COMMENTS ON THE REPORTED STATISTICS ON NARCOTIC DRUGS

Summary

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

The demand for natural alkaloids that are obtained from the opium poppy plant (morphine, codeine, thebaine and oripavine) continued to be high in 2012, in line with the trend of the preceding 20 years. About 83 per cent of the morphine and 91 per cent of the thebaine manufactured worldwide were obtained from poppy straw, while the rest was extracted from opium. Australia, France, Hungary, Spain and Turkey were the main producer countries in 2012, together accounting for about 90 per cent of global production of poppy straw rich in morphine. Australia, France and Spain were the main producers of poppy straw rich in thebaine, together accounting for about 97 per cent of global production of poppy straw rich in thebaine. India remained the only licit supplier of opium to the world market.

Manufacture of morphine followed a rising trend over the past two decades, reaching almost 440 tons in 2007; after 2007, morphine manufacture fluctuated and reached a record level of more than 474 tons in 2012. Morphine and codeine are used in therapy and for conversion into other opioids. Manufacture of thebaine increased sharply after the late 1990s and reached an all-time high of 158 tons in 2012. Manufacture of codeine stood at 414 tons in 2012, the highest level ever reported. Thebaine itself is not used in therapy, but it is an important starting material for the manufacture of a number of opioids. Australia, France, the United Kingdom of Great Britain and Northern Ireland and the United States of America continued to be the leading manufacturers of natural alkaloids.

Codeine has been the most commonly consumed opiate in the world in terms of the number of countries in which it is consumed. In 2012, its use reached 292 tons, the highest level ever reported. Global consumption of morphine for the treatment of severe pain rose by a factor of more than four over the past two decades, reaching the record level of 44 tons in 2012. That increase was due mainly to increasing consumption in high-income countries, while consumption levels in most other countries remained very low. Australia, Canada, Japan, New Zealand, the United States and some countries in Europe accounted for more than 93 per cent of total morphine consumption in 2012.

In 2012, the semi-synthetic opioid hydrocodone remained the narcotic drug with the highest consumption in terms of doses consumed. Global consumption of hydrocodone amounted to 46 tons in 2012. High global consumption of oxycodone and hydromorphone continued in 2011 (94.9 tons and 3.4 tons, respectively). As in the past, the United States was the principal consumer country of those three opioids. The use of dihydrocodeine (27.5 tons in 2012) decreased slightly, while that of pholcodine increased to 12 tons in 2012.

Fentanyl has been the synthetic opioid with the highest consumption in terms of doses consumed. Consumption of fentanyl has followed an increasing trend, reaching the all-time high of 1.7 tons in 2010 and standing at 1.3 tons in 2012. Consumption of methadone also followed a rising trend, stabilizing at 31.1 tons in 2012. Diphenoxylate consumption also increased in recent years, reaching a new all-time high in 2012 (25.2 tons). Global use of dextropropoxyphene (169 tons in 2012) and pethidine (6.7 tons in 2012) has shown a downward trend in the past 10 years.

1. The present comments are intended to facilitate the use of the statistical information on the licit production, manufacture, consumption,¹ utilization² and stocks of, as well as trade in, opiate raw materials, the main opioids, including synthetic narcotic drugs under international control, and cannabis, coca leaf and cocaine that is presented in the tables of reported statistics (see pages 123-242 and 397-432). Unless otherwise indicated, the comments refer to developments during the period 1993-2012.

2. The tables of reported statistics in part four of and annexes IV and V to the present report contain data furnished by Governments to the International Narcotics Control Board (INCB) in accordance with article 20 of the Single Convention on Narcotic Drugs of 1961.³ The most recent statistical data reflected in the comments are those relating to 2012. The failure by some Governments to submit reports or to provide precise and complete reports may have a bearing on the accuracy of some of the information presented below.⁴ The most pertinent conclusions and recommendations of INCB based on the analysis of statistical data are included in chapter II of its annual report.⁵

Opiate raw materials

3. Opium and poppy straw are the raw materials obtained from the opium poppy plant (*Papaver somniferum*), from which alkaloids such as morphine, thebaine, codeine and oripavine are extracted. Concentrate of poppy straw is a product obtained in the process of extracting alkaloids from poppy straw. It is controlled under the 1961 Convention.

4. The demand for alkaloids increased significantly over the 20-year period from 1993 to 2012. Throughout the period, the increased demand was covered mainly by poppy straw. In 2012, approximately 83 per cent of the morphine and about 91 per cent of the thebaine manufactured worldwide were obtained from poppy straw, while the rest was obtained from opium.

5. Details on trends in the production and use of opium and poppy straw, and on the manufacture and use of the principal opiates,⁶ including concentrate of poppy straw, are provided below. The current balance between the supply of opiate raw materials and the demand for opiates for medical and scientific needs is examined in a separate section of the present publication (see pages 93-100).

Opium

6. Opium (also called "raw opium") is the latex obtained by making incisions on the green capsules of opium poppy plants. For statistical and comparison purposes, data on the production of and trade in opium are reported at 10 per cent moisture content. When appropriate, the data on opium are also expressed in morphine equivalent,⁷ in order to enable comparison between opium and poppy straw. Figure 1 shows the licit production, stocks and use (consumption plus utilization) of opium during the period 1993-2012, expressed in morphine equivalent. Not included in the data on stocks and use are the amounts of illicitly produced opium that were seized and released for licit purposes. Global opium production remained stable in 2012, with only a slight decrease (from 789.1 to 765.2 tons). The amount of opium imported and exported increased. Almost all opium available globally was manufactured to produce other drugs, and only a small amount (23.3 tons) was used for Schedule III preparations.

7. India has been the leading licit producer of opium for several decades, accounting for 98 per cent of global production. Other opium-producing countries in recent times have been China,⁸ the Democratic People's Republic of Korea and Japan (see table I). Production, which fluctuated in the period 2000-2008, remained at a high level with a small decrease with respect to 2011 stabilizing at 765 tons in 2012 (or 84 tons in morphine equivalent), compared to 789 tons in 2011. In China, poppy straw has replaced

¹For the purposes of the Single Convention on Narcotic Drugs of 1961, a drug is regarded as "consumed" when it has been supplied to any person or enterprise for retail distribution, medical use or scientific research; and "consumption" is construed accordingly (art. 1, para. 2).

²The parties shall furnish the International Narcotics Control Board (INCB) with statistical returns on the utilization of narcotic drugs for the manufacture of other drugs, of preparations in Schedule III of the 1961 Convention and of substances not covered by the Convention and on the utilization of poppy straw for the manufacture of drugs.

³United Nations, *Treaty Series*, vol. 520, No. 7515.

⁴Details on the submission of statistical reports by individual Governments are contained in annex I to the present publication.

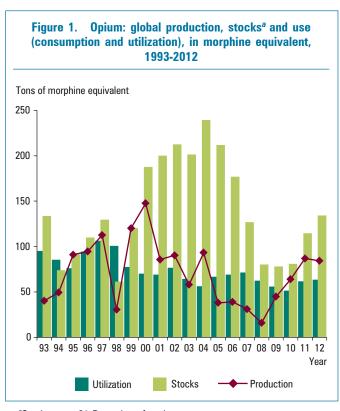
⁵*Report of the International Narcotics Control Board for 2013* (United Nations publication, Sales No. E.14.XI.1).

 $^{^{6^{\}rm co}}$ Opiate" is the term generally used to designate drugs derived from opium and their chemically related derivatives, such as the semi-synthetic alkaloids.

⁷The morphine or thebaine equivalent is calculated by INCB on the basis of the industrial yield of the respective alkaloid obtained from opium or poppy straw. Lesser alkaloids contained in opium or poppy straw that are convertible into morphine or thebaine have also been included, adjusted by appropriate conversion rates, whenever the Board has been informed of their extraction in commercially significant quantities.

⁸Data for China do not include statistics relating to the Hong Kong Special Administrative Region of China, the Macao Special Administrative Region of China or Taiwan Province of China.

opium as the main raw material for the manufacture of alkaloids; in 2012, China reported a small amount of production of opium (14 tons), and the Democratic People's Republic of Korea produced 516 kg of opium.



 $^{\rm a}{\rm Stocks}$ as at 31 December of each year.

8. India is the only licit supplier of opium to the world market, and most of the opium produced in India is destined for export. Opium exported from India contains morphine in a concentration of 9.5 to 12.0 per cent, codeine in a concentration of about 2.5 per cent and thebaine in a concentration of 1.0 to 1.5 per cent. As shown in figure 2, imports from India had fluctuated in recent years and stood at about 470 tons (or 52 tons in morphine equivalent) in 2012. The United States of America and Japan continued to be the main importing countries, accounting for 70 per cent and 25 per cent of total imports in 2012, respectively. The Islamic Republic of Iran imported opium irregularly; in 2012, it accounted for 2.85 per cent of total imports.

