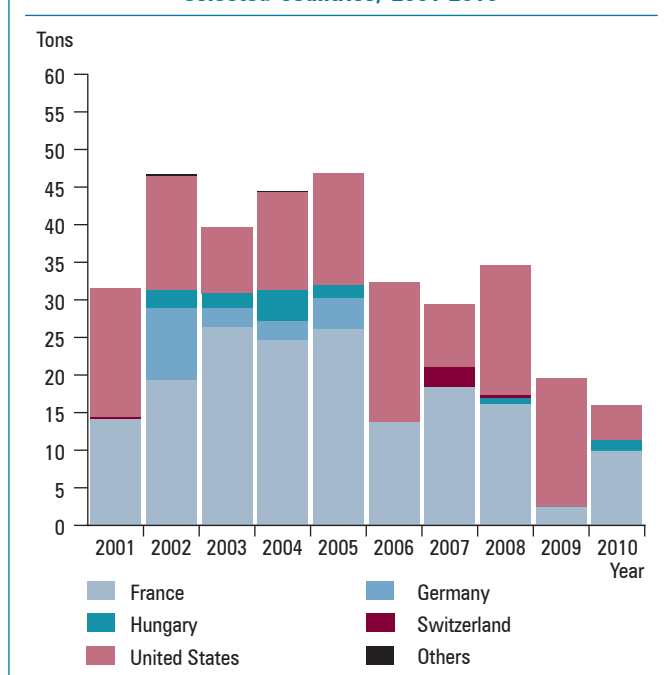
8. Both optical isomers of amphetamine (levamfetamine and dexamfetamine) and their racemic mixture (amphetamine), as well as both optical isomers of metamfetamine (levomethamphetamine and metamfetamine) and their racemic mixture (metamfetamine racemate), are listed in Schedule II. Statistical reports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

9. In 2010, the quantity of amphetamines listed in Schedule II that were manufactured worldwide continued to decline, to 16 tons (1.1 billion S-DDD), as a result of the decreased manufacture by the two main manufacturers, France and the United States, which reported output of 10 and 5 tons respectively in 2010, compared to a yearly average of 12 and 14 tons respectively during the period 2007-2009 (see figure 2). In 2010, dexamfetamine, amphetamine and metamfetamine racemate had almost the same share

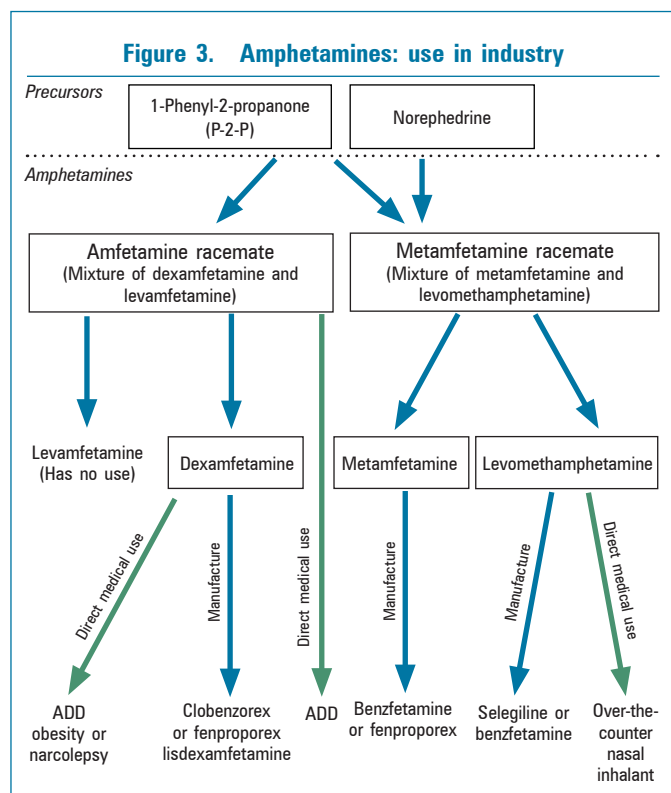
**Figure 1. Stimulants in Schedule II: total reported manufacture, by substance, 2001-2010**



**Figure 2. Amphetamines: total reported manufacture, selected countries, 2001-2010**



of total output of amphetamines (28, 27 and 26 per cent respectively), followed by levamfetamine (18 per cent). In 2010, France accounted for 62 per cent of the total manufacture of amphetamines, the United States for 29 per cent and Hungary for the remainder. Throughout the 10-year period 2001-2010, France was virtually the sole manufacturer of levamfetamine, which was used for reversion into amphetamines.



### 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 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, clonazepam, fenproporex and levopropylhexedrine) and antiparkinsonian drugs (selegiline).

### Direct 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 has traditionally been a major manufacturer of amphetamines, there is very limited medical use of amphetamines in that country, as almost all the amphetamines manufactured there are destined for export.

12. The countries with the highest levels of reported (i.e. furnished by Governments) and calculated consumption of amphetamines (calculated on the basis of statistics provided for 2010)<sup>1</sup> are listed in tables 1 and 2 in order of their calculated rate of use (expressed in S-DDD per 1,000 inhabitants per day)<sup>2</sup> in 2010.

**Table 1. Amphetamines: reported consumption rate, selected countries, 2010**

| Country       | Consumption rate<br>(S-DDD per 1,000 inhabitants per day) |
|---------------|---|
| United States | 14.93   |
| Chile         | 2.78  |
| Sweden        | 0.28  |
| Finland       | 0.08  |
| Denmark       | 0.04  |
| Israel        | 0.03  |
| Germany       | 0.04  |
| Austria       | 0.02  |

**Table 2. Amphetamines: calculated consumption rate, selected countries, 2010**

| Country     | Consumption rate<br>(S-DDD per 1,000 inhabitants per day) |
|-------------|---|
| Canada      | 1.73  |
| Australia   | 1.48  |
| Netherlands | 0.85  |
| Norway      | 0.39  |
| Belgium     | 0.11  |
| Croatia     | 0.05  |
| Kuwait      | 0.01  |

<sup>1</sup> The method used for calculating levels of consumption of psychotropic substances is explained in the explanatory note to table IV of the present publication.

<sup>2</sup> The list of defined daily doses for statistical purposes (S-DDD) used in these calculations is presented in table III of the present publication.



## Comments on amphetamines, by substance

13. The manufacture of amphetamine gradually increased until 1998, when it reached 30 tons. After 1998, it fell gradually to less than 4.3 tons in 2010, mostly in France and the United States. The United States subsequently replaced France as the leading manufacturer, accounting on average for 66 per cent of global output during the period 2008-2010. For medical purposes, amphetamine is used mainly in combination with dexamfetamine in the United States. In 2010, about 81 per cent of global stocks (8.7 tons) of amphetamine were held in the United States; the rest was held in France. Total imports of amphetamine in 2010 amounted to 148 kg, the main importers being, in descending order, Canada, Chile, Sweden and Germany.

14. While the manufacture of dexamfetamine was stable during the 1980s, at a level of approximately 350 kg annually, it rose, with fluctuations, after 1991, reaching 11 tons in 2009. In 2010, it decreased sharply to less than half (4.4 tons), owing to the drastic fall of output in the United States, which was the only manufacturer of the substance apart from France. Although, in 2010, the United States remained the main user of dexamfetamine for medical purposes, such use was also reported in a number of other countries, including, in descending order, Canada, Australia, the Netherlands, Sweden, Norway, Belgium, Finland, Germany, Switzerland and Denmark. Global stocks of dexamfetamine increased from 1 ton in 1995 to 11 tons in 2010. More than 20 countries reported imports of the substance, amounting in total to 508 kg in 2010. Canada and Australia remained the main importers, accounting for 53 and 32 per cent of the total, respectively.

15. Since 1999, when the total reported manufacture of metamfetamine stood at 9.5 tons, global output has fluctuated. Since 2008, total manufacture decreased sharply, reaching less than 500 g in 2010 after France and Switzerland had ceased manufacturing the substance. The main regular user of metamfetamine (mainly for industrial purposes) is the United States. International trade in metamfetamine has been limited in volume, fluctuating on average at about 2 kg. Nine countries reported imports of metamfetamine in 2010, ranging from 1 to 81 g.

16. In the period 1999-2005, the total reported manufacture of levomethamphetamine had fluctuated between 433 kg and 4.6 tons. From 2005, manufacture dropped sharply from 4.3 tons to no output in 2009 or 2010. In the past, Germany, France, the United States and the Czech Republic (in descending order) were the main manufacturers of the substance. The main user of levomethamphetamine for industrial purposes was Germany; it was followed by the United States, France and the Czech Republic. In the United States, levomethamphetamine was mainly used for the manufacture of over-the-counter nasal inhalers,

which are exempted in that country from certain control measures, in accordance with article 3 of the 1971 Convention. In 2010, about 600 kg of the substance were used for that purpose. In the five-year period 2006-2010, levomethamphetamine was also used in Italy, which had been the main importer of the substance until 2008, when it stopped importing the substance.

17. Metamfetamine racemate is mainly manufactured for export to the United States, where it is used for conversion into levomethamphetamine and metamfetamine. France and Hungary were the main manufacturers of metamfetamine racemate in the last decade. In 2010, global manufacture of metamfetamine amounted to 4.3 tons, of which France and Hungary accounted for 68 and 32 per cent respectively. Global stocks in 2010 stood at 3 tons. International trade averaged 1.3 tons in the five-year period 2006-2010; most of the imports were accounted for by the United States.

## Fenetylline

18. During the decade leading up to 2010, the Netherlands held most of the stocks of fenetylline; those stocks were gradually exported to Belgium and from there to other countries in Europe. Belgium, France, Germany and Luxembourg are the only countries to have reported use of fenetylline for medical purposes after 2003. In 2010, Canada and Switzerland were the only countries holding small stocks of fenetylline (1 and 7 g respectively).

## Methylphenidate

19. The use of methylphenidate<sup>3</sup> for medical purposes has increased 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 the result of developments in the United States, where the substance is heavily advertised, including directly to potential consumers. During the period 2001-2010, the use of methylphenidate for the treatment of ADD rose sharply in many other countries, such as Canada, the Netherlands and Germany. The calculated global consumption of the substance followed an upward trend and reached 43 tons (1.4 billion S-DDD) in 2010.

20. Global manufacture of methylphenidate started to increase rapidly in the first half of the 1990s, from 2.8 tons in 1990 to 19.1 tons in 1999. As a result of increasing use of amphetamines for the treatment of ADD, methylphenidate manufacture dropped to 16 tons in 2000. After that,

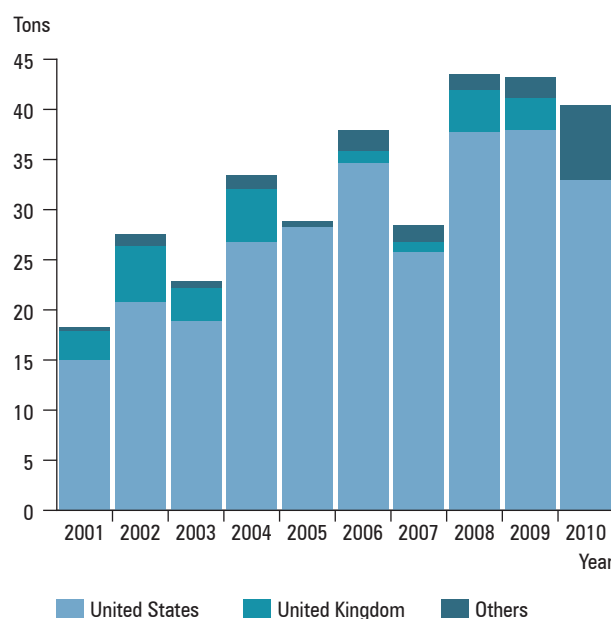
<sup>3</sup> See table IV for details of the consumption levels of methylphenidate.

total reported manufacture of the substance fluctuated, but remained stable at about 42 tons in the period 2008-2010 (see figure 4). During the period 1991-2010, the United States was the leading manufacturer of methylphenidate, increasing its output from 1.8 tons in 1990 to 38 tons in 2009. In 2010, total manufacture in that country decreased slightly, to 33 tons. The quantity of methylphenidate manufactured in the United Kingdom increased fourfold in 2008 compared with 2006 and 2007 and remained at about that level in 2009 (3.2 tons); however, in 2010, that country did not report manufacture of the substance. The other countries reporting manufacture of considerable amounts of methylphenidate in 2010 were Canada (3.8 tons), Switzerland (2.4 tons), and Spain and Japan (together totalling 1.2 tons); their combined output accounted for 18 per cent of global manufacture. Most of the methylphenidate manufactured in the United States continued to be used domestically, although exports from that country had increased in recent years. Global stocks of methylphenidate continued to increase, reaching 45 tons in 2010 as a result of an increase in stocks held in the United States. In 2010, that country held 35 tons of the substance in stocks, or 80 per cent of global stocks.

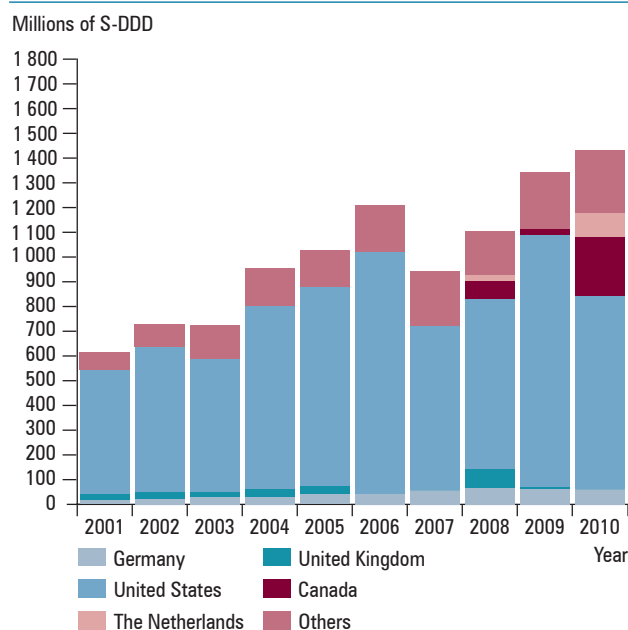
21. Despite increases in manufacture in several countries, the medical requirements for methylphenidate outside the United States continued to be mainly met by imports. International trade in methylphenidate increased during the period 1999-2010, from 6 to 21 tons. Germany, Switzerland, Canada, Spain and the Netherlands were the main importers of methylphenidate in 2010; together they accounted for 77 per cent of global imports. Although Switzerland was the main exporter of methylphenidate until 2006, in that year the United States became the leading exporter and in 2010 accounted for 42 per cent of total exports. Other major exporting countries in 2010 were, in descending order, Switzerland, Spain, Germany and India. The number of countries and territories importing methylphenidate continued to rise gradually during the period 2001-2010. In 2010, the Governments of 38 countries and 1 territory reported imports of methylphenidate in amounts exceeding 10 kg.