9. The bulk of opium is used for the extraction of alkaloids. Total utilization of licitly produced opium for the extraction of alkaloids followed a declining trend during the period under consideration. Utilization remained stable at 539 tons in 2012 (excluding the utilization of seized opium in the Islamic Republic of Iran),⁹ or 59 tons in morphine equivalent, in 2012 (see figure 3). Iran (Islamic Republic of), the United States, India and Japan, in descending order, are the main users of opium for the extraction of alkaloids, together accounting for 99 per cent of the global total in 2012. The Democratic People's Republic of Korea is the only other country reporting the use of opium (0.5 per cent) for the extraction of alkaloids in 2012. Details on the utilization of opium for the extraction of alkaloids and the alkaloids obtained are provided in table III.

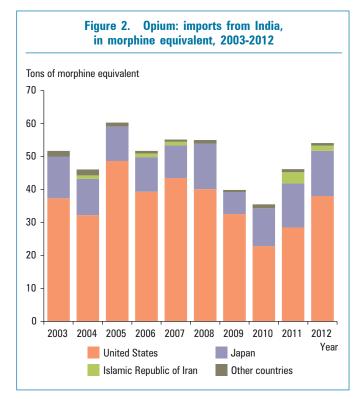
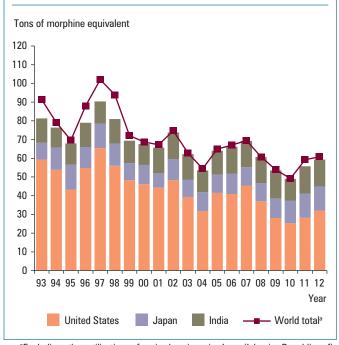


Figure 3. Opium: utilization for the extraction of alkaloids, in morphine equivalent, 1993-2012



 $^a\mathrm{Excluding}$ the utilization of seized opium in Iran (Islamic Republic of), Myanmar and Turkey.

⁹In the Islamic Republic of Iran, in addition to licitly produced opium imported from India, seized opium is released regularly in large quantities for the extraction of alkaloids. The yield of alkaloids extracted from seized opium is usually less than from licitly produced opium.

10. Opium is also consumed in many countries in the form of preparations, mainly for the treatment of diarrhoea and coughs. Most of those preparations are included in Schedule III of the 1961 Convention.¹⁰ Global consumption of opium has fluctuated, averaging about 16.8 tons per year since 2001. Total consumption in 2012 was over 23 tons, which corresponds to 230 million defined daily doses for statistical purposes (S-DDD).¹¹ In 2012, consumption and use of opium for the manufacture of preparations in Schedule III amounted to 13 tons in China and 4 tons in both France and India.

11. Global stocks of opium reached their peak of the last decade in 2004 (2,176 tons) and then began to decrease. In 2012, they increased slightly to 1,220 tons (or 134.2 tons of morphine equivalent), having stood at 1,041 tons in 2011. India continued to hold the largest stocks (950,000 tons, or 77 per cent of the global total), followed by the United States (137.2 tons), Japan (108.4 tons) and China (18.1 tons).¹²

Poppy straw

12. Poppy straw consists of all parts of the opium poppy plant after mowing except the seeds. Morphine is the predominant alkaloid found in the varieties of opium poppy plant cultivated in most producing countries. Commercial cultivation of the opium poppy plant with high thebaine content started in the second half of the 1990s. In the present publication, poppy straw produced from varieties of opium poppy plant rich in morphine is referred to as "poppy straw (M)", poppy straw produced from varieties of opium poppy plant rich in thebaine is referred to as "poppy straw (T)", and the poppy straw produced from varieties of opium poppy plant rich in codeine is referred to as "poppy straw (C)". Some of those varieties contain, in addition to their main alkaloid (morphine, thebaine or codeine), other alkaloids that can be extracted, such as morphine, codeine, thebaine or oripavine.

13. The concentration of alkaloids in poppy straw varies significantly among the producing countries.¹³ Production levels of poppy straw among those countries can be

compared only by use of a common denominator, which is the morphine or thebaine equivalent of the quantity of poppy straw produced in each country. Commercial cultivation of the opium poppy plant with a high codeine content started in Australia in 2010. For statistical purposes, the quantities of poppy straw produced from that variety of opium poppy are recorded under "poppy straw (M)".

Poppy straw produced from opium poppy rich in morphine (poppy straw (M))

14. Although the submission of statistics on the production of poppy straw is voluntary, most countries cultivating opium poppy plants for the extraction of alkaloids provide such information. Global production of poppy straw (M) expressed in morphine equivalent followed an increasing trend in the two decades prior to 2012. Production fluctuated sharply, mainly because of weather conditions and in response to the demand in manufacturing countries. Production reached about 430 tons in morphine equivalent in 2003 and declined to about 218 tons in 2008. Production then increased strongly, reaching 394 tons in 2012 after a peak of about 454 tons in 2011 (see figure 4). Throughout the two decades prior to 2012, Australia, France, Spain and Turkey were the main producer countries. In 2012, the leading producer was Australia (174 tons in morphine equivalent, accounting for 44 per cent of global production), followed by France (92 tons, or 23 per cent), Spain (83 tons, or 21 per cent) and Turkey (14 tons, or 4 per cent). Other main producers of poppy straw (M) in 2012 were Austria, China, Hungary, Slovakia, the former Yugoslav Republic of Macedonia and the United Kingdom of Great Britain and Northern Ireland, together accounting for the remaining 8 per cent of global production in morphine equivalent.

15. In 2012, production of poppy straw (M) increased in Australia, France and Spain, while it decreased in Turkey (from 164 to 14 tons). Changes in the area cultivated with the opium poppy plant, the amounts of poppy straw (M) harvested and the yields obtained in producing countries are shown in table II.

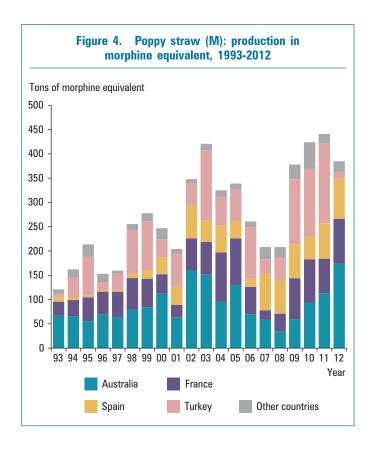
16. International trade in poppy straw (M) as a raw material continues to be limited, with the Czech Republic being the major exporter of poppy straw for the purpose of extraction of alkaloids (see annex IV, table 1). The Czech Republic, which cultivates opium poppy plants primarily for the production of seeds, produces poppy straw as a by-product and exports it to Slovakia, where it is used for the extraction of alkaloids. Such poppy straw has a significantly lower morphine content than poppy straw obtained from opium poppy plants cultivated for the production of alkaloids. In 2012, imports by Slovakia of poppy straw (M) from the Czech Republic decreased to 1,586 tons (in gross weight).

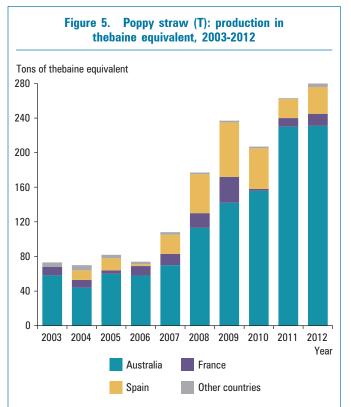
¹⁰Preparations included in Schedule III of the 1961 Convention are exempt from several control measures that are otherwise mandatory for preparations containing narcotic drugs, including reporting on their consumption and international trade.

¹¹The list of defined daily doses for statistical purposes and an explanation of that concept are contained in the notes to table XIV.1.

¹²For production of, stocks of and demand for opium, see also the section entitled "Supply of opiate raw materials and demand for opiates for medical and scientific purposes", on pages 93-100.

¹³For example, in the period 2009-2012, the industrial yield of anhydrous morphine alkaloid obtained from poppy straw (M) during the manufacture of anhydrous morphine alkaloid contained in concentrate of poppy straw (AMA (CPS)) averaged 1.41 per cent in Australia, 1.35 per cent in France, 1.22 per cent in Spain and 0.39 per cent in Turkey.





17. In 2012, utilization of poppy straw (M) in the main user countries amounted to 26,139 tons in gross weight in Turkey, 9,362 tons in Australia,¹⁴ 6,550 tons in France and 5,315 tons in Spain. Further details on the utilization of poppy straw (M) for the extraction of alkaloids and the yields obtained are contained in table IV.

Poppy straw produced from opium poppy rich in thebaine (poppy straw (T))

18. Australia and France started to report to INCB the production of poppy straw (T) in 1999. Spain reported the production of poppy straw (T) for the first time in 2004. China and Hungary have reported sporadic production in recent years. More details on the production of poppy straw (T) can be found in table II.

19. Global production of poppy straw (T) expressed in thebaine equivalent during the period 2003-2012 is shown in figure 5. In 2012, total production amounted to about 288 tons in thebaine equivalent.¹⁵ Australia remained the leading producer of thebaine equivalent (231 tons, accounting for 80 per cent of global production), followed by Spain (31 tons, or 10.7 per cent) and France (14 tons, or 4.8 per cent).

20. All poppy straw (T) is used in the producing and manufacturing countries for the extraction of alkaloids. The quantities used, the alkaloids obtained from poppy straw (T) and the respective yields are shown in table V.

Poppy straw produced from opium poppy rich in codeine (poppy straw (C))

21. In 2009, Australia reported for the first time the cultivation of poppy straw (C) for commercial purposes, and was the sole producer in the world. This new variety was cultivated specifically to meet the high global demand for codeine. In 2010, 415 tons were produced and in 2011, 1,390 tons. In 2012 the level remained the same as in 2011.

Poppy straw used for decorative purposes

22. In some countries, poppy straw is used for decorative purposes. Austria was the main exporter of poppy straw for such purposes in 2012. The main importers in 2012 were Germany and Switzerland.

Concentrate of poppy straw

23. Most countries using poppy straw for the extraction of alkaloids first manufacture an intermediate product called "concentrate of poppy straw", although in some countries morphine or thebaine is manufactured directly

¹⁴This figure is being clarified with the Government.

¹⁵The thebaine equivalent of the thebaine and oripavine alkaloids contained in poppy straw (M) is also included, where appropriate, in the data referred to in this paragraph.

from poppy straw in a continuous process, which may involve a number of other intermediate products (for details, see tables IV and V). Until the second half of the 1990s, only concentrate of poppy straw containing morphine as the main alkaloid was manufactured. Since then, concentrate of poppy straw containing mainly thebaine, oripavine or codeine has started to be manufactured. Concentrate of poppy straw may contain a mixture of alkaloids, and more alkaloids than just the principal alkaloid may be extracted in industrial processes. The different types of concentrate of poppy straw are referred to by the main alkaloid contained in them.¹⁶

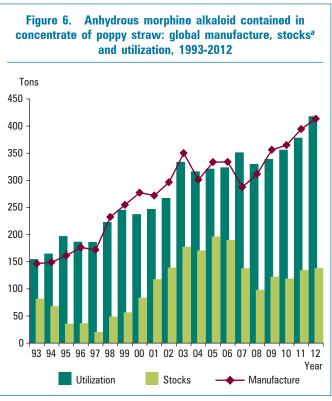
24. Since the actual content of alkaloids in concentrate of poppy straw may vary significantly, for purposes of comparison and for statistical purposes, all data referring to concentrate of poppy straw are expressed in terms of the quantity of the respective anhydrous alkaloid contained in the material. The quantities of anhydrous morphine alkaloid contained in concentrate of poppy straw are referred to as AMA (CPS), those of anhydrous thebaine alkaloid as ATA (CPS), those of anhydrous oripavine alkaloid as AOA (CPS) and those of anhydrous codeine alkaloid as ACA (CPS). The totals of all the individual alkaloids contained in concentrate of poppy straw are examined below, expressed in terms of 100 per cent of the respective anhydrous alkaloid content.¹⁷

Anhydrous morphine alkaloid contained in concentrate of poppy straw (AMA (CPS))

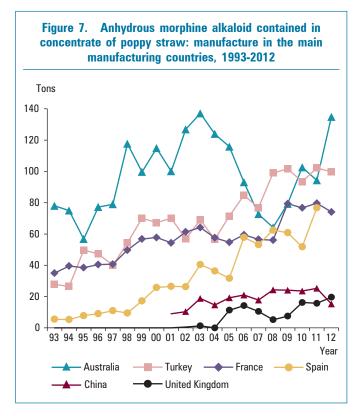
25. AMA (CPS) continues to be the most important and most widely used alkaloid among the alkaloids contained in concentrate of poppy straw. Figure 6 shows the trends in its manufacture, stocks and utilization in the period from 1993 to 2012.

26. Global manufacture of AMA (CPS) has risen sharply since the 1990s and fluctuated between 270 and 413 tons (which was the level in 2012) in the period 2001-2012. Trends in the manufacture of AMA (CPS) in the main manufacturing countries in the period 1993-2012 are presented in figure 7. Australia and Turkey alternate as leading manufacturer. In 2012, Australia accounted for 134.8 tons, or 32.6 per cent of global manufacture of 413 tons, followed by Turkey (99.6 tons, or 24 per cent),

France (74 tons, or 17.9 per cent) and Spain (69.5 tons, or 16 per cent). Other countries reporting manufacture of AMA (CPS) for 2012 were the United Kingdom (19.5 tons), China (15.3 tons) and the former Yugoslav Republic of Macedonia (173 kg).



^aStocks as at 31 December of each year.

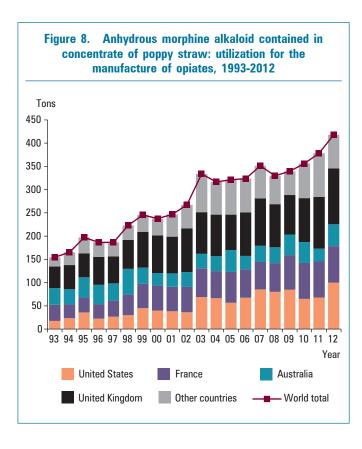


¹⁶Currently, the following types are traded: (*a*) concentrate of poppy straw containing morphine as the main alkaloid; (*b*) concentrate of poppy straw containing thebaine as the main alkaloid; (*c*) concentrate of poppy straw containing oripavine as the main alkaloid; and (*d*) concentrate of poppy straw containing codeine as the main alkaloid.

¹⁷The comments on concentrate of poppy straw in this publication are not directly comparable with comments on concentrate of poppy straw contained in editions of this publication prior to 2005, since at that time concentrate of poppy straw was expressed at 50 per cent of the main alkaloid contained therein.

27. Global exports of AMA (CPS) increased to 240 tons in 2003 and have fluctuated since then. In 2012, they amounted to 239 tons. Turkey remained the main exporting country in 2012 (with 102.7 tons, accounting for 42.9 per cent of global exports), followed by Australia (72.6 tons, or 30 per cent) and Spain (62.6 tons, or 26 per cent). The United Kingdom and the United States have been the leading importers of AMA (CPS), together accounting for 76 per cent of the world total in 2012. Other major importing countries were, in descending order, Norway, France, South Africa, Italy, Switzerland and Slovakia. Further details on international trade in AMA (CPS) can be found in annex IV, tables 1 and 2.

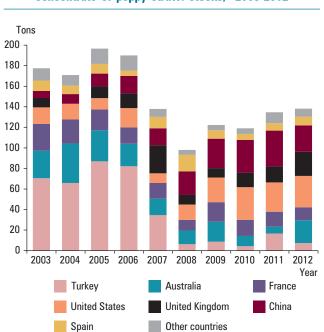
28. AMA (CPS) is an intermediate product for the manufacture of morphine. It is also used in continuous manufacturing processes for the manufacture of codeine. Utilization of AMA (CPS) increased steadily until 2003 and has been fluctuating since then (see figure 8). In 2012, total world utilization amounted to 418 tons. The United Kingdom, at 120.4 tons, accounted for 28 per cent of the global utilization of AMA (CPS), followed by the United States (99.8 tons, or 23 per cent), France (78.6 tons, or 18 per cent) and Australia (46 tons, or 11.2 per cent).



29. Global stocks of AMA (CPS) reached 138 tons in 2012 (see figure 9). The United States held the largest stocks in 2012 (30.5 tons, or 22 per cent of the global total); other countries holding significant stocks of AMA (CPS) in 2012

were China (25.7 tons, or 18.6 per cent) and the United Kingdom (23 tons, or 16.9 per cent).





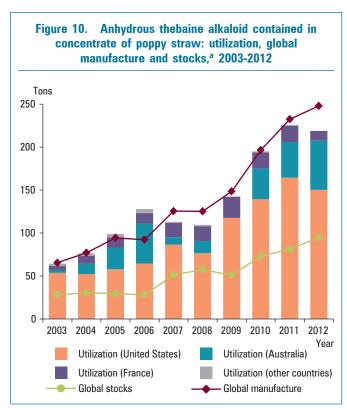
^aStocks as at 31 December of each year.