22. The calculated consumption of methylphenidate, expressed in S-DDD, has traditionally been highest in the United States (see figure 5). In the three-year period 2008-2010, that country accounted, on average, for 66 per cent of the calculated worldwide use of methylphenidate. The level of methylphenidate use in the rest of the world averaged about 453 million S-DDD per year in the same period. The main users of methylphenidate during the period 2006-2010 were Canada, Iceland, the Netherlands, Israel, Switzerland, Denmark, Sweden and Norway, with sharply increasing use reported by Canada, Iceland and Switzerland.

**Figure 4. Methylphenidate: total reported manufacture, selected countries, 2001-2010**



**Figure 5. Methylphenidate: calculated medical consumption,<sup>a</sup> 2001-2010**



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

23. The countries with the highest level of reported (i.e. furnished by Governments) and calculated consumption of methylphenidate (calculated on the basis of statistics provided for 2010) are listed in tables 3 and 4 in order of their level of consumption (expressed in S-DDD per 1,000 inhabitants per day) in 2010.



**Table 3. Methylphenidate: reported consumption rate, 2010**

| Country       | Consumption rate<br>(S-DDD per 1,000 inhabitants per day) |
|---------------|---|
| United States | 15.05   |
| Iceland       | 14.78   |
| Israel        | 7.37  |
| Denmark       | 5.10  |
| Sweden        | 4.81  |
| Germany       | 2.00  |
| Finland       | 1.23  |
| Chile         | 1.08  |
| Austria       | 0.44  |
| Singapore     | 0.20  |

**Table 4. Methylphenidate: calculated consumption rate, 2010**

| Country     | Consumption rate<br>(S-DDD per 1,000 inhabitants per day) |
|-------------|---|
| Canada      | 20.21   |
| Netherlands | 16.38   |
| Switzerland | 5.93  |
| Norway      | 5.35  |
| New Zealand | 3.19  |
| Belgium     | 2.08  |
| Andorra     | 2.05  |
| Spain       | 2.01  |
| Australia   | 1.97  |

## Anti-emetics

### *delta*-9-Tetrahydrocannabinol and its stereochemical variants

24. During the period 2001-2010, manufacture of *delta*-9-THC fluctuated between 106 and 318 kg. In 2010, global manufacture was 106 kg (3.5 million S-DDD), a slight decrease compared with the figure for 2009 (114 kg). The United States remained the main manufacturer of *delta*-9-THC in 2010 (101 kg), accounting for 95 per cent of the global total, while Germany (5 kg) accounted for the rest. The majority of the *delta*-9-THC manufactured in the United States was for domestic consumption. In 2010, stocks of *delta*-9-THC held in the United States amounted to 364 kg, accounting for 81 per cent of global stocks; other

countries holding stocks of the substance were Germany (12 per cent of global stocks) and Switzerland (6 per cent).

25. International trade in *delta*-9-THC remained limited in 2010. A total of 7 kg of the substance were exported by the United States, Germany, Switzerland and France (in that order) to 15 countries, with Austria and Canada being the main importers and users.

## Hallucinogens

### Phencyclidine

26. Phencyclidine is primarily used as an anaesthetic agent in veterinary medicine. After 2006, manufacture and international trade in phencyclidine amounted to less than half a kilogram per year.

## Sedative-hypnotics

### Mecloqualone

27. Mecloqualone stopped being manufactured after 1980. In 2010, global stocks of the substance amounted to a few grams.

### Methaqualone

28. The latest significant manufacture of methaqualone was reported in 1997 by Switzerland (340 kg) and the Czech Republic (43 kg). After that, only small quantities (amounts of just a few grams) were manufactured intermittently in the United States, mainly for domestic consumption. In 2010, a total of 3 g were manufactured in the United States. Global stocks of methaqualone have fluctuated between 355 g and 575 g since 2006. In 2010, global stocks stood at about 400 g, with 86 per cent held by the United States. Germany and Malaysia imported a total of 2 g in 2010.

### Secobarbital

29. Since 2000, Germany has been the main manufacturer of secobarbital. Its annual output accounted for between 54 and 99 per cent of the global total during the period 2001-2010. In 2010, Germany (721 kg) and Japan (4.4 kg) reported manufacture of the substance. In 2010, global stocks of secobarbital stood at 845 kg, held mainly by Germany (65 per cent) and the United Kingdom (26 per cent).

30. During the period 2008-2010, total trade volume of secobarbital gradually declined from 776 kg (7.8 million S-DDD) in 2008 to 618 kg (6.2 million S-DDD) in 2010. Germany continued to be the leading exporter of the substance, and Sweden was the main importer in 2010. The United Kingdom remained the main user of secobarbital in 2010; it was followed by the United States, Sweden and Germany.

## Antitussives

### Zipeprol

31. The Republic of Korea, which had stopped manufacturing zipeprol in 1999, resumed its manufacture in 2008

and 2009 for domestic consumption. In 2010, no manufacture was reported. The only country reporting imports of zipeprol in 2010 was the Plurinational State of Bolivia (23 kg, for domestic use only).

## Antidepressants

### Amineptine

32. 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 its manufacture has ever been reported. In 2010, Switzerland reported having imported very small quantities of amineptine (9 g) from China.

## Substances listed in Schedule III

33. 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

34. Cathine is used as a stimulant and for industrial purposes. Manufacture of cathine fluctuated considerably during the period 2001-2010, reflecting the manufacturing levels of Germany, the only manufacturer of the substance until 2003. Global manufacture averaged 4 tons per year in the period 2005-2007. After a peak in 2007 (5.9 tons), global output fell in 2009 to 55 kg, all of which was manufactured in China. For 2010, China reported output of 300 kg of cathine, mainly for export. Global stocks of cathine stood at 2.4 tons in 2010; those stocks were held mainly in Germany and Mexico.

35. Germany and Italy were the main exporters of cathine in the period 2006-2010; they were followed by India and China. Global exports of the substance averaged 5.5 tons during the period 2005-2008; between 2009 and 2010, however, total exports averaged only 1.3 tons, as lower imports were reported by Italy, Mexico and South Africa, which had been the main importers of the substance.

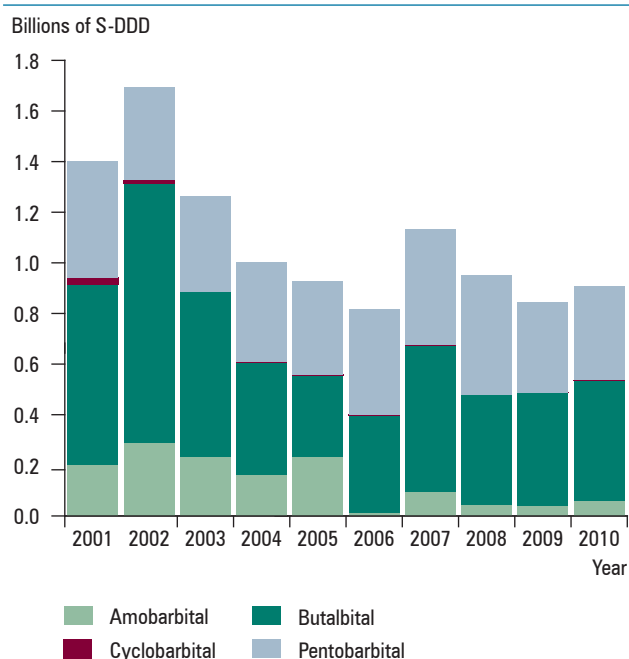
## Sedative-hypnotics

36. Classified as sedative-hypnotics, barbiturates used to be prescribed for the treatment of anxiety and stress and, in some cases, as anaesthetics for short surgery interventions (ultra-short-acting substances). Nowadays, they are 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.

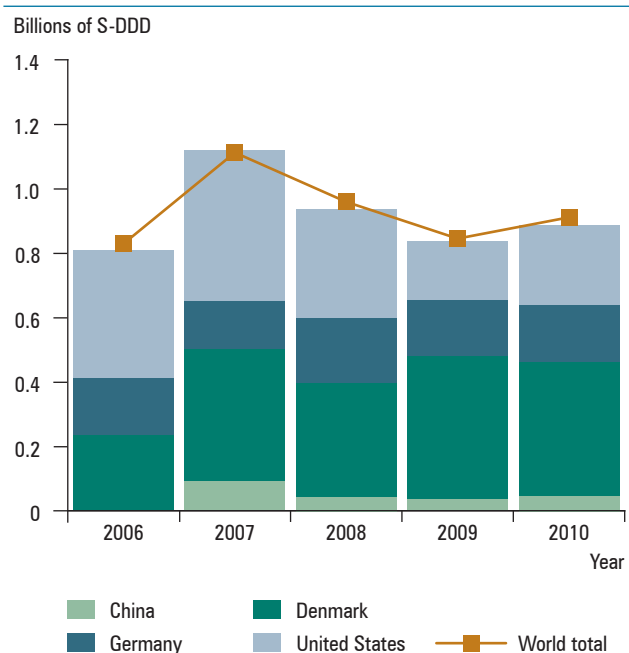
### Amobarbital, butalbital, cyclobarbital and pentobarbital

37. In 2010, total reported manufacture of amobarbital, butalbital, cyclobarbital and pentobarbital amounted to 905 million S-DDD (see figure 6), an increase of 7 per cent compared with 2009. Manufacture in China, Denmark,

**Figure 6. Barbiturates listed in Schedule III: total reported manufacture, by substance, 2001-2010**



**Figure 7. Barbiturates listed in Schedule III: total reported manufacture, selected countries, 2006-2010**



Germany, Poland and the United States accounted for over 97 per cent of global manufacture of these four substances combined. Figure 7 shows the share of the main manufacturing countries, in total output, during the period 2006-2010.

38. China and Japan had been the main countries manufacturing and using amobarbital. Global output of amobarbital had fluctuated between 20 and 30 tons during the period 1999-2005 and then declined significantly, to 4.2 tons, in 2009. In 2010, global manufacture of the sub-

stance increased to 5.8 tons, which were manufactured solely by China and Japan. China accounted for 86 per cent (5 tons) of global manufacture, the majority of which was for domestic use. The total calculated consumption of the substance reached 7 tons (70 million S-DDD) in 2010. Global imports of amobarbital declined from a peak of 10 tons in 2002 to 159 kg in 2010. Thailand and the Netherlands continued to be the main importers of the substance in 2010. China, Germany and the Netherlands were the three main exporting countries in 2010.

39. Having declined during the period 2002-2007, global manufacture of butalbital gradually increased between 2008 and 2010, from 32 tons to 36 tons, mainly because of increased manufacture in Denmark, the leading manufacturer of the substance. Another major manufacturer of the substance during the period 2001-2010 was the United States. Other manufacturing countries in 2010 included Canada and Germany. About two thirds of the butalbital manufactured in Denmark and Germany in 2010 were for export. The butalbital manufactured in the United States was used mainly for domestic consumption; for example, some of the substance was used for the manufacture of preparations exempted from certain control measures, in accordance with article 3 of the 1971 Convention. Italy and Canada (in descending order) were the main importers of butalbital in 2010.

40. Cyclobarbital continued to be mainly manufactured and used in Europe, although the quantities manufactured decreased considerably after 1998. The sole manufacturer of cyclobarbital after 2004 was Poland (its manufacture of the substance was used mainly for export), after Germany and Latvia stopped manufacturing the substance in 2003. In 2010, Poland manufactured 150 kg of cyclobarbital (0.75 million S-DDD) and was the only country exporting the substance to other countries, including Georgia, Latvia and the Russian Federation, the three main users of the substance. The Russian Federation continued to be the main importer of cyclobarbital in 2010, accounting for 79 per cent of global imports of the substance. Global stocks of cyclobarbital stood at 179 kg at the end of 2010; over 90 per cent of those stocks were held in Poland.

41. Total reported manufacture of pentobarbital fluctuated between 36 and 47 tons during the decade up to 2010. In 2010, total manufacture amounted to 36.8 tons (368 million S-DDD), a slight increase compared with 2009, mainly as a result of increased manufacture in the United States. Three countries reported manufacture of the substance in 2010, namely the United States, Germany and Japan (in descending order). Manufacture in the United States and Germany, the two leading manufacturers of the substance in the previous decade, accounted for about 58 and 41 per cent of the global output in 2010 respectively. Global stocks stood at 24.8 tons in 2010; about 66 per cent of those stocks

were held in Germany and the United States. During the period 2008-2010, Australia, Canada, Ireland, New Zealand, Switzerland and the United States were the main users of the substance.

42. During the period 2008-2010, international trade in pentobarbital continued to decrease. Total reported exports of the substance declined from 27.3 tons in 2008 to 22.3 tons in 2010. As in previous years, Germany, Canada, France and Denmark (in descending order) together accounted for about 91 per cent of global exports of the substance in 2010. France (4,141 kg), Canada (3,922 kg), the United States (2,383 kg), Australia (2,366 kg) and the Netherlands (1,905 kg) remained the main countries importing pentobarbital, together accounting for 68 per cent of global imports of the substance. Canada, the main country trading in the substance, reported that its imports of the substance declined significantly (by 46 per cent) from 2009 to 2010.

### Glutethimide

43. During the early 1980s, several dozen tons of glutethimide were manufactured annually, mainly for conversion into aminoglutethimide, a non-psychotropic substance used as an antineoplastic agent. Global manufacture of glutethimide declined steadily during the 1990s and stopped in 1998. After that year, sporadic manufacture of the substance took place in Hungary (700 kg in 2001) and China (240 kg in 2005). No manufacture was reported in 2010. Global stocks of glutethimide at the end of 2010 stood at 1.2 kg; most of those stocks were held in the United States. International trade in glutethimide decreased from a peak of about 15 tons per year during the period 1997-1998 to several hundred kilograms during the period 2002-2005. No international trade in the substance was reported for the period 2006-2010.