Anhydrous thebaine alkaloid contained in concentrate of poppy straw (ATA (CPS))

30. Figure 10 provides an overview of the manufacture, stocks and utilization of ATA (CPS) during the period 2003-2012. Industrial manufacture of ATA (CPS) started in 1998 and has increased rapidly since then, peaking at 247 tons in 2012, which represented an increase of 15 tons over the level in 2011. Australia, Spain and France, in descending order, have been the only manufacturing countries, accounting for 92 per cent, 3.6 per cent, and 3.5 per cent, respectively, of the global total in 2012. Australia was the main exporter, accounting for 180 tons, or 93.2 per cent, of global exports in 2012. The United States has been the leading importer of ATA (CPS); in 2012 it accounted for 98 per cent of total imports.

31. ATA (CPS) is an intermediate product for the manufacture of thebaine. Global utilization of ATA (CPS) increased sharply from 22 tons in 2000 to 218 tons in 2012, slightly less than the highest level ever, 226 tons, which was reported in 2011. This reflects the growing demand for thebaine and the substances that may be obtained from it. The United States continued to be the main user in 2012 (accounting for 68 per cent of global utilization), followed by Australia (26 per cent) and France (5 per cent). Global stocks of ATA (CPS) stood

at 94.7 tons in 2012. The United States (57 tons) and Australia (34 tons) and accounted for 96 per cent of global stocks.



^aStocks as at 31 December of each year.

Anhydrous oripavine alkaloid contained in concentrate of poppy straw (AOA (CPS))

32. Manufacture of AOA (CPS) in commercially usable quantities started in 1999. Australia was the main manufacturing country in 2012, with 91.7 per cent of the world total of 23.4 tons. Spain manufactured 1.9 tons. Total utilization of AOA (CPS) in 2012 amounted to 28.4 tons. AOA (CPS) has been used in Switzerland (48.9 per cent), the United States (47.5 per cent) and Australia (3.5 per cent) for the manufacture of other drugs. Global stocks of AOA (CPS) have been fluctuating since 2001. In 2012, they stood at 9.4 tons, of which 66 per cent was held in the United States and 33 per cent in Australia.

Anhydrous codeine alkaloid contained in concentrate of poppy straw (ACA (CPS))

33. Manufacture of ACA (CPS) amounted to 36 tons in 2012. Australia, France, Turkey and Spain have been the only countries manufacturing ACA (CPS), accounting, respectively, for 61 per cent, 20 per cent, 18 per cent and 1.2 per cent of the global total in 2012. ACA (CPS) is used for the extraction of codeine. Global utilization of ACA (CPS) amounted to 10.6 tons in 2012, of which 94 per cent was accounted for by France and 5.5 per cent by Norway. Global stocks of ACA (CPS) in 2012 stood at 9.4 tons, most of which was held in the United States (4.4 tons) and Australia (3.8 tons).

Opiates and opioids

34. "Opiate" is the term generally used to designate drugs derived from opium and their chemically related derivatives, such as the semi-synthetic alkaloids, while "opioid" is a more general term for both natural and synthetic drugs with morphine-like properties, although the chemical structure may differ from that of morphine.¹⁸

35. Opioids are used mostly for their analgesic properties to treat severe pain (fentanyl, hydromorphone, methadone, morphine and pethidine), moderate to severe pain (buprenorphine¹⁹ and oxycodone) and mild to moderate pain (codeine, dihydrocodeine and dextropropoxyphene), as well as to induce or supplement anaesthesia (fentanyl

and fentanyl analogues such as alfentanil and remifentanil). They are also used as cough suppressants (codeine, dihydrocodeine and, to a lesser extent, pholcodine and ethylmorphine), to treat gastrointestinal disorders, mainly diarrhoea (codeine and diphenoxylate) and to treat addiction to opioids (buprenorphine and methadone).

Natural alkaloids

36. Morphine, codeine, thebaine, noscapine, oripavine, papaverine and narceine are alkaloids contained in opium or poppy straw. Morphine and codeine are under international control because of their potential for abuse, while thebaine and oripavine are under such control because of their convertibility into opioids subject to abuse. Noscapine, papaverine and narceine are not under international control. Morphine is the prototype of natural opiates and many opioids, and because of its strong analgesic potency, it is used as a reference parameter for comparative purposes.

¹⁸From a clinical point of view, opioids may be classified according to their actions compared with those of morphine: similar affinity (agonist), competitive (antagonist) or mixed (agonist/antagonist) for the same receptor sites (the so-called opioid receptors) in the central and peripheral nervous system.

¹⁹Buprenorphine is controlled under the Convention on Psychotropic Substances of 1971. Comments on its licit movement are contained in para. 96 below.

English — Comments Part two Deuxième partie

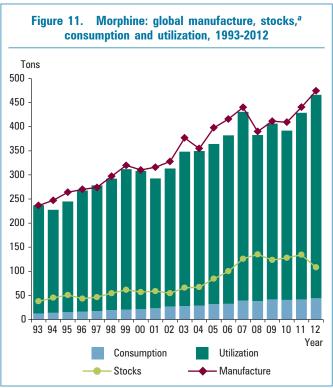
Segunda

parte

Morphine

37. Figure 11 presents data on the manufacture,²⁰ stocks, consumption and utilization of morphine in the period 1993-2012. Global manufacture of morphine doubled during the 20-year period, increasing from about 236 tons in 1993 to 474.2 tons in 2012, a further increase from the 440.3 tons recorded in 2011. Almost 90 per cent of the morphine manufactured globally is converted into other narcotic drugs, as well as into substances not covered by the 1961 Convention (see paras. 42-44 below). The rest is used for medical purposes.

38. In 2012, the leading manufacturing country of morphine was the United Kingdom (110.6 tons, or 23 per cent of global manufacture), followed by the United States (89 tons, or 19 per cent), France (76.4 tons, or 16 per cent), Australia (48.5 tons, or 10 per cent), China (28 tons, or 6 per cent) and Iran (Islamic Republic of) (25.5 tons, or 5 per cent). Together, those six countries accounted for 79 per cent of global manufacture. Five other countries reported the manufacture of morphine in 2012 in quantities of more than 10 tons: Norway (18.1 tons), Japan (14.4 tons), Hungary (14 tons), India (11.5 tons)²¹ and South Africa (10.3 tons).

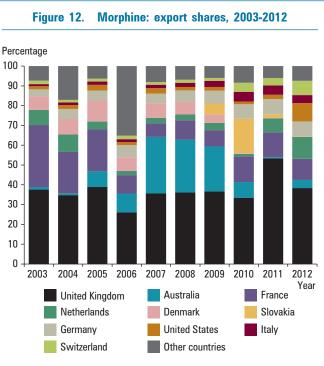


^aStocks as at 31 December of each year.

²⁰In Australia, Brazil, China, Iran (Islamic Republic of), Italy, Norway, Portugal, Turkey and the United Kingdom, concentrate of poppy straw is used in continuous industrial processes for the manufacture of other narcotic drugs, without first separating morphine. For statistical and comparative purposes, the theoretical quantity of morphine involved in such conversions is calculated by INCB and included in the present publication in the statistics on global manufacture and utilization of morphine.

²¹This figure was calculated by INCB using available data series; it is being clarified with the Government.

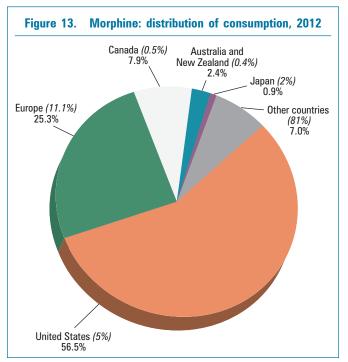
39. Total exports of morphine amounted to 10.1 tons in 2012. As can be seen in figure 12, the leading exporting country continued to be the United Kingdom (38 per cent of global exports), followed by the Netherlands (11 per cent). Seven countries imported more than 1 ton of morphine in 2012: Canada (5.2 tons), Germany (4.1 tons), Netherlands (3.1 tons), Austria (2.2 tons), the United Kingdom (1.6 tons), Norway (1.5 tons) and Hungary (1.2 tons). Further details on exports and imports of morphine can be found in tables 3 and 4, respectively, of annex IV.



40. Global consumption of morphine, excluding preparations included in Schedule III of the 1961 Convention, increased by a factor of 3.5 between 1993 and 2012. Consumption grew steadily from 12.5 tons in 1993, reaching 44 tons (or 440 million S-DDD) in 2012. The differences in consumption levels between countries continued to be very significant (see figure 13 and table XIV), owing to various economic, knowledge, regulatory and other factors influencing the use of morphine in the treatment of pain.