### Flunitrazepam

44. Flunitrazepam continues to be one of the most frequently abused benzodiazepines. The substance is diverted mainly from domestic distribution channels. Preparations containing flunitrazepam have often been diverted from the licit market in one country and smuggled into countries in which there is an illicit demand for such preparations. As it was frequently diverted and abused, flunitrazepam was transferred from Schedule IV to Schedule III in 1995. Several countries, including major manufacturers and importers of the substance, adopted strict control policies for flunitrazepam, in close cooperation with the pharmaceutical industry. Nowadays, most of the preparations purportedly containing flunitrazepam that are sold on the illicit market are counterfeit products that do not contain that substance.

45. In medical practice, flunitrazepam, like diazepam, is used in some countries for pre-medication and to induce general anaesthesia. Prior to 1996, flunitrazepam was manufactured in several countries. After 1996, only Italy and Switzerland, which started to manufacture flunitrazepam in 1997, reported its manufacture. The manufacture of flunitrazepam in Switzerland, the main manufacturer of the substance, fluctuated greatly; in some years, such as 2010, no manufacture of the substance took place in that country. Despite those fluctuations, global manufacture of flunitrazepam increased, reaching 1.9 tons in 2009, the largest amount ever reported. In 2010, global manufacture of flunitrazepam dropped to 231 kg, all of which was manufactured in Italy (see figures 22 and 23 and paragraph 91 below).

46. International trade in flunitrazepam reached a record high of 1.2 tons in 2010. Switzerland remained the leading exporter of flunitrazepam, averaging over 65 per cent of global exports of the substance during the period 2006-2010. In 2010, that country exported 791 kg of flunitrazepam. Italy was the second biggest exporter of flunitrazepam, exporting 328 kg of the substance in 2010. Those two countries together accounted for over 90 per cent of global exports of flunitrazepam in the period 2008-2010. Japan remained the leading importer of flunitrazepam in 2010, importing 870 kg and accounting for 75 per cent of global imports of the substance. About 40 countries reported imports of flunitrazepam in 2010. The combined flunitrazepam imports of Brazil, Germany, Switzerland, Nigeria, the Republic of Korea and Greece, each ranging between 20 and 45 kg, accounted for 17 per cent of global imports of the substance in 2010.

## Analgesics

### Buprenorphine

47. Buprenorphine belongs to the family of opioids used mainly as analgesics. In the late 1990s, total reported manufacture of buprenorphine increased significantly, as the substance started to be used in higher doses for the treatment of pain and opioid addiction. In 2010, seven countries reported manufacture of buprenorphine, including Belgium (1,098 kg), the Czech Republic (397 kg), Germany (127 kg), Switzerland (49 kg), the United States (147 kg), China (4 kg) and Denmark (0.4 kg). The United Kingdom and Australia, once the two main manufacturers of buprenorphine, together accounting for over 86 per cent of total reported manufacture of the substance in 2009, did not report data on its manufacture for 2010. As a result, total reported manufacture of buprenorphine amounted to 1.8 tons (228 million S-DDD) in 2010 (see figure 8). However, of the countries that reported manufacture of buprenorphine in 2010, Belgium reported that its



manufacture of the substance significantly increased, by 77 per cent, over the figure reported for 2009 and the Czech Republic reported an increase of nearly 70 per cent. Global stocks of the substance continued to increase in 2010, reaching 3.8 tons, the highest level reported in 10 years. The majority of the stocks were held in the United Kingdom, the United States, Germany, France, the Czech Republic and Switzerland (in descending order).

48. Total exports of buprenorphine started to increase in 1996 and amounted to 3.4 tons in 2009, the highest amount ever reported. In 2010, the total volume of trade in the substance decreased to about 1.7 tons, mainly as a result of the significant decline in exports reported by the United Kingdom. The main exporting countries in 2010 included Belgium (575 kg), Germany (418 kg), the Czech Republic (371 kg), Australia (112 kg) and Switzerland (76 kg), which together accounted for 90 per cent of the global total. The United Kingdom had been the main exporter of buprenorphine; however, in 2010, exports of the substance from the United Kingdom decreased to 42 kg, only 1.8 per cent of in the level it had reported for 2009. During 2010, more than 60 countries reported imports of buprenorphine. The United States, a major importer of the substance, reported considerably fewer imports in 2010 (405 kg) than in 2009 (1,878 kg). Other major importers of buprenorphine in 2010 included Germany (698 kg), France (391 kg), Spain (103 kg), Australia (93 kg), the United Kingdom (86 kg), Italy (85 kg) and Belgium (84 kg).

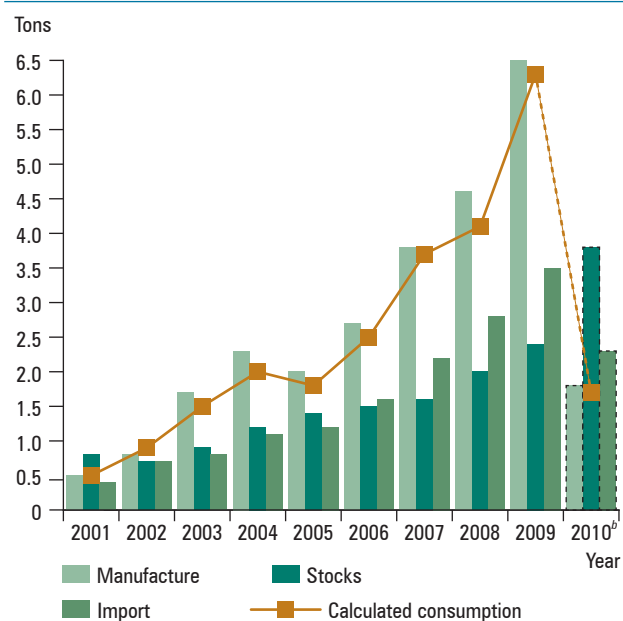
49. The major consumers of buprenorphine continued to be Australia, the United States and several European countries such as Belgium, France, Germany and the United Kingdom. In 2010, the global calculated consumption of buprenorphine was 218 million S-DDD.<sup>4</sup> Buprenorphine is used in several countries in detoxification and substitution treatment programmes for opioid dependence, including Austria, Australia, Denmark, France, Germany, Hungary, Malaysia, Ireland, Switzerland and the United States. Small seizures of preparations of buprenorphine have been reported by a few countries; some of those seized consignments had been smuggled by mail out of other countries. Abuse of the substance, which is mainly diverted from licit distribution channels, including from opioid substitution treatment, remains a risk in some countries.

## Pentazocine

50. Pentazocine is an opioid analgesic with properties and uses similar to those of morphine. Total reported

<sup>4</sup>In recent years, calculated consumption of buprenorphine has been less reliable than the calculated consumption of other substances, owing to the limited number of manufacturers of buprenorphine, lack of data from some of those manufacturers in 2010 and inconsistent stock data reported by some major consumers.

**Figure 8. Buprenorphine: total reported manufacture, stocks and calculated global consumption,<sup>a</sup> 2001-2010**



<sup>a</sup>Statistical 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).

<sup>b</sup>The data for 2010 are incomplete.

manufacture of the substance was about 2.1 tons (10.5 million S-DDD) in 2010. India and Italy have been the main manufacturers of pentazocine; however, data for 2010 are missing for India, possibly explaining the decrease in global manufacture of the substance (for 2009, India reported the manufacture of 5.5 tons of pentazocine). Italy accounted for 64 per cent of global manufacture of pentazocine in 2010; it was followed by the United States (33 per cent) and China (1.2 per cent). The pentazocine manufactured in Italy was mainly destined for export. The United States reported manufacture of the substance for the first time since 2003. With the increased stocks held by Italy and the States, global stocks of the substance increased by 36 per cent, to 4.5 tons, in 2010.

51. Global trade in pentazocine declined between 2009 and 2010. Total imports of pentazocine amounted to 1.9 tons in 2010, decreasing by 63 per cent compared with the figure for 2009. The United States, the main importing country of pentazocine, reported having imported 574 kg of the substance in 2010, or only 23 per cent of its total imports of the substance in 2009. Canada, Japan, Nigeria, Portugal and Switzerland together accounted for over 57 per cent of global imports of pentazocine in 2010. Data for 2010 from Pakistan, another major importer of the substance, has not yet been received. The United Kingdom became the largest exporter of pentazocine in 2010, when



it reported having exported 1.2 tons of the substance, the highest figure reported by that country since 1999. Italy remained a major exporter of the substance in 2010. The

main countries consuming pentazocine over the past three years included Canada, India, Japan, Nigeria, Pakistan, Portugal and the United States.

## Substances listed in Schedule IV

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

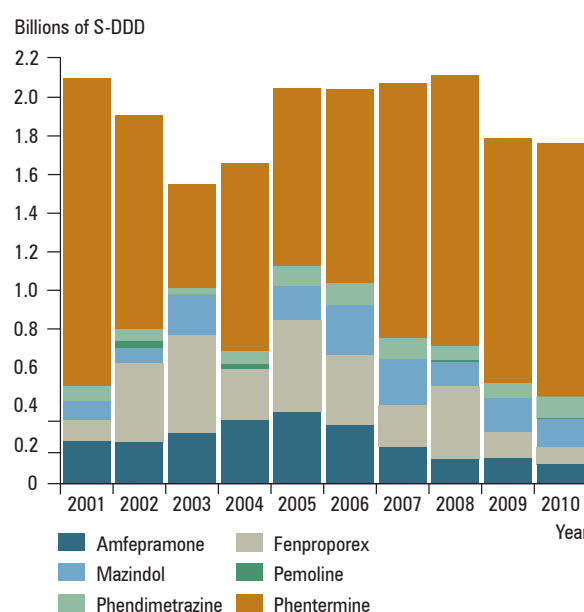
### Central nervous system stimulants

53. Fourteen stimulants are listed in Schedule IV: amfepramone, aminorex, benzfetamine, etilamfetamine, fencamfamin, fenproporex, mazindol, mefenorex, meso-carb, pemoline, phendimetrazine, phentermine, pipradrol and pyrovalerone. The stimulants in Schedule IV are essentially used as anorectics or for the treatment of ADD.

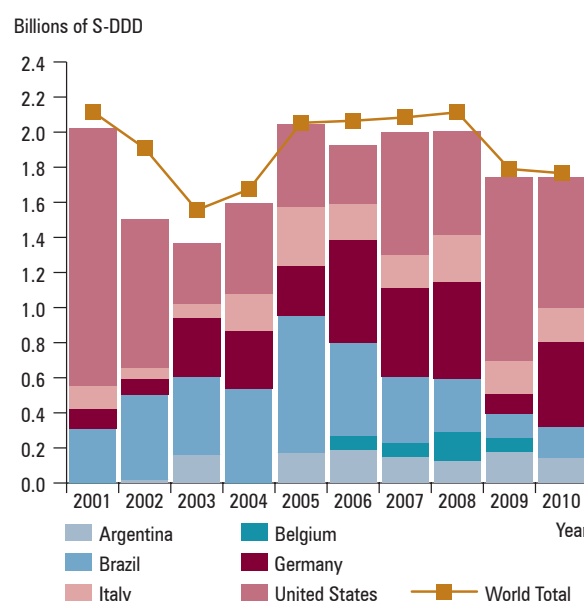
54. In the 1990s, total reported manufacture of stimulants in Schedule IV was very unstable, primarily reflecting the developments of phentermine manufacture in the United States. In the period 2001-2010, total reported manufacture of central nervous system stimulants continued to fluctuate, as a result of changes in manufacture in Brazil, in addition to those observed in the United States. Brazil, Germany and the United States were the main manufacturers of this group of substances. During the period 2006-2008, total manufacture was fairly stable, averaging 2.07 billion S-DDD. However, it then dropped, reaching 1.8 billion S-DDD in 2010 (see figures 9 and 10).

55. In 2010, of the total reported manufacture of the 14 stimulants in Schedule IV (1.8 billion S-DDD), phentermine (1.3 billion S-DDD) accounted for 74 per cent; it was followed by mazindol (143 million S-DDD, or 8 per cent of total reported manufacture), phendimetrazine and amfepramone (109 million S-DDD and 100 million S-DDD, or 6 per cent each) and fenproporex (88 million S-DDD, or 5 per cent) (see figures 9 and 11). Pemoline and benzfetamine accounted for less than 1 per cent of total reported manufacture.

**Figure 9. Main central nervous system stimulants in Schedule IV: total reported manufacture, by substance, 2001-2010**

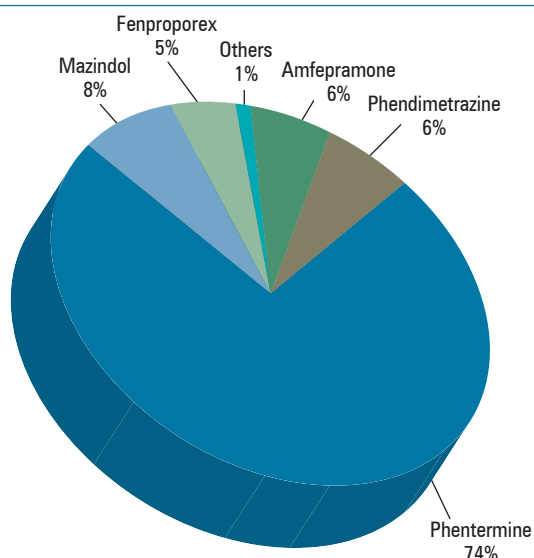


**Figure 10. Main central nervous system stimulants in Schedule IV: total reported manufacture, by country, 2001-2010**

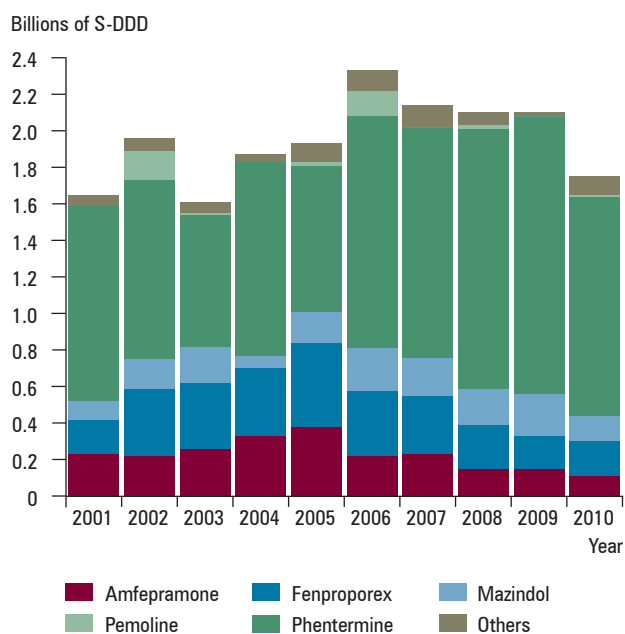


56. The fluctuations in the total calculated consumption of central nervous system stimulants listed in Schedule IV (see figure 12) mainly reflect changes in the use of phentermine in the United States and the use of amfepramone and fenproporex in Brazil. A total of 1.75 billion S-DDD of central nervous stimulants listed in Schedule IV were used in 2010. Of those, phentermine (1.2 billion S-DDD) accounted for 69 per cent; it was followed by fenproporex (190 million S-DDD or 11 per cent), mazindol

**Figure 11. Main central nervous system stimulants in Schedule IV: share of total reported manufacture, selected substances, 2010**



**Figure 12. Main central nervous system stimulants calculated global consumption,<sup>a</sup> by substance, 2001-2010**



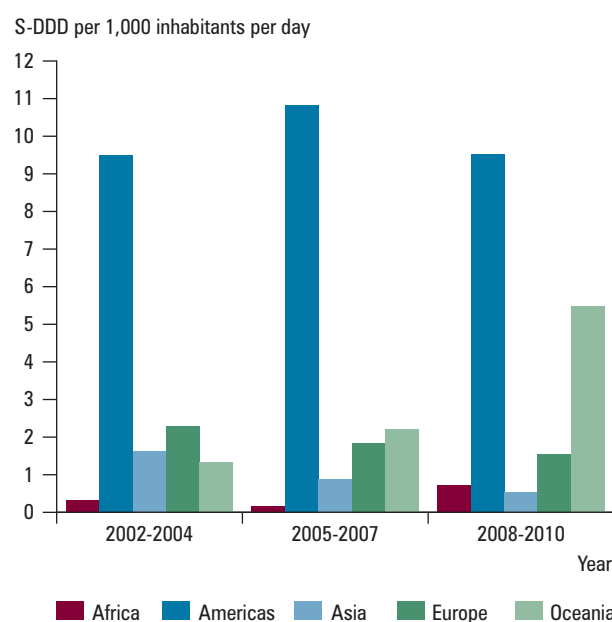
<sup>a</sup>Statistical data submitted by Governments are used to calculate the approximate global consumption in a given year, which is expressed in defined daily doses for statistical purposes (S-DDD).

(140 million S-DDD, or 8 per cent) and amfepramone (107 million S-DDD or 6 per cent).

57. Consumption of Schedule IV stimulants in the Americas remained the highest worldwide. This is mainly a result of high consumption levels in the United States and Argentina. Overall, an average of 9.53 S-DDD per 1,000 inhabitants per day were consumed in the Americas during the period 2008-2010 (see figure 13). Levels of consumption decreased in the Americas, Asia and Europe during the three-year period 2008-2010 compared with the period 2005-2007, although they increased markedly in Africa and Oceania, mainly as a result of increased consumption in South Africa and Australia. In 2010, the highest calculated consumption rates expressed in S-DDD per 1,000 inhabitants per day were observed in Australia (9.8), Argentina (9.2), the United States (9.0), the Republic of Korea (6.5), Brazil (3.9), the Hong Kong Special Administrative Region of China (2.9) and Singapore (2.8).

58. Phentermine has been the most manufactured substance in the group of stimulants in Schedule IV, although its share of total manufacture within this group fluctuated widely, between 0 and 70 per cent in the previous two decades. 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 ceased in 1998. After 1999, global reported manufacture of the substance continued to fluctuate. It amounted

**Figure 13. Central nervous system stimulants listed in Schedule IV: average national consumption,<sup>a</sup> by region, 2002-2004, 2005-2007 and 2008-2010**



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

to nearly 20 tons in 2010. In the period 2008-2010, the United States, Germany, Italy and India, in descending order, were the main manufacturers of the substance.

59. During the three-year period 2008-2010, the volume of trade in phentermine averaged 11 tons. Germany, Italy and the United States, in descending order, were the main exporters of phentermine; in 2010, their exports totalled 9.5 tons, accounting for 87 per cent of total exports of the substance in that year. Other major exporters in 2010 were Australia and Switzerland. Thirty countries reported imports of phentermine at least once during the three-year period 2008-2010. In 2010, the United States remained the main importer of the substance (5.6 tons), followed by Australia and the Republic of Korea (1.6 and 1.4 tons respectively).

60. After steady growth, from 3 tons in 1998 to 10 tons in 2003, total reported manufacture of fenproporex fluctuated between 9.5 tons in 2005 and 1.76 tons in 2010. Belgium and Brazil, the two main countries manufacturing fenproporex, accounting for about 99 per cent of global manufacture of the substance in the period 2006-2009. In 2010, Brazil was the sole manufacturer of fenproporex. Germany was the leading importer of the substance in every year after 2006, except 2009, when Brazil was the leading importer. Total reported imports of the substance fell sharply from 5.9 tons in 2009 to less than 1 ton in 2010.

61. Total reported manufacture of amfepramone decreased from 28 tons in 2005 to an average of about 11 tons during the three-year period 2007-2009. In the period 2001-2010, Brazil was the largest manufacturer of the substance; it was followed by Switzerland and Italy. In 2010, global manufacture of amfepramone decreased further, to 7.5 tons, most of which was manufactured in Brazil (87 per cent) and Italy. Switzerland was the main exporter of amfepramone in the period 2001-2010, exporting 2.5 tons of the substance, or 78 per cent of the global exports, in 2010; it was followed by Italy and Germany. The largest imports of amfepramone in 2010 were reported by the United States (1.5 tons), Germany and Mexico (485 kg each) and Chile (170 kg), the four countries together accounting for 89 per cent of global imports.

62. In 2010, global manufacture of phendimetrazine stood at 7.6 tons, of which Italy accounted for more than 66 per cent. Germany was the second largest manufacturer of the substance. Italy was also the main exporter of the substance, accounting for 88 per cent of global exports during the period 2008-2010. Traditionally, the main importers of the substance have been the United States and the Republic of Korea. After a sharp fall in phendimetrazine imports in 2009 in both countries, imports of the substance in 2010 reached previous levels (3.5 tons and 560 kg in the United States and the Republic of Korea respectively). Canada and Italy also imported significant

amounts of phendimetrazine in 2010. Calculated per capita consumption of this substance for the period 2008-2010 were highest in the Republic of Korea (0.56 S-DDD per 1,000 inhabitants per day), followed by Italy (0.35 S-DDD) and the United States (0.26 S-DDD).

63. Global manufacture of pemoline during the period 2001-2010 ranged from no manufacture to a few tons. During that period, the Netherlands was the main manufacturer of pemoline. The Netherlands and Switzerland were the main exporters of the substance. Global trade in pemoline amounted to 295 kg in 2010. The main importers of pemoline during the three-year period 2008-2010 were Japan, which imported a total of 440 kg in that period, followed by Chile (37 kg) and Switzerland (23 kg). In addition to being used as a stimulant, pemoline is used for the treatment of ADD.

64. During the period 2006-2010, mazindol was manufactured almost exclusively in Argentina. An average of 157 kg of mazindol was manufactured in Argentina each year during that period, for domestic consumption and, to a lesser extent, for export. Global use of the substance fell sharply, from 707 kg in 1998 to an annual average of 191 kg in the three-year period 2008-2010. Global stocks of mazindol at the end of 2010 amounted to 175 kg; those stocks were held in Brazil, France, Mexico and Switzerland.

65. Until 2004, only the United States reported manufacture of benzphetamine, averaging 1.1 tons annually during the period 2000-2004. In 2006, benzphetamine was manufactured in Italy and Switzerland, in addition to the United States; subsequently, in the three-year period 2008-2010, the United States was once more the sole manufacturer, manufacturing on average 448 kg per year. During the period 2001-2010, international trade in benzphetamine was limited, with only the United States reporting imports of the substance (16 kg in 2010) from stocks held by Italy. The United States was also virtually the sole consumer of benzphetamine in the period 2008-2010, consuming an average of 862 kg of the substance per year.

66. The reporting of manufacture of and trade in the other stimulants listed in Schedule IV has been sporadic. Following exports from France to Canada in 2004 and 2007, all stocks of pipradol at the end of 2010 were held in Canada (9 kg). Since 2003, the only reported manufacture of etilamfetamine was 6 g in 2009 and the only reported manufacture of pyrovalerone was 5 g in 2010. No manufacture of aminorex, fencamfamin, mefenorex, mesocarb or pipradol was reported. Small and irregular trade transactions were reported for fencamfamin, mefenorex and pipradol, while no international trade was reported for aminorex, etilamfetamine, mesocarb or pyrovalerone.

## Benzodiazepines

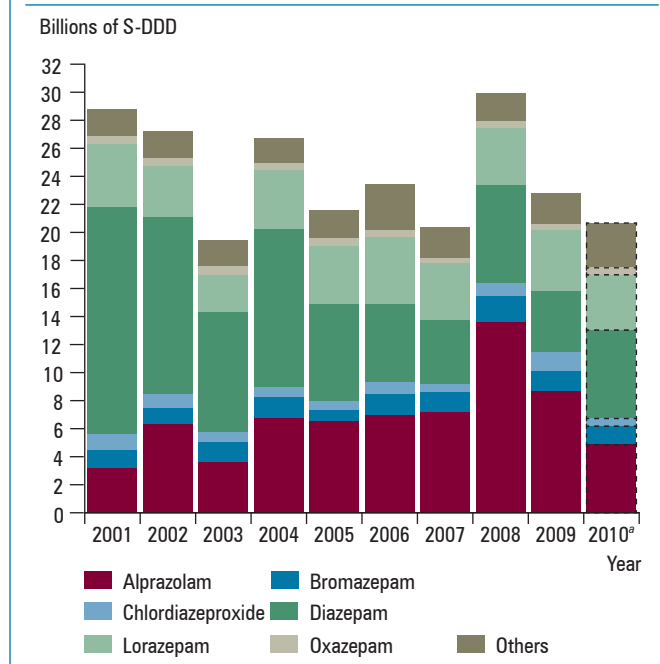
67. Thirty-three benzodiazepines were included in Schedule IV in 1984. Midazolam was added to Schedule IV in 1990 and brotizolam was added in 1995. Flunitrazepam was transferred from Schedule IV to Schedule III in 1995. During the decade ending in 2010, practically all countries and territories that reported to the Board manufactured or traded in benzodiazepines in quantities of more than 1 kg at least once. Benzodiazepines are frequently diverted for subsequent smuggling and abuse.

### Benzodiazepine-type anxiolytics

68. Twenty-two benzodiazepines are generally classified as anxiolytics. Total reported manufacture of this group of substances rose steadily until 2001, when it reached a peak of 28.8 billion S-DDD. Global manufacture then fluctuated between 18.9 billion and almost 30 billion S-DDD in the period 2002-2008, and then dropped to 22.9 billion S-DDD in 2009. Those fluctuations mainly reflect fluctuations in the manufacture of alprazolam and diazepam, the main substances in this group, which together accounted, on average, for almost 60 per cent of the total in the period 2007-2009. In 2010, because data on manufacture were not received for that year from India, which in 2009 accounted for 25 per cent of global manufacture of that group of substances, total reported manufacture of benzodiazepine-type anxiolytics stood at 19.7 billion S-DDD (see figure 14).

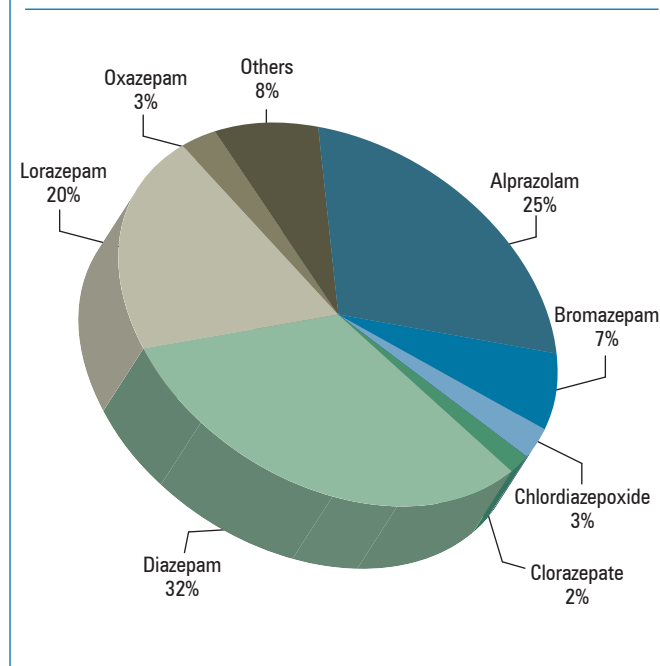
69. In 2010, diazepam accounted for almost 32 per cent (6.3 billion S-DDD) of total reported manufacture of benzodiazepine-type anxiolytics, alprazolam for 25 per cent (5 billion S-DDD), lorazepam for 20 per cent (3.9 billion S-DDD), bromazepam for 7 per cent, chlordiazepoxide for 2.8 per cent, oxazepam for 2.5 per cent and clorazepate for 2.4 per cent (see figure 15). Nordazepam accounted for 1.7 per cent of total reported manufacture of benzodiazepine-type anxiolytics, tetrazepam for 1.5 per cent, clobazam for 1.1 per cent and ethyl loflazepate and prazepam for 1 per cent each. The remaining six substances in that group (clotiazepam, delorazepam, halazepam, ketazolam, medazepam and oxazolam) together accounted for 2 per cent of total reported manufacture of benzodiazepine-type anxiolytics, calculated in S-DDD. No manufacture of camazepam, fludiazepam or pinazepam was reported for 2010. As shown in figure 17, China, India and Italy were the leading manufacturers of benzodiazepine-type anxiolytics in the period 2001-2009. In the absence of data from India, China and Italy together accounted for almost 59 per cent of global manufacture of that group of substances in 2010 (see figure 16).