41. In 2012, the United States was the country with the highest consumption of morphine (24.9 tons, or 57 per cent of global consumption), followed by Canada (3.5 tons, or 8 per cent). Thus, together they accounted for almost two thirds of the global consumption of morphine, excluding preparations included in Schedule III of the 1961 Convention. A quarter of the world's morphine is consumed in Europe, and significant consumption was reported by the United Kingdom (2.4 tons, or 6 per cent), France (2 tons, or 5 per cent), Austria (1.6 tons, or 3 per cent), Germany (1.5 tons, or 3 per cent) and Italy (1 ton, or 2 per cent).

On the basis of defined daily doses for statistical purposes consumed per million inhabitants per day, the country with the highest consumption was Austria (5,508 S-DDD), where morphine is used for the treatment of pain as well as in substitution treatment for opioid addiction. In six other countries, morphine consumption was over 1,000 S-DDD per million inhabitants per day in 2012: Canada (2,838 S-DDD), Denmark (2,291 S-DDD), United States (2,153 S-DDD), Australia (1,174 S-DDD), Switzerland (1,107 S-DDD) and United Kingdom (1,089 S-DDD).



Note: Percentages in parentheses refer to share of the world population (i.e. total population of all reporting countries).

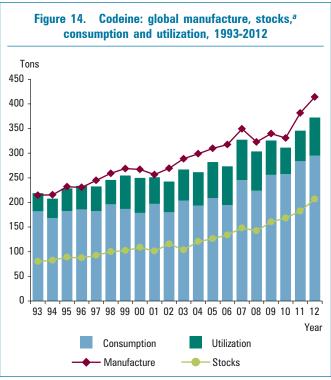
42. In some countries, morphine is used for the manufacture of preparations included in Schedule III of the 1961 Convention. In 2012, countries using morphine for that purpose in significant quantities were China, which reported the use of 7.4 tons of morphine for the manufacture of such preparations, and Italy (974 kg).

43. The largest share of morphine is used for conversion into other opiates, such as codeine, ethylmorphine and pholcodine (see table VI). The amounts utilized for that purpose, which fluctuated around the level of 200 tons per year until the beginning of the 1990s, have increased steadily since then, reaching 419 tons in 2012. Of the quantity utilized in 2012, 94 per cent was converted into codeine. The six main countries reporting conversion of morphine into codeine in 2012 were the United Kingdom (92.8 tons, or 23 per cent), France (78 tons, or 20 per cent), Australia (46.5 tons, or 12 per cent), the United States (42.9 tons, or 11 per cent), Iran (Islamic Republic of) (26 tons, or 7 per cent) and Norway (17.1 tons, or 4 per cent), which together accounted for 77 per cent of global utilization. 44. Morphine is also used for the manufacture of substances not controlled under the 1961 Convention, such as noroxymorphone, nalorphine and naloxone. The quantity of morphine utilized for that purpose fluctuated considerably in the last two decades, amounting to 2,637 kg in 2012, of which 1,910 kg was used by the United States and 265 kg by France.

45. Global stocks of morphine stood at 108 tons in 2012, a decline from the 133 tons reported in 2011. The largest stocks were held by the United States (57.3 tons, or 53 per cent of global stocks), the United Kingdom (8.9 tons, or 8 per cent) and France (8.3 tons, or 7 per cent).

Codeine

46. Codeine is a natural alkaloid of the opium poppy plant, but most (90-95 per cent) of the codeine currently being manufactured is obtained from morphine through a semi-synthetic process. Codeine is used mainly for the manufacture of preparations in Schedule III of the 1961 Convention, while a smaller quantity is used for the manufacture of other narcotic drugs, such as dihydrocodeine and hydrocodone. The trends in global manufacture, consumption, utilization and stocks of codeine during the period 1993-2012 are shown in figure 14.

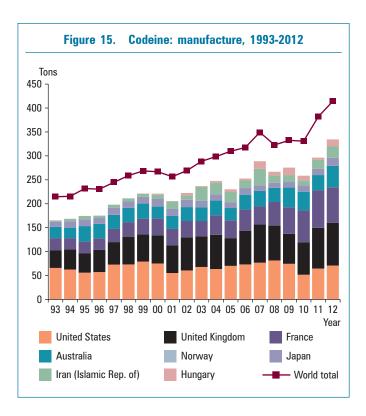


^aStocks as at 31 December of each year.

47. After a general upward trend in the 1990s and an increase to 381 tons in 2011, global codeine manufacture grew further, to a peak of 414 tons in 2012 (see figure 15).

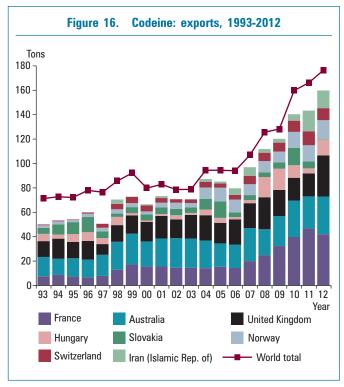
The main manufacturing country was the United Kingdom (89 tons, or 22 per cent of global manufacture), followed by France (74.6 tons, or 18 per cent), the United States (70.8 tons, or 17 per cent) and Australia (44.7 tons, or 11 per cent).

for the manufacture of preparations listed in Schedule III are not necessarily the countries of consumption of those preparations. Large quantities of those preparations are exported from some of those countries.



48. World exports of codeine followed a rising trend, reaching 176.4 tons in 2012, the highest level ever reported (see figure 16). France remained the leading exporting country of codeine in 2012, with 42.1 tons, accounting for 24 per cent of world exports, followed by the United Kingdom (33.6 tons, or 19 per cent), Australia (30.7 tons, or 17 per cent), Norway (15.5 tons, or 8 per cent) and Iran (Islamic Republic of) (14.5 tons, or 8 per cent). The main importing countries of codeine in 2011 were India (61.3 tons),²² Canada (16.8 tons), Germany (12.3 tons), Switzerland (11.7 tons) and Hungary (10 tons). Sixteen other countries reported imports of between 1 and 9 tons in 2012. More details on international trade in codeine can be found in annex IV, tables 3 and 4.

49. Codeine is used mainly in the form of preparations listed in Schedule III of the 1961 Convention. In 2012, preparations listed in Schedule III accounted for 99 per cent of the total consumption of codeine. The consumption of codeine grew from 182 tons in 1993 to 295 tons in 2012 (see figure 14), making it the second most widely used opiate in medical practice globally in terms of defined daily doses for statistical purposes (2.9 billion S-DDD). It should be noted that countries reporting the utilization of codeine



50. The main countries reporting the use of codeine for the manufacture of preparations listed in Schedule III in 2012 were India (60 tons),²³ the United Kingdom (50 tons), France (28 tons), Iran (Islamic Republic of) (24 tons), Canada (18 tons) and the United States (16 tons), which together accounted for 68 per cent of global use in 2012. Other major user countries were, in descending order of quantity used, Germany, China, Spain, Viet Nam and Australia (see figure 17).

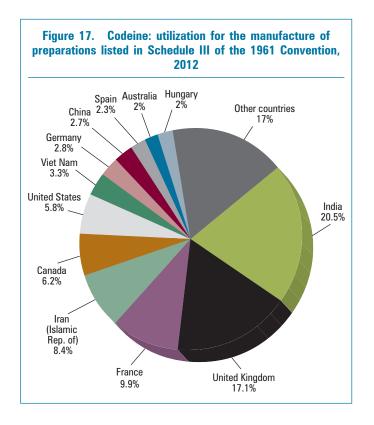
51. Utilization of codeine for the manufacture of other narcotic drugs, mainly dihydrocodeine and hydrocodone, increased steadily until reaching its highest level in 2007 (81.8 tons). Utilization stood at 77.5 tons in 2012. Of the amount reported for 2012, 41.3 tons was used in the United States, 13.2 tons in Japan and 12 tons in the United Kingdom. Other major user countries were, in descending order of quantity used, Italy, Slovakia, Belgium and Hungary.

52. Global stocks of codeine amounted to 206 tons in 2012. About 59 per cent of global stocks were held by four countries: United States (43 tons), India (28 tons), France (22 tons) and United Kingdom (20 tons). Seventeen other countries held stocks of codeine in quantities of more than

 $^{^{\}rm 22}{\rm This}$ figure was calculated by INCB using available data series; it is being clarified with the Government.

²³This figure was calculated by INCB using available data series; it is being clarified with the Government.

1 ton: in descending order of quantity of stocks, Hungary, Australia, Japan, Canada, South Africa, Switzerland, Romania, China, Norway, Germany, Italy, Viet Nam, Turkey, Brazil, Spain, Russian Federation and Ukraine.