**Figure 14. Benzodiazepine-type anxiolytics: total reported manufacture, 2001-2010**



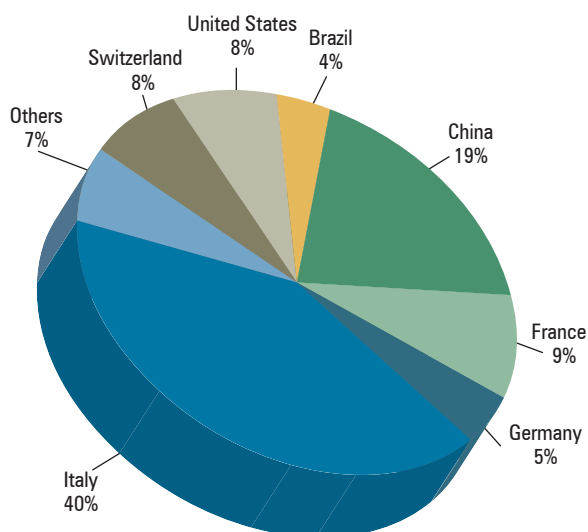
<sup>a</sup>The data for 2010 are incomplete.

**Figure 15. Benzodiazepine-type anxiolytics: share of total reported manufacture, by substance, 2010**

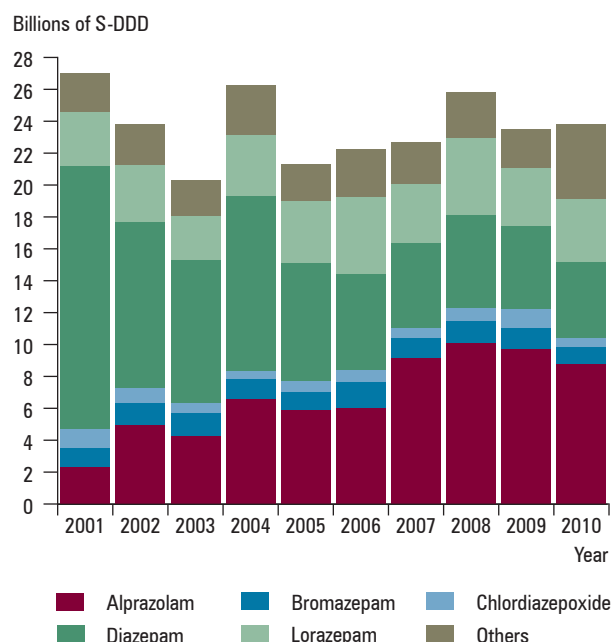


70. Total approximate consumption of benzodiazepine-type anxiolytics calculated by the Board was more stable than global manufacture, although it follows the same overall trend. In the three-year period 2008-2010, total calculated consumption of this group of substances gradually decreased, from 25.8 billion S-DDD in 2008 to 23.8 billion S-DDD in 2010 (see figure 18). The calculated consumption

**Figure 16. Benzodiazepine-type anxiolytics: share of total reported manufacture, by country, 2010**

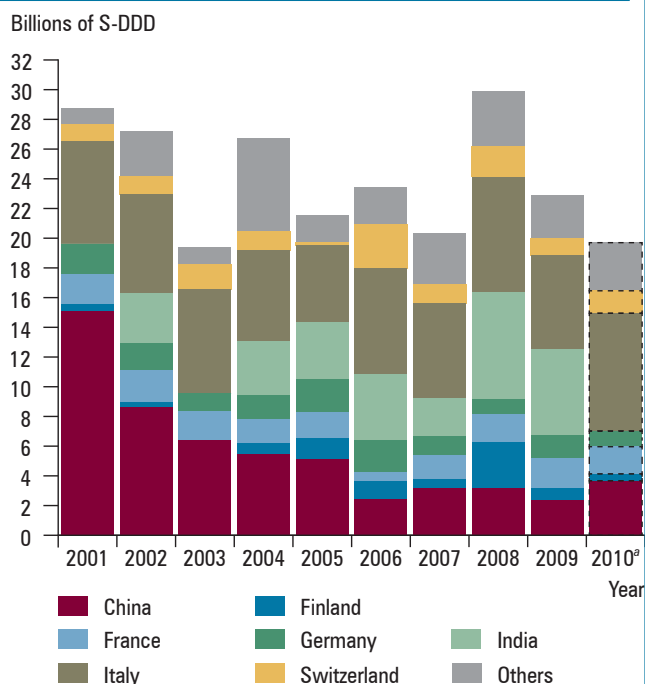


**Figure 18. Benzodiazepine-type anxiolytics: calculated global consumption,<sup>a</sup> 2001-2010**



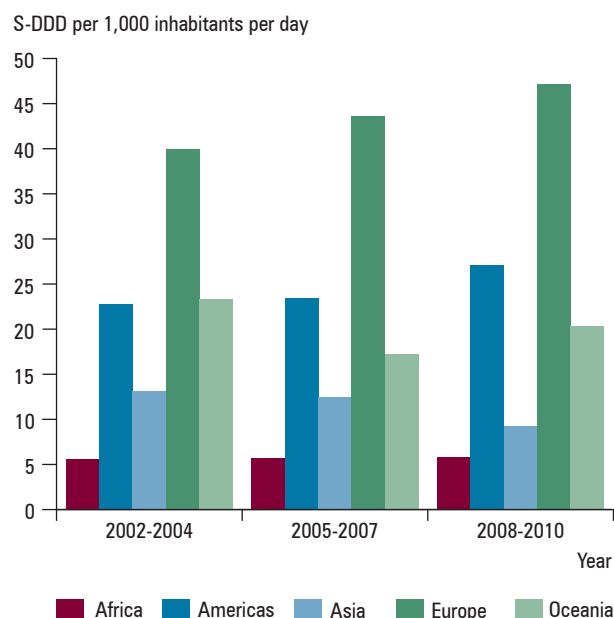
<sup>a</sup>Statistical data submitted by Governments are used to calculate the approximate global consumption in a given year. These consumption figures are expressed in defined daily doses for statistical purposes (S-DDD).

**Figure 17. Benzodiazepine-type anxiolytics: reported manufacture, selected countries, 2001-2010**



<sup>a</sup>The data for 2010 are incomplete.

**Figure 19. Benzodiazepine-type anxiolytics: average national consumption,<sup>a</sup> by region, 2002-2004, 2005-2007 and 2008-2010**



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

of benzodiazepine-type anxiolytics in S-DDD per 1,000 inhabitants per day is shown in table IV.3 of the present publication. Europe has consistently been the region with the highest calculated average national consumption rates for benzodiazepine-type anxiolytics (see figure 19).

## Alprazolam

71. Total reported manufacture of alprazolam grew from about 1 ton per year in 1986 to a one-time peak of 13.6 tons in 2008, which was the result of increased



output by all manufacturing countries and unprecedented increases in Finland and India in that year. In 2009, total manufacture dropped to 8.7 tons, as output declined across the board in all the major manufacturing countries. In 2010, total reported manufacture of alprazolam was 5 tons, as only eight countries reported manufacture of the substance (down from 12 countries in 2008) and no data were submitted by India. The main manufacturers of alprazolam in 2010 were Italy (1.9 tons), the United States (1.2 tons), France (928 kg) and Finland (463 kg), which together accounted for almost 90 per cent of global manufacture.

72. International trade in alprazolam averaged 8.4 tons during the period 2008-2010. In 2010, global imports of alprazolam stood at 8.2 tons, with more than 140 countries and territories in all regions reporting imports of the substance. The main importers of alprazolam continued to be the United States (2.7 tons), Italy (907 kg) and Belgium (887 kg), which together accounted for 55 per cent of total imports of the substance. Global calculated consumption, which had averaged 4.8 billion S-DDD during the period 2000-2005, reached an average of 9.7 billion S-DDD in the period 2008-2010. The largest consumers of alprazolam in absolute terms in 2010 continued to be the United States (3.6 billion S-DDD), followed by Canada (1.2 billion S-DDD) and Hungary (850 million S-DDD).

## Diazepam

73. Diazepam continued to be the most traded substance in the group of benzodiazepine-type anxiolytics. It is consumed in all regions of the world. Together with alprazolam, diazepam is among the benzodiazepines that are often diverted from domestic distribution channels to be sold on unregulated markets and to be abused. Global manufacture of diazepam declined from 162.6 tons in 2001 to 43.5 tons in 2009, reflecting declining use of the substance. In 2010, global reported manufacture increased again, to 63 tons, owing to increased output in China (31.3 tons, or almost 50 per cent of global manufacture) and Italy (20.6 tons or 33 per cent), the leading manufacturers of diazepam. The only other countries reporting manufacture of diazepam in quantities exceeding 1 ton were Brazil (5.4 tons), Switzerland (3.6 tons) and the United States (1.5 tons). India, which had manufactured 7.9 tons of the substance in 2009, did not report any manufacture for 2010.

74. Exports of diazepam fluctuated between 51 and 60 tons during the five-year period 2006-2010, reflecting varying levels of exports reported by China and Italy, the world's leading exporters of the substance. In 2010, China exported 23.8 tons of diazepam and Italy exported 18.8 tons. About 45 other countries reported exports of diazepam in excess of 1 kg in 2010, among them

Switzerland (5.1 tons), Denmark (3.3 tons), Germany (2.6 tons) and India (2.6 tons), which together accounted for 23 per cent of global exports.

75. Practically all countries and territories imported diazepam at least once in the period 2008-2010. About 115 countries and territories reported imports of diazepam of more than 2 kg for 2010. The main importers of diazepam in that year were Denmark (10.3 tons), the United States (4.7 tons), Germany (3.4 tons), Switzerland (2.8 tons), Brazil (2.7 tons), Ghana (2.5 tons), Spain (2.2 tons), the Democratic Republic of the Congo (1.9 tons), the Czech Republic (1.8 tons), Serbia (1.4 tons) and Thailand and Bangladesh (1.2 tons each). Together, those countries accounted for 65 per cent of global imports. Global calculated consumption of diazepam decreased from 16.4 billion S-DDD in 2001 to 5.7 billion in 2010. China (748 million S-DDD), Brazil (681 million S-DDD), the United States (640 million S-DDD) and the United Kingdom (273 million S-DDD) were the largest consumers of diazepam in that year.

## Lorazepam

76. Total reported manufacture of lorazepam was fairly stable in recent years, averaging 10.7 tons per year in the period 2004-2009. Italy and Germany were the two main manufacturers of the substance; they were followed by India. In 2010, total output of the substance was 9.9 tons, of which Italy accounted for 66 per cent and Germany 23 per cent. India had traditionally reported about 1.5 tons of lorazepam manufacture every year, although no manufacture was reported for 2010. Other countries reporting manufacture of lorazepam in 2010 were Brazil, Canada, China, Israel, Poland, Spain and the United States.

77. Between 2001 and 2009, total exports of lorazepam had been between 9 and 11.6 tons. In 2010, total reported exports of lorazepam stood at 10.2 tons. The main exporters of lorazepam in the decade up to 2010 had been Italy, Germany, Ireland and India (in that order), together accounting for 88 per cent of total exports of the substance. The main importers of lorazepam in 2010 remained the United States, Ireland, Spain, Germany, Italy, France and Canada, together accounting for 68 per cent of all imports of the substance. About 55 other countries imported lorazepam in quantities exceeding 5 kg. During the period 2001-2010, global calculated consumption averaged 3.9 billion S-DDD per year; in 2010 it amounted to 4.1 billion S-DDD. The largest consumers of lorazepam in that year were the United States (906 million S-DDD), Germany (587 million S-DDD), Spain (450 million S-DDD), Canada (355 million S-DDD) and Italy (341 million S-DDD).

## Bromazepam

78. Total reported manufacture of bromazepam fluctuated significantly during the period 2001-2010. After attaining a peak of 18.3 tons in 2008, total reported manufacture of bromazepam was 13.1 tons in 2010. Italy (4.4 tons) and Switzerland (6.9 tons) remained the leading manufacturers of the substance in 2010, accounting for 34 per cent and 53 per cent, respectively, of the reported total; they were followed by Brazil (1.4 tons), China (420 kg) and Canada (86 grams). India, the other major manufacturer of bromazepam in the recent past, did not report any manufacturing data for 2010.

79. Global exports of bromazepam were very stable during the period 2001-2010, averaging 16.3 tons annually. In 2010, as in previous years, the main manufacturing countries were also the leading exporters of the substance: Switzerland (7.3 tons), Italy (5.5 tons) and India (2.1 tons) accounted for 89 per cent of global exports. About 110 countries reported imports of bromazepam in 2010; 23 of those countries imported more than 100 kg of the substance. The main importers of bromazepam in 2010 included France (2.5 tons), Switzerland (2.2 tons), Italy (1.8 tons), Brazil (1.2 tons), Germany (836 kg) and Japan (795 kg), which together accounted for 59 per cent of global imports of the substance. Calculated global consumption of bromazepam was fairly stable during the period 2001-2008, averaging 1.3 billion S-DDD. After that, it decreased slightly, amounting to 1.2 billion S-DDD in 2010.

## Chlordiazepoxide

80. Total reported manufacture of chlordiazepoxide decreased from 43 tons in 2000 to 19 tons in 2007 and then increased to 40 tons in 2009. In 2010, total reported output of that substance was 16.5 tons, 98 per cent of which was accounted for by China (8.5 tons) and Italy (7.6 tons) together. Three other countries reported manufacture of the substance in 2010, namely Iraq (259 kg), Poland (149 kg) and Canada (15 kg). India, which had reported the manufacture of 10.9 tons of chlordiazepoxide for 2009, did not report any manufacture of the substance for 2010. China, India, Italy and Switzerland were the largest exporters of chlordiazepoxide during the period 2001-2010. During that decade, global exports of chlordiazepoxide fluctuated, but declined overall, from an average of 22 tons in the period 2001-2003 to 15.8 tons in 2010.

81. More than 100 countries reported imports of chlordiazepoxide in the three-year period up to 2010. The main importers of the substance in 2010 were Cuba (2 tons), the United States (1.9 tons), Switzerland (1.8 tons), Iraq (1.1 tons) and Egypt (884 kg). Together, those

countries accounted for 58 per cent of global imports. Calculated global consumption of the substance, which had decreased from 1.2 billion S-DDD in 2001 to 715 million S-DDD in 2006, rose again in 2009 to 2.1 billion S-DDD. In 2010, calculated global consumption of the substance stood at 613 million S-DDD.

## Oxazepam

82. In the period 1991-2010, total reported manufacture of oxazepam was fairly stable, averaging 27.3 tons per year. After reaching a low of 20.7 tons in 2009, global reported manufacture of the substance amounted to 25.3 tons in 2010, owing to increased output reported by Italy. Italy, which manufactures the substance mainly for export, and France remained the main manufacturers of oxazepam in 2010, reporting manufacture of 18.3 tons and 5.2 tons of the substance respectively. The volume of trade in oxazepam, which had averaged about 40 tons annually during the five-year period 2001-2005, declined between 2006 and 2009, when it dropped to 17.3 tons. It picked up again slightly in 2010, reaching 24.6 tons. More than 50 countries imported oxazepam in 2010. The main importers of oxazepam in 2010, together accounting for 64 per cent of the global imports of the substance, were Germany (6.6 tons), France, Canada, the Netherlands, Australia and Norway (in that order). Those countries were also the largest consumers of oxazepam in 2010.

## Clorazepate

83. Total reported manufacture of clorazepate averaged 8.4 tons during the period 2000-2005. After declining to 5 tons in 2006 and 2007, global output started to increase again, reaching a peak of 11.3 tons in 2009 before dropping again to 9.4 tons in 2010. France and Italy were the leading manufacturers of clorazepate during the period 2001-2010. In 2010, those two countries accounted for over 98 per cent of global manufacture of clorazepate. International trade in clorazepate stood at 5.6 tons in 2010. France and Spain remained the largest users of clorazepate; about 60 other countries reported the import and use of the substance.

## Clobazam

84. During the decade leading up to 2010, total reported manufacture of clobazam fluctuated between 3 and 6 tons. In 2010, total output stood at 4.2 tons. France, Germany and India were the main manufacturers of clobazam during the period 2001-2009. For 2010, in the absence of the data on the manufacture of clobazam in India, total reported manufacture of the substance was almost entirely comprised of output from Germany (2.3 tons) and France

(1.9 tons). International trade in clobazam fluctuated during the period 2001-2010, when it averaged 5 tons. Over 80 countries reported imports of the substance in 2010; France, India, Brazil, Bangladesh and Japan reported having imported the largest quantities.

## Other anxiolytics

85. Total reported manufacture of nordazepam fluctuated widely in the 10-year period up to 2010, reflecting changing output reported by Switzerland. In 2010, global manufacture of the substance amounted to 4.9 tons (328 million S-DDD), 94 per cent of which was manufactured in Switzerland. Global output of tetrazepam stood at 305 million S-DDD, and total reported manufacture of ethyl loflazepate amounted to 190 million S-DDD. Camazepam has not been manufactured since 1991; manufacture of fludiazepam was last reported by Japan for 2007. India was the only country that reported manufacture of pinazepam during the period 2007-2009; no manufacture of the substance was reported in 2010. The combined manufacture of the remaining eight substances in that group (clotiazepam, cloxazolam, delorazepam, halazepam, ketazolam, medazepam, oxazolam and prazepam) amounted to 619 million S-DDD in 2010.

## Meprobamate

86. Meprobamate, the only non-benzodiazepine-type substance in Schedule IV that is used as an anxiolytic, has gradually been replaced by benzodiazepines, leading to a substantial decline in manufacture from 750 tons in the late 1970s to an annual average of 290 tons during the 1990s. After 2000, total manufacture of meprobamate fluctuated around an annual average of 230 tons and the decreasing trend continued. In 2010, total reported manufacture of the substance amounted to 137 tons (114 million S-DDD). China, Denmark and India were the main countries manufacturing meprobamate, although the quantities manufactured declined. In 2010, Denmark reported having manufactured 71.9 tons of meprobamate, while China reported having manufactured 63.5 tons. India did not report any data on manufacture for 2010. Global stocks of meprobamate stood at 146 tons in 2010, 93 per cent of which was held in Denmark (59 tons), South Africa (34 tons), France (30 tons) and Hungary (12 tons).

87. International trade in meprobamate also continued to decline. Global exports of the substance decreased from 199 tons in 2009 to 177 tons in 2010. China and Denmark were the main exporters of meprobamate in 2010. France (58.7 tons), Cuba (54 tons) and South Africa (37 tons) remained the leading importers of meprobamate, together

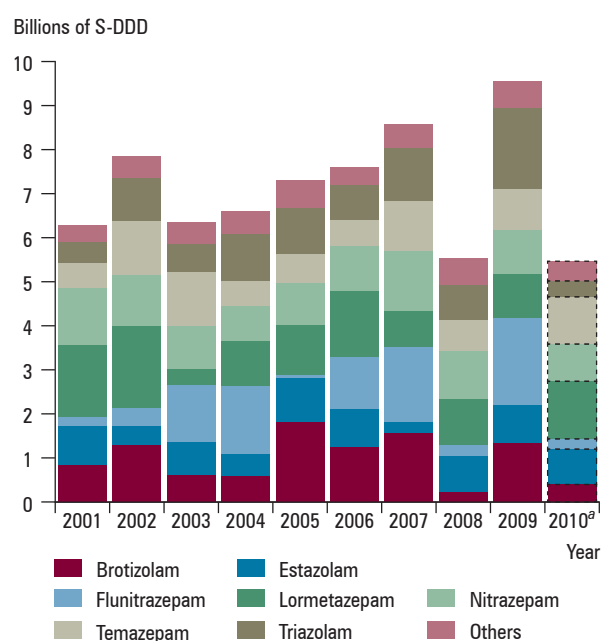
accounting for 80 per cent of total imports of the substance in 2010. Other main importers of the substance in 2010 included Hungary, Romania, Tunisia, Algeria, the Democratic Republic of the Congo, Iraq and Switzerland (in descending order). In 2010, global calculated consumption of meprobamate amounted to 258 tons (215 million S-DDD). Hungary, France, Cuba and South Africa (in that order) had the highest calculated consumption of the substance in 2010.

## Benzodiazepine-type sedative-hypnotics

88. Twelve benzodiazepines are generally used as sedative-hypnotics: brotizolam, estazolam, flunitrazepam, flurazepam, haloxazolam, loprazolam, lormetazepam, midazolam, nimetazepam, nitrazepam, temazepam and triazolam. Comments on flunitrazepam, a substance that was transferred from Schedule IV to Schedule III in 1995, are provided in paragraphs 44-46 above.

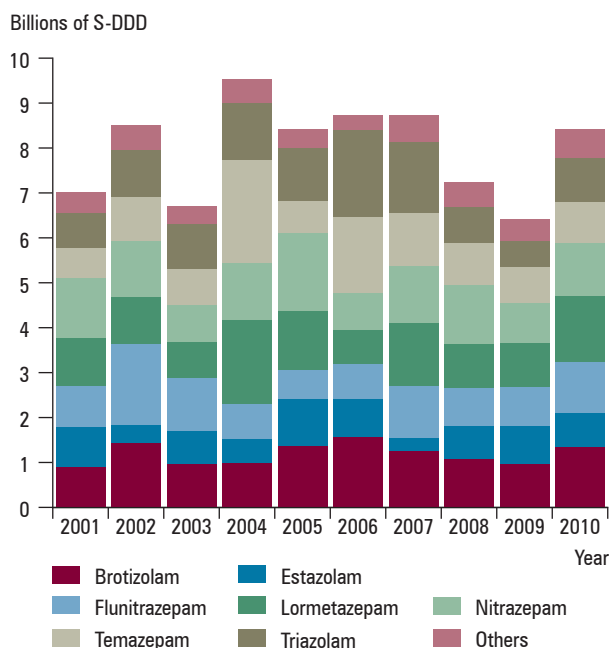
89. Total reported manufacture of the 12 substances in the group gradually increased from 6.4 billion S-DDD in 1999 to over 8.5 billion S-DDD in 2007 and subsequently fluctuated, mainly as a result of changes in manufacture in Germany and Switzerland. In 2002, Switzerland started reporting to the Board on the manufacture of benzodiazepines. In 2010, total reported manufacture of this group of substances fell to 5.5 billion S-DDD, as a result of lower output reported by several manufacturing countries and because of missing data on manufacture from India (see figure 20). Calculated consumption of this group of sub-

**Figure 20. Benzodiazepine-type sedative-hypnotics: total reported manufacture, by substance, 2001-2010**



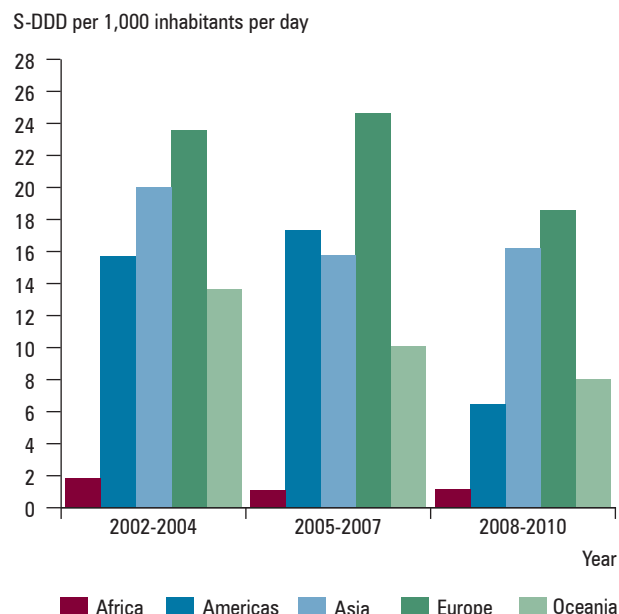
<sup>a</sup>The data for 2010 are incomplete.

**Figure 21. Benzodiazepine-type sedative-hypnotics: calculated global consumption,<sup>a</sup> 2001-2010**



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

**Figure 22. Benzodiazepine-type sedative-hypnotics: average national consumption,<sup>a</sup> by region, 2002-2004, 2005-2007 and 2008-2010**



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

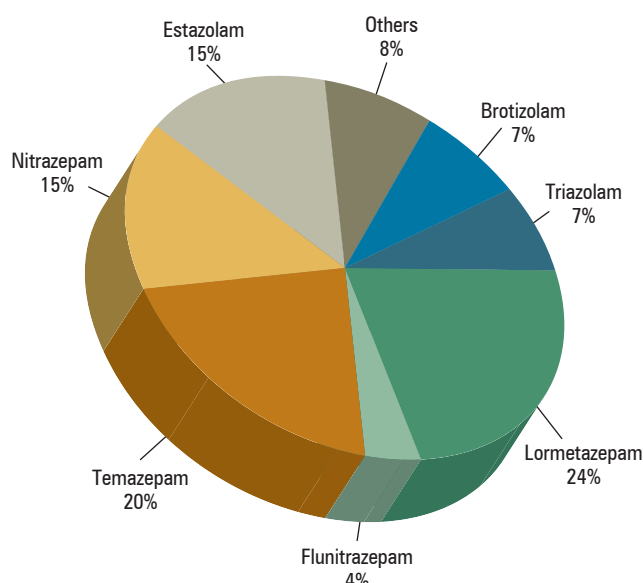
stances was less volatile and fluctuated around an annual average of 7.9 billion S-DDD during the period 2001-2010. In 2010, it stood at 8.4 billion S-DDD (see figure 21).

90. The calculated average national consumption of benzodiazepine-type sedative-hypnotics, expressed in S-DDD per 1,000 inhabitants per day, has traditionally been higher in Europe than in other regions. The marked decline in the calculated consumption levels in Europe, which was observed in the period 2007-2009, did not continue in 2010. Average levels of consumption of this group of substances had also declined in the other regions, compared with the period 1998-2000, but increased again in 2010 (see figure 22). Calculated consumption levels of benzodiazepine-type sedative-hypnotics in S-DDD per 1,000 inhabitants per day in individual countries are shown in table IV.2 of the present publication.

91. The reported manufacture of individual substances in this group has varied greatly over the years, as manufacturers tend to produce large quantities of a substance at a time, keeping in stocks those quantities that are not used within the year. The trends in total manufacture of flunitrazepam, in particular, showed significant fluctuations. In 2010, lormetazepam became the most manufactured substance in the group of benzodiazepine-type sedative-hypnotics, accounting for 1.3 billion S-DDD, or 24 per cent of global manufacture of this group of substances. Temazepam came second, with an output of 1.1 billion S-DDD,

or 20 per cent of global manufacture in 2010. Nitrazepam was third in that group (844 million S-DDD or 15 per cent); it was followed by estazolam (802 million S-DDD or 15 per cent) and brotizolam and triazolam (7 per cent each). Flunitrazepam, which in 2009 was the most manufactured substance in this group, accounted for 4 per cent of the total (see figure 23).

**Figure 23. Benzodiazepine-type sedative-hypnotics: share of total reported manufacture, by substance, 2010**

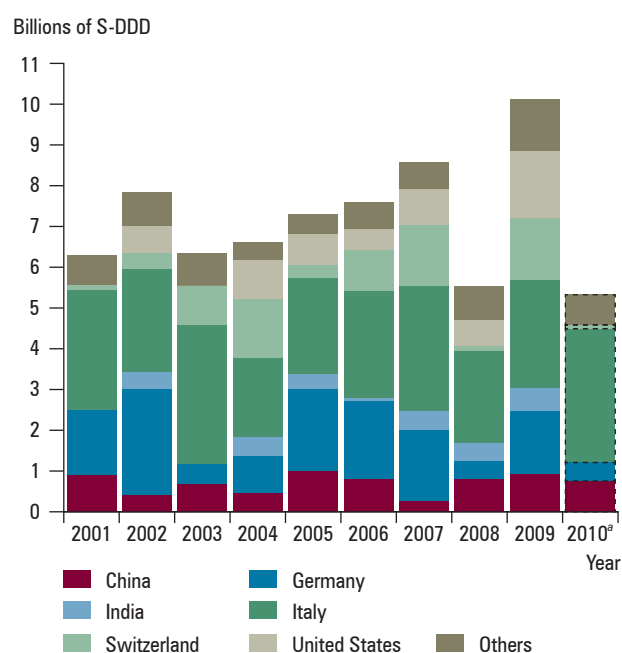




92. For the remaining substances, total reported manufacture amounted to 240 million S-DDD of midazolam, 168 million S-DDD of flurazepam, 18 million S-DDD of loprazolam and 13 million S-DDD of both haloxazolam and nimetazepam. Together, those substances accounted for 8 per cent of global reported manufacture of benzodiazepine-type sedative-hypnotics in 2010.