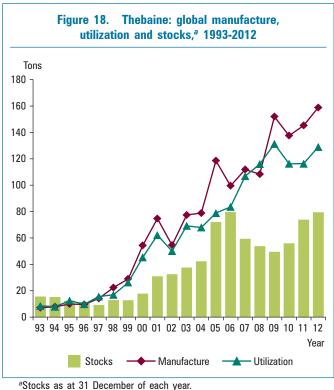


Thebaine

53. Until the 1990s, thebaine was manufactured mainly from opium; since 1999, it has been obtained primarily from poppy straw. Thebaine may also be obtained through the conversion of oripavine or from semi-synthetic opioids, such as hydrocodone. Thebaine itself is not used in therapy, but it is an important starting material for the manufacture of a number of opioids, mainly codeine, dihydrocodeine, etorphine, hydrocodone, oxycodone and oxymorphone (all of which are substances controlled under the 1961 Convention) and buprenorphine (which is a substance controlled under the Convention on Psychotropic Substances of 1971),²⁴ as well as for substances not under international control, such as the derivatives naloxone, naltrexone, nalorphine and nalbuphine.

54. Global manufacture of thebaine has increased sharply since the late 1990s, as a consequence of the growing demand for oxycodone and other drugs and substances that may be derived from it. In 2012, global manufacture rose to 158 tons, a sharp increase from the 145 tons recorded in 2011. The United States continued to be the

leading manufacturing country, accounting for 75.4 tons, or 47 per cent of global manufacture, in 2012. The other major manufacturers of thebaine were Australia (55.9 tons, or 35 per cent) and Spain (20 tons, or 12 per cent). Global exports of thebaine reached 67 tons in 2012. Australia and Spain remained the main exporting countries in 2012, together accounting for 98 per cent of the world total. The main importing country of thebaine was the United Kingdom (31.5 tons).²⁵

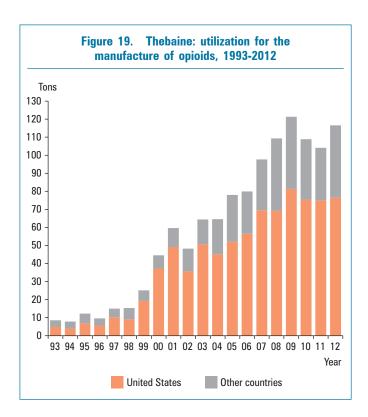


55. Utilization of thebaine for the manufacture of other narcotic drugs reached 104 tons in 2012 (see figure 19 and table VII). The United States was the main user country of thebaine during the 20-year period from 1993 to 2012. In 2012, the United States accounted for 72 per cent of global use, followed by the United Kingdom, which accounted for 18 per cent. The quantity of thebaine reported as used for the manufacture of substances not covered under the 1961 Convention (mainly buprenorphine) fluctuated during the 10-year period from 2003 to 2012; in 2012, it amounted to 12.3 tons, with Germany and the United Kingdom together accounting for 89 per cent of the world total.

56. Global stocks of thebaine stood at 78 tons in 2012. Major stocks were held in the United States (28 tons), the United Kingdom (23 tons), Switzerland (11 tons), France (5 tons) and Japan (4 tons).

²⁴United Nations, *Treaty Series*, vol. 1019, No. 14956.

²⁵This figure is based on data submitted by the exporting countries; it is being clarified with the Government.



Oripavine

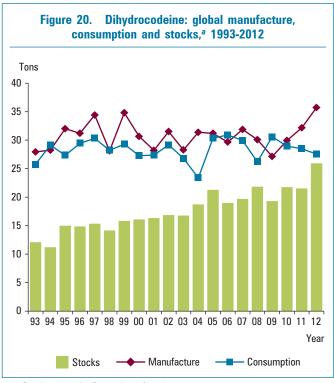
57. In 2007, oripavine was included in Schedule I of the 1961 Convention. The United States (10.9 tons) and Switzerland (0.3 tons) were the only countries reporting significant manufacture of oripavine in 2012. The use of oripavine in significant quantities for the manufacture of other drugs was reported in 2012 by the United States (6.6 tons, for oxymorphone and hydromorphone) and Switzerland (0.2 tons, mainly for hydromorphone). In 2012, global stocks of oripavine amounted to 7.5 tons, of which 96 per cent was held in the United States.

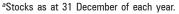
Semi-synthetic opioids

58. Semi-synthetic opioids are made by relatively simple chemical modifications of natural opiates, such as morphine, codeine and thebaine. Some examples of these derivatives are dihydrocodeine, ethylmorphine, heroin, hydrocodone, oxycodone and pholcodine. It should be noted that large losses²⁶ have been reported to occur during the processing of some semi-synthetic opioids by some of the major manufacturers. Those manufacturing losses account for the difference between the total quantities of hydrocodone and oxycodone manufactured and consumed, as reflected in figures 22 and 23.

Dihydrocodeine

59. Global manufacture of dihydrocodeine rose between 1993 and 1999, when it reached 34.8 tons. After 2000, the annual manufacture fluctuated between 27.1 tons and 31.9 tons and stood at 35.7 tons in 2012 (see figure 20). Japan (12.2 tons), the United Kingdom (10.3 tons) and the Republic of Korea (2.4 tons) have been the main manufacturing countries, together accounting for 93 per cent of total world dihydrocodeine manufacture in 2012. Global exports of dihydrocodeine amounted to 12.2 tons in 2012. The main exporting country remained Italy, accounting for 40 per cent of world exports, followed by the United Kingdom, Belgium and France. The United Kingdom became the leading importing country of dihydrocodeine in 2012 (3.9 tons); other main importers were the Republic of Korea (2.7 tons) and France (1.6 tons).





60. Dihydrocodeine is consumed mainly in the form of preparations included in Schedule III of the 1961 Convention, accounting for 95 per cent of total consumption. In 2012, use of dihydrocodeine reached 26.8 tons (about 186.6 million S-DDD). The main user countries of dihydrocodeine, in descending order, were Japan, the United Kingdom and the Republic of Korea, together accounting for 92.7 per cent of total global utilization. In 2012, global stocks of dihydrocodeine amounted to 25.9 tons; major stocks were held in Japan (10.8 tons) and the United Kingdom (4.4 tons).

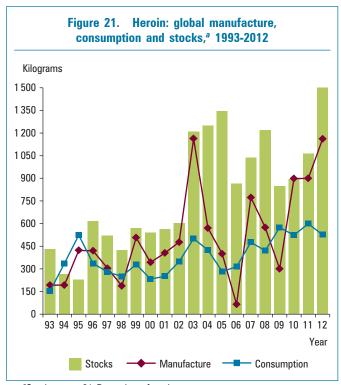
²⁶Manufacturing losses are those occurring: (*a*) during the process of refining a drug; (*b*) during the process of transformation of a drug into its salts, isomers, esters and ethers, as applicable according to the Schedules; and (*c*) during the manufacture of preparations other than those included in Schedule III. They may be also due to the chemical decomposition of a drug, leakage, evaporation, quality requirements or accidents.

Ethylmorphine

61. Global manufacture of ethylmorphine has followed a downward trend in the last 20 years, decreasing slightly from the 2011 level to 928.5 kg in 2012. France and Hungary, the main manufacturing countries in 2012, accounted for 96 and 3.5 per cent of global manufacture, respectively. France, at 744.2 kg, continued to be the leading exporting country, accounting for 82 per cent of global exports. The two largest importers in 2012, Sweden and Belgium, imported 525.4 and 197.9 kg of ethylmorphine, respectively. Ethylmorphine is consumed mainly in the form of preparations listed in Schedule III of the 1961 Convention (about 94 per cent of total consumption). Global utilization reached 849 kg in 2012 (16.9 million S-DDD). The main user countries in 2012 were Sweden (47 per cent of the world total) and France (25 per cent). In 2012, global stocks of ethylmorphine totalled 734.9 kg; the largest holder of stocks was France (28 per cent of global stocks).

Heroin

62. From 1993 to 2002, global licit manufacture of heroin fluctuated between 192.6 kg and 477 kg. In 2003, it increased sharply to 1.2 tons, the largest amount ever reported. After 2003, manufacture declined and fluctuated, reflecting the changes in the manufacture reported by Switzerland and the United Kingdom. In 2012, global manufacture amounted to 1.16 tons (see figure 21). In 2012, the United Kingdom continued to be the main exporting country of heroin (611 kg, or 77 per cent of global exports). Other exporters



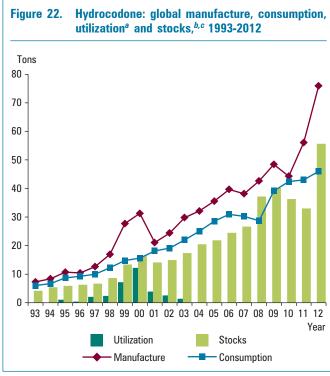
^aStocks as at 31 December of each year.

of heroin in amounts exceeding 10 kg were Switzerland (150 kg) and Germany (17 kg). Switzerland remained the main importing country of heroin in 2012 (331 kg), followed by the Netherlands (234 kg) and the United Kingdom (147 kg).

63. Global consumption of heroin amounted to 526 kg in 2012. Switzerland, where heroin is prescribed for longterm opiate addicts, reported consumption of 250 kg in 2012. Other countries with significant heroin consumption in 2012 were the Netherlands (138 kg), Germany (53 kg), the United Kingdom (48 kg) and Denmark (26 kg). In 2012, global stocks of heroin amounted to 1.7 tons. The countries holding significant stocks in 2012 were Switzerland (805 kg), the United Kingdom (613 kg) and the Netherlands (188 kg).

Hydrocodone

64. Global manufacture of hydrocodone has followed an upward trend in the last 20 years, reaching 75.9 tons in 2012 (see figure 22), with the United States accounting for almost 100 per cent of global manufacture.



^aUtilization for the manufacture of other drugs.

^bStocks as at 31 December of each year.

^cThis substance is subject to losses during the manufacturing process. This explains some gaps between manufacture and consumption/stocks.

65. Global consumption of hydrocodone stood at 46 tons in 2012, with the United States accounting for more than 99 per cent of the total. The high consumption in the United States makes hydrocodone the most used narcotic drug in medical practice in terms of defined daily doses for statistical purposes (about 3 billion S-DDD). Ranked according to defined daily doses for statistical purposes consumed per million inhabitants per day, the country with the highest consumption of hydrocodone in 2012 was the United States (26,437 S-DDD). In the past, hydrocodone had been used in the United States for the manufacture of thebaine for the purpose of manufacturing other narcotic drugs; no such use was reported after 2003, as extraction of thebaine from poppy straw had increased since the late 1990s and replaced the use of hydrocodone in the manufacture of thebaine. In 2012, global stocks of hydrocodone accounted for 55 tons, more than 99 per cent of which was held by the United States.

Hydromorphone

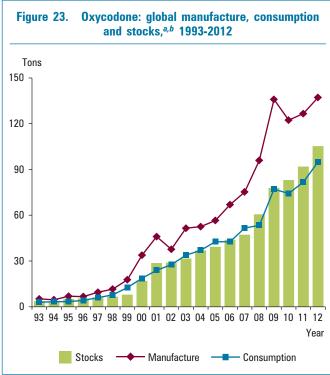
66. Global manufacture of hydromorphone increased sharply over recent years, reaching 5.8 tons in 2012. The United States (68 per cent of global manufacture) and the United Kingdom (24 per cent) were the leading manufacturing countries in 2012. Total exports of hydromorphone have risen steadily, reaching 2.8 tons in 2012. The leading exporting countries were the United Kingdom (34 per cent of world exports) and the United States (15 per cent). Canada remained the main importing country (950 kg) in 2012, followed by Germany (662 kg) and Switzerland (422 kg).

67. Global consumption of hydromorphone increased steadily, reaching 3.4 tons (170 million S-DDD) in 2012. The United States remained the main consumer country in 2012 (42 per cent of global consumption), followed by Canada (30 per cent) and Germany (13 per cent). Ranked according to defined daily doses for statistical purposes consumed per million inhabitants per day, the countries with the highest consumption of hydromorphone in 2012 were Denmark (4,241 S-DDD) and Canada (4,158 S-DDD). Global stocks of hydromorphone reached 5.8 tons in 2012, of which 49 per cent was held in the United States, 13 per cent in the United Kingdom and 10 per cent in Canada.

Oxycodone

68. Global manufacture of oxycodone has increased sharply over recent years, reaching a record 137.1 tons in 2012 (see figure 23). In 2012, the United States accounted for 75 per cent of total world manufacture, followed by France (9 per cent), the United Kingdom (9 per cent) and Switzerland (6 per cent). Total exports of oxycodone have risen steadily and stood at 28.7 tons in 2012. The United Kingdom continued to be the main exporting country in 2012 (53 per cent of world exports), followed by the United States (14 per cent). Canada and Germany were the major importers of oxycodone in 2012, accounting for 20 per cent

and 16 per cent of global oxycodone imports, respectively. Tables XVI.3 and XVI.4 provide further details on exports and imports, respectively, of oxycodone.



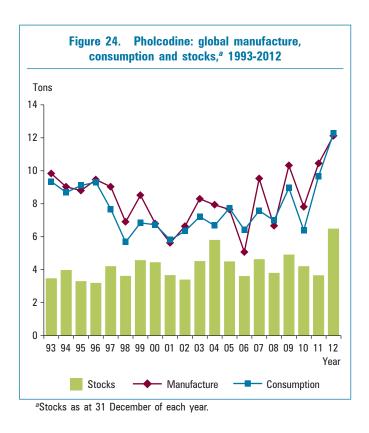
^aStocks as at 31 December of each year.

^bThis substance is subject to losses during the manufacturing process. This explains some gaps between manufacture and consumption/stocks.

69. Global consumption of oxycodone has been rising steadily. In 2012, global oxycodone consumption rose sharply to 94.9 tons (1.26 billion S-DDD). The United States, which continued to be the principal consumer country of oxycodone, accounted for 82 per cent of the world total. Other major consumer countries in 2012 were Canada (4.9 tons), Germany (2.8 tons) and Australia (2 tons). Ranked according to defined daily doses for statistical purposes consumed per million inhabitants per day, the countries with the highest consumption of oxycodone in 2012 were the United States (8,902 S-DDD), Canada (5,281 S-DDD) and Australia (3,338 S-DDD). Global stocks of oxycodone increased to 105.3 tons in 2012—the highest level ever recorded—with the United States accounting for 76 per cent of the world total.

Pholcodine

70. Global manufacture of pholcodine has fluctuated in the past 20 years, amounting to 11.9 tons in 2012 (see figure 24). The main manufacturers in 2012 were France (4.7 tons) and Norway (2.8 tons). Total exports of pholcodine reached 10.8 tons in 2012, the main exporting countries being Norway (27 per cent of total exports), Hungary (27 per cent), France (24 per cent) and the United Kingdom (14 per cent). The main importers in 2012 were the Hong Kong Special Administrative Region of China (5.4 tons) and Australia (1.1 tons). Further details on exports and imports of pholocodine are provided in tables 3 and 4, respectively, of annex IV.



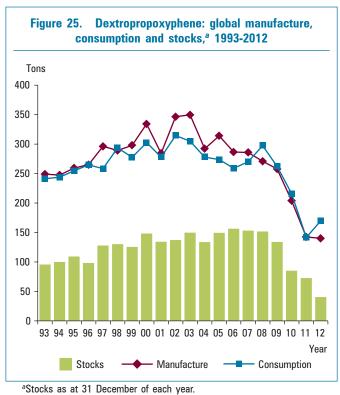
71. Most pholcodine is consumed in the form of preparations listed in Schedule III of the 1961 Convention; in 2012, such preparations accounted for 99 per cent of total consumption. Global utilization of pholcodine amounted to 12 tons (239 million S-DDD) in 2012. The major user countries and territories in 2012 were the Hong Kong Special Administrative Region of China (53 per cent of the world total), France (11 per cent) and Pakistan (8 per cent). Global stocks of pholcodine increased to 6.4 tons in 2012. Major stocks were held by France (26 per cent of global stocks) and the Hong Kong Special Administrative Region of China (17 per cent).

Synthetic opioids

72. Synthetic opioids are used in the treatment of chronic, moderate or severe pain. They are also used for the induction of general anaesthesia and in the treatment of specific conditions such as gastrointestinal disorders. In addition, methadone is used in treatment related to drug dependency.

Dextropropoxyphene

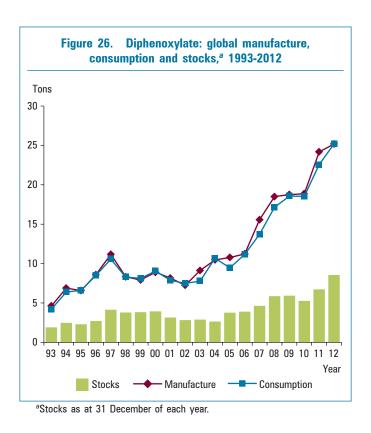
73. Global manufacture of dextropropoxyphene has followed a downward trend since 2003, when 349.6 tons was manufactured. This decline is to be attributed to the fact that the substance has been banned in several countries owing to concerns over serious side effects. It declined sharply in 2011 and reached 140 tons in 2012. India was the only country reporting manufacture in significant quantities in 2012. Global exports also continued to decline in 2012 and amounted to less than 3 tons. Exports from India, the principal exporting country of dextropropoxyphene, accounted for 46 per cent of global exports in 2012. Exports from France and Italy accounted for about 33 and 10 per cent of the global total, respectively. The United Kingdom and Mexico were the main importing countries of dextropropoxyphene in 2012 (956 kg and 945 kg, respectively), followed by Cambodia (226 kg) and Argentina (216 kg).