93. The main manufacturers of benzodiazepine-type sedative-hypnotics during the decade up to 2010 are shown in figure 24. Throughout that decade, Italy was the leading manufacturer of benzodiazepine-type sedative-hypnotics, accounting in some years for more than half of global manufacture of such substances. In 2010, Italy manufactured benzodiazepine-type sedative-hypnotics amounting to 3.3 billion S-DDD, accounting for 60 per cent of global manufacture of such substances (see figure 25).

**Figure 24. Benzodiazepine-type sedative-hypnotics: reported total manufacture, selected countries, 2001-2010**

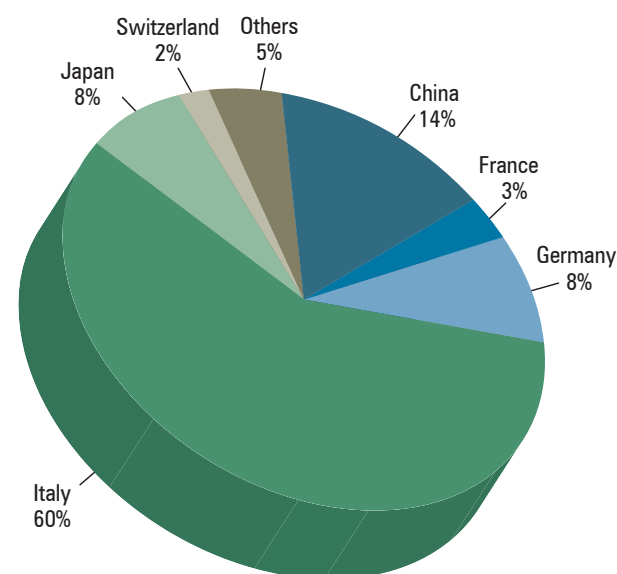


<sup>a</sup>The data for 2010 are incomplete.

## Lormetazepam

94. In the period 2001-2010, total reported manufacture of lormetazepam was consistently above 1 ton, except in 2003 (380 kg) and 2007 (809 kg). In 2010, manufacture of the substance amounted to 1.3 tons, an increase of 29 per cent over the figure reported in 2009. The fluctuations were caused by changes in output reported by Germany and Italy, the two main manufacturers of lormetazepam. No other country reported manufacture of that substance in 2010. Germany and Italy also continued

**Figure 25. Benzodiazepine-type sedative-hypnotics: total reported manufacture, selected countries, 2010**



to be the main exporters of lormetazepam in 2010. The main importers of lormetazepam were Spain, France, and Belgium; in all of those countries, the substance was imported partly for re-export. Calculated global consumption of lormetazepam followed an increasing trend. In 2010 it amounted to 1.5 tons. The highest calculated rates of consumption in 2010, measured in S-DDD per 1,000 inhabitants per day, were recorded in Belgium (49.3), Spain (34.6), Italy (16.3) and the Netherlands (11.3).

## Temazepam

95. During the period 2001-2010, Italy was the leading manufacturer and exporter of temazepam; Poland, the United Kingdom and the United States reported intermittent manufacture of the substance for some years. In 2010, global reported manufacture of temazepam amounted to 21.4 tons, with Italy accounting for about 82 per cent of the total. Canada, which reported manufacture of temazepam for the first time in 2010, manufactured 1.4 tons of the substance and Poland and the United States manufactured 124 and 1.5 kg, respectively. The United States continued to be the largest importer of temazepam in 2010, when it imported 7.7 tons. The second largest importer of temazepam in that year was Canada, followed by Finland, Hungary, Ireland, Germany, Australia and the Netherlands, all of which imported the substance in quantities of between 600 kg and 1.4 tons. The United States remained the main user; it was followed by Canada, the Netherlands and Italy. Together, those four countries accounted for almost 90 per cent of global consumption of temazepam (903 million S-DDD).



## Nitrazepam

96. In the period 2001-2010, global reported manufacture of nitrazepam ranged between 7 and 4 tons per year. In 2010, that figure stood at 4.2 tons, of which Italy accounted for 76 per cent. China, Canada and the Russian Federation (in that order) were the other countries manufacturing nitrazepam in 2010. India, a major manufacturer of nitrazepam during the period 2001-2009, did not report any manufacture of the substance for 2010. Exports of nitrazepam, which had averaged about 5 tons annually during the period 2000-2008, dropped to 3.7 tons in 2009 and picked up slightly in 2010, when they amounted to 4.4 tons. As in previous years, Italy and China, in that order, were the main exporters of the substance, together accounting for more than 80 per cent of all nitrazepam exports. About 80 countries reported importing over 1 kg of nitrazepam at least once in the period 2008-2010. Imports of nitrazepam reported by Japan and Cuba, traditionally the largest importers and users of the substance, increased during the period 2001-2010 and in 2010 reached the highest values reported so far (for Japan, 2,465 kg and for Cuba, 625 kg).

## Estazolam

97. During the period 2001-2010, global reported manufacture of estazolam fluctuated, as a result of developments in the manufacturing countries (China, Japan, Poland and the United States). The United States stopped manufacturing estazolam after 2006, causing global manufacture to drop to 790 kg in 2007, the lowest level recorded since 1994. However, global manufacture of the substance picked up again afterwards, amounting to 2.4 tons in 2010. China remained the leading manufacturer of estazolam during the period 2001-2010. China manufactured estazolam mainly for domestic use, whereas Italy and Japan manufactured the substance mainly for export. Fewer than 20 countries reported the use of estazolam in the period 2008-2010. In 2010, Poland, Italy, Japan, Portugal and the United States (in descending order) together accounted for 87 per cent of total imports of the substance.

## Brotizolam

98. Brotizolam is a potent hypnotic. Together with triazolam, it has the lowest S-DDD of all psychotropic substances (0.25 mg). 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, to a much lesser extent, by Italy and Japan. In 2008 and 2010, Germany did not manufacture brotizolam. Global reported manufacture of brotizolam reached 330 kg in 2009; in 2010,

when only Italy and Japan reported having manufactured the substance, the total reported manufacture was 99 kg. Germany remained the main exporter of brotizolam in 2010, accounting for 78 per cent of total exports of the substance, which amounted to 193 kg. In 2010, as in previous years, Japan was the largest importer of brotizolam (134 kg, or 72 per cent of total imports of the substance); it was followed by France and Italy, which imported the substance for re-export. In 2010, only six other countries reported having imported more than 1 kg of brotizolam. Calculated global consumption of brotizolam in 2010 amounted to 1.3 billion S-DDD, of which Japan, the main user of the substance during the period 2001-2010, accounted for 61 per cent.

## Triazolam

99. In the decade up to 2010, total reported manufacture of triazolam increased until 2009, when it reached a peak of 460 kg (1.8 billion S-DDD), the largest quantity reported after 1990. In 2010, that figure stood at 90 kg (361 million S-DDD). The United States had been the leading manufacturer of triazolam throughout the period 2000-2009, accounting for over 90 per cent of global manufacture of the substance in 2009. Then, in 2010, the United States did not manufacture triazolam, and Italy and France together accounted for over 99 per cent of global manufacture of the substance.

100. The United States continued to be the main exporter of triazolam in 2010; it was followed by France, Italy and Belgium. More than 40 countries reported imports of triazolam in the period 2008-2010. Throughout that period, Japan was the largest importer of triazolam, accounting for over 50 per cent of global imports of the substance. Belgium and Italy also imported large quantities of the substance for re-export. Japan accounted for almost 50 per cent of global use of the substance in 2010. Belgium was the country with the highest per capita use of triazolam (over 30 S-DDD per 1,000 inhabitants per day); it was followed by Japan (10.3 S-DDD).

## Midazolam

101. Total reported manufacture of midazolam had never exceeded a few hundred kilograms until 1996. After 1997, it fluctuated at about 6.9 tons per year. In 2010, that figure stood at 4.8 tons, of which 1.8 tons (or 37.5 per cent) were accounted for by Switzerland, the largest manufacturer of the substance; it was followed by Brazil (1.3 tons, or 29 per cent of the total), Israel (953 kg, or 20 per cent), Italy and China. Midazolam is used in many countries and was imported by about 140 countries in the period 2008-2010. In 2010, global reported imports of the substance stood at 5.7 tons. In 2010, Germany continued

to be the main importer of midazolam; it was followed by the United States, France, Switzerland, Brazil, Argentina, Spain, Portugal, Hungary, Mexico and Bangladesh. Together, those countries accounted for 71 per cent of global imports of midazolam.

## Flurazepam

102. Global reported manufacture of flurazepam, which had followed a declining trend, dropped in 2009 to 2.8 tons, the lowest level ever recorded. In 2010, it increased again, to 5.1 tons. Fluctuations in the reported manufacture of flurazepam reflected changes of manufacture in Italy, the largest manufacturer and exporter of the substance. In 2010, Italy accounted for 82 per cent of global reported manufacture of the substance, and Brazil and Canada accounted for the remainder. About 40 countries reported having imported flurazepam in the period 2008-2010. In 2010, the main importers of flurazepam continued to be Spain (1,300 kg), the United States (457 kg) and Germany (412 kg), which together accounted for over 50 per cent of total imports of the substance. Switzerland, Portugal, Canada, Italy and Belgium (in that order) imported between 190 and 300 kg of flurazepam during 2010.

## Loprazolam

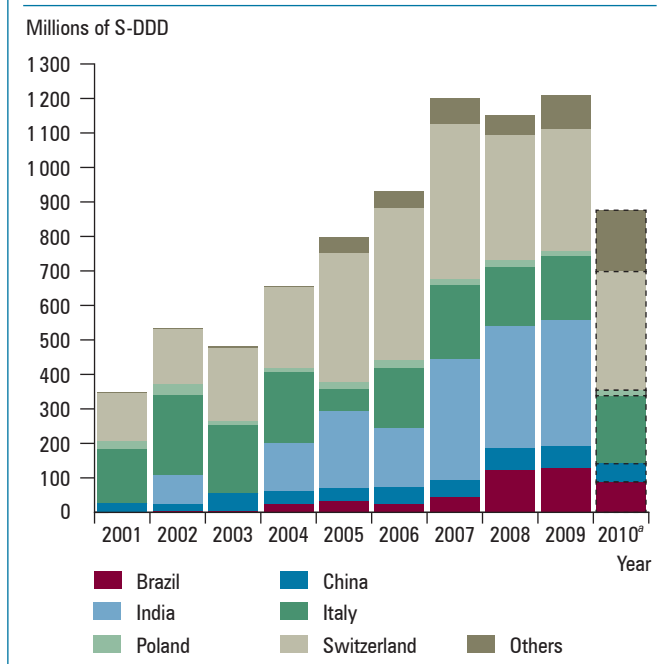
103. Total reported manufacture of loprazolam in 2010 amounted to 17.5 kg. France has traditionally been the main manufacturer and leading exporter of loprazolam, although manufacture of the substance has occasionally been reported by Spain (in 1993) and the United Kingdom (25 kg in 2000 and 34 kg in 2009). About 25 countries used loprazolam in the period 2008-2010. International trade in loprazolam in 2010 amounted to 117 kg, 86 per cent of which was accounted for by Poland, France, Italy and Spain.

## Benzodiazepine-type anti-epileptics

### Clonazepam

104. Clonazepam is a benzodiazepine that is used mainly as an anti-epileptic. During the period 1998-2003, global reported manufacture of clonazepam averaged about 4 tons per year. That figure more than doubled in the period 2007-2009, when it averaged 9.5 tons per year. In 2010, global reported manufacture of clonazepam stood at 7 tons, mainly as a result of missing reports on manufacture from India. Switzerland, which has been the world's leading manufacturer of clonazepam, manufactured 2.7 tons of

**Figure 26. Clonazepam: total reported manufacture, selected countries, 2001-2010**



<sup>a</sup>The data for 2010 are incomplete.

that substance in 2010; it was followed by Italy, Israel, Brazil, China, Canada and Poland, which reported the manufacture of between 120 kg and 1.6 tons of the substance for 2010 (see figure 26).

105. Global exports of clonazepam increased from about 0.5 ton in 1995 to 10.1 tons in 2009, Switzerland and Italy being the major exporters. In 2010, total exports of the substance amounted to 10 tons. In 2010, the United States and Switzerland remained the largest importers of clonazepam, with imports of 1.7 and 1.6 tons, respectively; Brazil, Mexico, Spain, Argentina, France, Italy, Canada, Japan, Bangladesh, Chile, Hungary and India (in that order) imported the substance in quantities of over 100 kg. Use of clonazepam expanded from about 50 countries in 1995 to more than 140 countries in the period 2008-2010. Global calculated consumption of clonazepam reached a record high of 1.1 billion S-DDD in 2008 and then levelled off. In 2010, it stood at 1 billion S-DDD. The largest users in 2010 were the United States (209 million S-DDD), Brazil (206 million S-DDD), Argentina (73 million S-DDD), Canada (71 million S-DDD), Hungary (71 million S-DDD) and France (66 million S-DDD). The highest rates of calculated consumption of clonazepam, measured in S-DDD per 1,000 inhabitants per day, were observed in Hungary (19), Uruguay (6), Canada (6) and Argentina (5). Calculated consumption levels of this substance in S-DDD per 1,000 inhabitants per day in individual countries are shown in table IV.4 of the present publication.

## Barbiturate-type sedative-hypnotics and anti-epileptics

### Allobarbitol, barbitol, butobarbitol, methylphenobarbitol, phenobarbitol, secbutabarbitol and vinylbitol

106. The seven barbiturates listed in Schedule IV are pharmacologically related to those included in Schedule III. Five of the seven substances, namely allobarbitol, barbitol, butobarbitol, secbutabarbitol and vinylbitol, are intermediate-acting barbiturates and are mainly used as hypnotics (to induce sleep). They are no longer used as daytime sedatives. The other two substances, methylphenobarbitol and phenobarbitol,<sup>5</sup> have additional properties and are also used as anti-epileptics (long-acting barbiturates). Phenobarbitol continued to be the most widely used substance in the group of barbiturates in 2010; it was followed by barbitol.

107. Total reported manufacture of those seven barbiturates (for both direct medical use and the manufacture of non-psychotropic substances) fell below 4 billion S-DDD in the period 1999-2000, then gradually rose to an average of 5.1 billion S-DDD in 2006 before declining in 2010 to 4.5 billion S-DDD. In 2010, as in previous years, phenobarbitol accounted for over 94 per cent of global manufacture of the barbiturates in Schedule IV (expressed in S-DDD); barbitol accounted for approximately 5 per cent. Methylphenobarbitol and secbutabarbitol together accounted for the remainder. No manufacture of butobarbitol or vinylbitol was reported in 2010. Manufacture of butobarbitol was last reported in 2008 (by Germany: 117 kg). No manufacture of vinylbitol was reported after 1996.

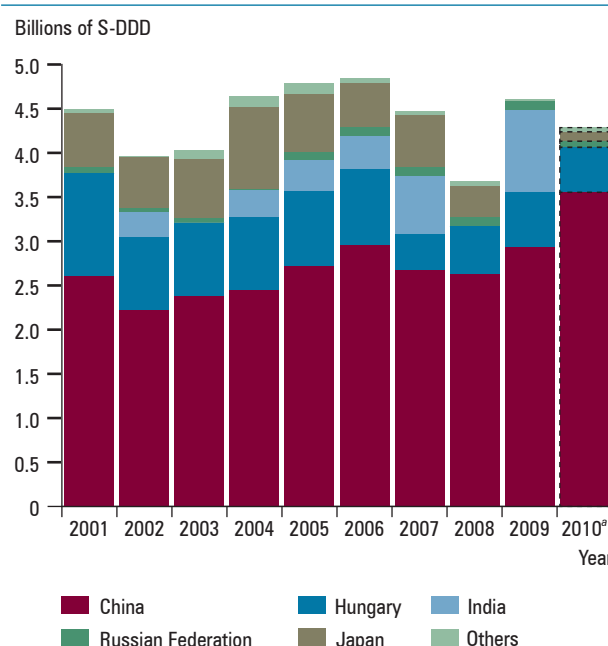
108. The countries with the highest calculated consumption rates of barbiturate-type sedative-hypnotics listed in Schedule IV during the period 2008-2010 were (in descending order) Jordan, Hungary, China, Yemen, Lebanon, Israel and Japan, which had consumption rates ranging between 0.5 and 4.7 S-DDD per 1,000 inhabitants per day. With respect to the barbiturate-type anti-epileptics listed in Schedule IV, the calculated consumption levels by country in S-DDD per 1,000 inhabitants per day are shown in table IV.4.

109. Total reported manufacture of phenobarbitol fluctuated between 370 tons and 450 tons during the period 2001-2010. In 2010, global reported manufacture of phenobarbitol amounted to 429 tons (4.29 billion S-DDD). China continued to be the leading manufacturer of phenobarbitol, accounting, on average, for over 70 per cent of global manufacture during the period 2008-2010. In the

period 2001-2010, the manufacture of phenobarbitol in China increased steadily. In 2010, it amounted to 355 tons, an increase of 21 per cent over the 2009 level (see figure 27). The second largest manufacturer of phenobarbitol in 2010 was Hungary, which reported having manufactured a total of 51 tons of the substance. Another major manufacturer of phenobarbitol, the Russian Federation, reported having manufactured 11 tons of the substance in 2010, significantly less than its average of 61 tons per year during the period 2001-2008. Other major manufacturers of phenobarbitol in 2010 included Japan (7 tons), Germany (2.6 tons) and Brazil (2.1 tons). Iraq and Canada also reported having manufactured small quantities of the substance in 2010. India, another major manufacturer of phenobarbitol, did not report any data on manufacture for 2010.

110. Phenobarbitol continues to be one of the most widely traded psychotropic substances, with an average trade volume of over 300 tons per year. International trade in phenobarbitol fluctuated during the period 2008-2010, with a slight decline between 2009 and 2010. During the period 2006-2010, an average of 145 countries reported imports of the substance every year. In 2010, total imports of phenobarbitol amounted to 343 tons (3.4 billion S-DDD), the largest importer being Switzerland (67.6 tons), followed by Brazil (59 tons), the Russian Federation (36.9 tons), Ukraine (20.6 tons), Germany (20.4 tons), Denmark (18.6 tons), the United States (14.8 tons) and Japan (10 tons). Those countries together accounted for over 72 per cent of total imports of the substance. A total of 45 countries reported exports of

**Figure 27. Phenobarbitol: total reported manufacture, selected countries, 2001-2010**



<sup>a</sup>The data for 2010 are incomplete.

<sup>5</sup> See table IV for details of the calculated consumption levels of phenobarbitol.

phenobarbital in 2010. China, Switzerland, India, Hungary, Germany, Denmark, Singapore, France, Jordan and Ireland (in descending order) remained the main exporters of phenobarbital, accounting for 99 per cent of global exports of the substance.

111. Global manufacture of barbital fluctuated during the period 2001-2010 around an annual average of 96 tons. After 2008, global manufacture of barbital slowly increased, from 79 tons (158 million S-DDD) to 116 tons (233 million S-DDD) in 2010, mainly owing to increased manufacture in China, the leading manufacturer of the substance. During the period 2008-2010, China accounted for 98 per cent of global manufacture of barbital. Japan was the other key manufacturer; it manufactured barbital mainly for domestic consumption, including for use in the manufacture of non-psychotropic substances and preparations exempted from certain control measures in accordance with article 3 of the 1971 Convention. Total calculated consumption of barbital averaged 94 tons per year during the period 2008-2010. China, Japan, Italy, France, the United States and Thailand (in descending order) remained the main users of barbital during that period.

112. International trade in barbital grew significantly from approximately 10 tons (20 million S-DDD) in 2008 to 17 tons (34 million S-DDD) in 2010. In 2010, as in previous years, China (11.5 tons) and Germany (3.9 tons) were the main exporters of barbital; they were followed by Japan (1.2 tons). Together, those three countries accounted for 97 per cent of global exports of barbital. Exports of barbital from China increased considerably, by 130 per cent, between 2009 and 2010. Germany and Japan were the leading importers of barbital in 2010; they were followed by Italy, Thailand, France and the United States.

113. Manufacture of methylphenobarbital fluctuated between 0.8 and 22 tons during the period 2001-2010. Those fluctuations were the result of significant changes in output reported by the manufacturing countries, namely India, Switzerland and the United States. For instance, India manufactured 21.7 tons of methylphenobarbital in 2008, but reported no data on manufacture for 2010. In 2010, global manufacture of methylphenobarbital amounted to 3.4 tons, all of which was reported by Switzerland. Switzerland also accounted for over 95 per cent of global stocks of methylphenobarbital at the end of 2010. Croatia, Switzerland, Slovenia and Italy (in descending order) were the main users of the substance in 2010.

114. International trade in methylphenobarbital also fluctuated during the period 2001-2010, averaging about 2.9 tons per year between 2008 and 2010. The main exporters of methylphenobarbital in 2010 included Switzerland, the United States, Germany and India (in descending

order). Nine countries reported imports of methylphenobarbital in 2010. In 2010, the main importers of methylphenobarbital continued to be the United States, Croatia, Germany (for re-export) and Italy (in descending order); their imports together accounted for 96 per cent of global imports of the substance.

115. From 1996 to 2005, Germany was the sole manufacturer of allobarbital, manufacturing between 393 kg and 4 tons of the substance each year. In 2006 and 2007, Belgium started manufacturing the substance, reporting an output of 2.5 tons (25 million S-DDD) in 2006 and 1.4 tons (14 million S-DDD) in 2007 (mainly for export). While it reported no manufacture of allobarbital during the period 2006-2008, Germany resumed its manufacture of the substance in 2009 (1.1 tons, or 11.3 million S-DDD). In 2010, no manufacture of allobarbital was reported by any country. As a result, global stocks of the substance decreased from 2.6 tons in 2009 to 1.2 tons in 2010; those stocks were held mainly in Germany, Switzerland and Turkey. During the period 2008-2010, Hungary, Israel, Poland, Turkey and Yemen were the main consumers of the substance.

116. International trade in allobarbital decreased significantly, from 1.6 tons in 2008 to 825 kg in 2010. Germany was the leading exporter of the substance in 2010 (475 kg); it was followed by Switzerland (200 kg) and Jordan (149 kg). The major importers of allobarbital in 2010 were Switzerland (400 kg), Turkey (200 kg) and Yemen (149 kg).

117. Secbutabarbital was manufactured intermittently during the period 2001-2010. No manufacture of the substance was reported for 2000, 2004 or 2005. After Germany stopped manufacturing the substance in 2003, the United States became the sole manufacturer, reporting an output of 31 kg in 2010. Lebanon continued to be the main importer of secbutabarbital, and it reported imports of 25 kg of the substance in 2010.

118. Manufacture of butobarbital was last reported by Denmark in 1998 (1.3 tons) and by Germany in 2008 (117 kg). No manufacture of that substance was reported after 2009. About 21 kg of butobarbital were traded in 2010; Jordan, the Netherlands and Belgium (in descending order) were the importing countries. Germany and the Netherlands were the major exporters of the substance in 2010.

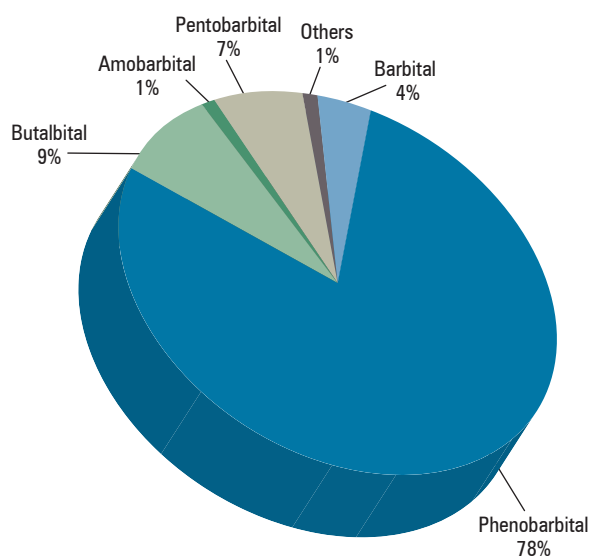
## **Barbiturates in Schedules II, III and IV**

119. Of the 12 barbiturates listed in Schedules II, III and IV of the 1971 Convention, the following five substances accounted, on average, for 99 per cent of the total reported manufacture of those barbiturates in the five-year

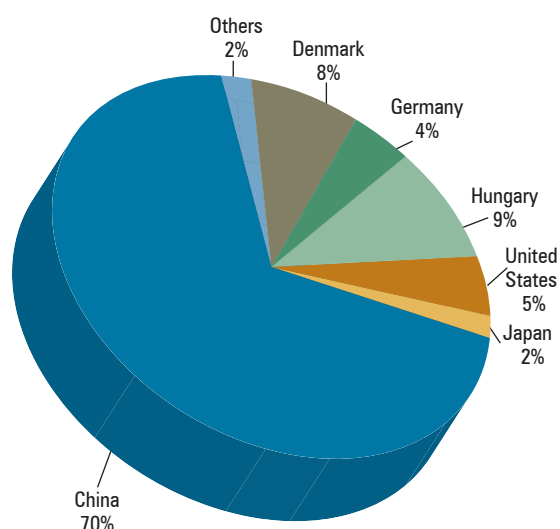


period 2006-2010: phenobarbital (77 per cent), butalbital (9.4 per cent), pentobarbital (7.8 per cent), barbital (3.4 per cent) and amobarbital (1.6 per cent). The shares of total manufacture of those substances in 2010 are presented in figure 28. In 2010, China (70 per cent), Hungary (9 per cent), Denmark (8 per cent), the United States (5 per cent), Germany (4 per cent) and Japan (2 per cent) together accounted for 98 per cent of the total manufacture of the entire group of barbiturates (see figure 29).

**Figure 28. Barbiturates in Schedules II, III and IV: share of total reported manufacture, by substance, 2010**



**Figure 29. Barbiturates in Schedules II, III and IV: total reported manufacture, selected countries, 2010**



## Other sedative-hypnotics

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

121. GHB is mainly used in the treatment of narcolepsy and, more rarely, alcoholism. Data for GHB may still be incomplete, although most countries have now extended all national control measures to this substance. Reported manufacture of GHB increased steadily during the period 2006-2010, reaching a peak of 59 tons in 2010, a significant increase of over 60 per cent compared with 2009 (36.9 tons). The United States, a major manufacturer of GHB, accounted for almost 80 per cent of global manufacture of the substance in 2010. Other major manufacturing countries in 2010 included Germany and Ukraine. International trade in GHB also increased. In 2010, about 30 countries reported imports of GHB totalling 15.8 tons, with Italy, France, the Russian Federation and the United Kingdom (in descending order) being the main importers of the substance. Germany, Ukraine and the United States (in descending order) were the leading exporters of GHB in 2010. United States, Italy, the Russian Federation and the United Kingdom (in descending order) had the highest calculated consumption of GHB in 2010.

122. Zolpidem is used to induce sleep. Global manufacture of zolpidem fluctuated between 24.2 and 51 tons during the period 2001-2010, reflecting the changing output of France, the main manufacturer of the substance. In 2010, total reported manufacture of zolpidem amounted to 46 tons (4.6 billion S-DDD), 86 per cent of which was accounted for by France (31.5 tons) and Israel (8 tons). Other major manufacturers of the substance were the Czech Republic (3.2 tons) and Argentina (2.8 tons). Other countries, including Japan, Italy, the United States, Canada, Brazil and China (in descending order), also reported manufacture of zolpidem in 2010. Zolpidem is one of the more widely traded and used psychotropic substances, with more than 100 countries reporting imports of the substance in the period 2008-2010. France and India were the two main exporters of zolpidem in 2010, accounting for about 52 per cent of global exports of the substance. France and the United States were also the largest consumers of the substance in 2010; they were followed by Japan, Spain, Hungary and Germany in 2010.

123. The manufacture of ethchlorvynol was last reported by the United States in 1999 (1.3 tons). The manufacture of ethinamate was last reported by Germany in 1988



(500 kg), and the manufacture of methypylon was last reported by the United States in 1990 (2.1 tons). Very small stocks of ethinamate and methypylon were reported by Canada and the United States in 2010. There were no reports of international trade in ethchlorvynol, ethinamate or methypylon after 1991.

## **Analgesics**

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