74. Dextropropoxyphene is consumed mainly in the form of preparations listed in Schedule III of the 1961 Convention (more than 99 per cent of total consumption in 2012). Global use of dextropropoxyphene peaked at 315 tons in 2002 and followed a sharp downward trend thereafter. From 2011 to 2012 it increased slightly to 169 tons (about 845 million S-DDD). The countries reporting the highest utilization in 2012 were India (82 per cent of the global total), Italy (8 per cent), the United States (8 per cent) and Mexico (1 per cent). Global stocks of dextropropoxyphene continued decreasing to 40.5 tons in 2012. The largest stocks were held by India (30 tons), France (2.4 tons) and the United States (2.3 tons).

Diphenoxylate

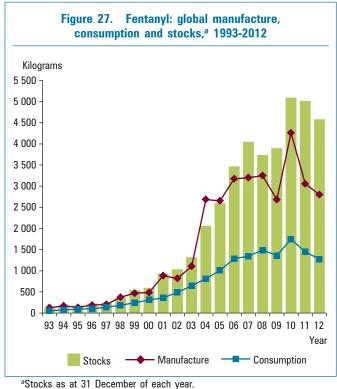
75. Global manufacture of diphenoxylate has followed a generally rising trend during the last two decades, reaching a peak of 25.9 tons in 2012 (see figure 26). India remained the main manufacturing country in 2012, contributing 89 per cent of the global total, followed by China (8 per cent) and the United States (3 per cent). India was also the main exporting country, accounting for 1.4 tons, or 94 per cent of world exports. In 2012, the Islamic Republic of Iran was again the principal importing country of diphenoxylate (541 kg), followed by Singapore (151 kg) and Malaysia (55 kg).



76. Diphenoxylate is consumed mainly in the form of preparations listed in Schedule III of the 1961 Convention (more than 99 per cent of total consumption in 2012). Global use in 2012 reached the record level of 25.2 tons, corresponding to 1.7 billion S-DDD. The countries reporting the highest utilization in 2012 were India (83 per cent of the global total), China (8 per cent), Pakistan (3 per cent), the United States (2 per cent) and Iran (Islamic Republic of) (2 per cent). Global stocks of diphenoxylate in 2012 amounted to 8.6 tons, 76 per cent of which was held by India, 16 per cent by Pakistan and 4 per cent by the United States.

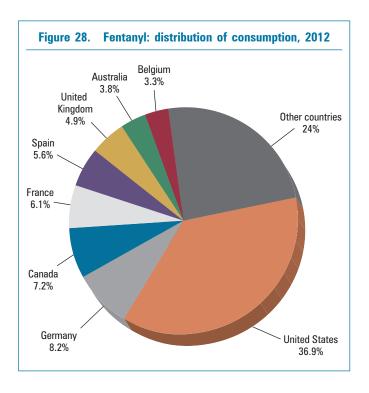
Fentanyl

77. Fentanyl, when used as an analgesic, is about 100 times as potent as morphine and is therefore used only in very small doses (for example, 0.005-0.1 mg in injectable form). Until the 1980s, fentanyl was used mainly for the induction of anaesthesia and, in combination with other substances, for balanced anaesthesia in short-term surgical interventions. Since the early 1990s, however, controlled-release preparations (patches) of fentanyl have been increasingly used in all parts of the world for the treatment of severe pain.



78. Global manufacture of fentanyl increased slowly until 1992, when it reached 77 kg. After that, manufacture of fentanyl grew rapidly, reaching the record level of 4.3 tons in 2010; it then decreased to 2.8 tons in 2012 (see figure 27). In 2012, the United States was the main manufacturing country of fentanyl (53 per cent of global manufacture), followed by Germany (21 per cent), South Africa (11 per cent) and Belgium (8 per cent). Germany was the principal exporting country, exporting 342 kg of fentanyl in 2012, followed by Belgium (322 kg) and South Africa (292 kg). In 2012, the United Kingdom was the leading importing country of fentanyl (740 kg),²⁷ followed by Germany (652 kg) and Canada (92 kg). Tables 3 and 4 of annex IV provide further details on exports and imports, respectively, of fentanyl.

 $^{^{\}rm 27}{\rm This}$ figure is based on data submitted by the exporting countries; it is being clarified with the Government.



79. Global consumption of fentanyl followed a steady increasing trend and reached a peak of 1.7 tons in 2010. Global consumption stood at 1.3 tons (corresponding to 2.1 billion S-DDD) in 2012, which made fentanyl the synthetic opioid with the highest consumption in terms of defined daily doses. The United States, accounting for 37 per cent of the world total, continued to be the main consumer country in 2012, followed by Germany, Canada, France and Spain (see figure 28). Ranked according to defined daily doses for statistical purposes consumed per million inhabitants per day, the countries and territories having the highest consumption of fentanyl in 2012 were Belgium (18,119 S-DDD), Gibraltar (13,148 S-DDD) and Canada (12,299 S-DDD). In 2012, global stocks of fentanyl stood at 5.2 tons, which was the same level as in 2011. The largest stocks were held by Belgium (30 per cent of global stocks), followed by the United States (26 per cent).

Fentanyl analogues

80. The fentanyl analogues alfentanil, remifentanil and sufentanil are used mainly as anaesthetics.

Alfentanil

81. Global manufacture of alfentanil has fluctuated sharply from year to year; it declined from 38.5 kg in 2010 to 11.9 kg in 2011. In 2012, global manufacture increased sharply to 78.3 kg. The principal manufacturers in 2012 were Belgium (71 per cent of global manufacture), the United States (25 per cent) and the United Kingdom

(2 per cent, a sharp decrease from 34 per cent in 2011). Global consumption of alfentanil remained stable, at 20.3 kg, in 2012. The United Kingdom was the main consumer country of alfentanil (36 per cent of global consumption),²⁸ followed by Italy (20 per cent), Germany (7 per cent) and France (6 per cent). Detailed information on the consumption of fentanyl analogues is provided in table XIII.1. In 2012, global stocks of alfentanil almost doubled to 84 kg, of which 68 per cent was held by Belgium, followed by the United States (12 per cent) and Germany (8 per cent).

Remifentanil

82. In 2012, global manufacture of remifentanil decreased slightly to 82 kg from the record level of 93 kg reached in 2011, which was a sharp increase from 32.2 kg in 2010. The United Kingdom accounted for 42 per cent of the global total, followed by Belgium (26 per cent), China (16 per cent), Spain (10 per cent) and Switzerland (3 per cent). Germany, the main manufacturing country in 2011 (20 kg), reported no manufacture in 2012. Global consumption of remifentanil followed a rising trend and reached a peak of 48 kg in 2012. China was the leading consumer (accounting for 18 per cent of global consumption), followed by Japan (12 per cent), Italy (12 per cent), Germany (9 per cent) and Brazil (5 per cent). In 2012, global stocks of remifentanil increased to 138 kg, of which 30 per cent was held by the United Kingdom, 13 per cent by Italy, 11 per cent by China, 9 per cent by Germany and 8 per cent by Hungary.

Sufentanil

83. Global manufacture of sufentanil amounted to 6 kg in 2012, with the United States and China accounting for 60 per cent and 26 per cent of global manufacture, respectively. Global consumption of sufentanil increased to 4.3 kg in 2012. China, France, Germany, Italy and the United States were the five largest consumers of sufentanil, together accounting for 84 per cent of the global total. In 2012, global stocks of sufentanil totalled 13 kg, most of which was held by the United States (56 per cent) and Belgium (16 per cent).

Ketobemidone

84. Global manufacture of ketobemidone reached 507 kg in 2003, the highest level in 10 years. In the past five years, manufacture was reported only in 2008, by Denmark,

²⁸This figure was calculated by INCB using available data series; it is being clarified with the Government.

English — Comments Part two Deuxième partie

Segunda

parte

-

which manufactured less than 1 kg, and in 2011, by the United Kingdom, which manufactured 182 kg. There was no reported manufacture of ketobemidone in 2012. Germany was the main exporting country of ketobemidone in 2012, accounting for 52 kg, or 79 per cent, of global exports,²⁹ followed by France (12 kg, or 21 per cent of global exports). The main importing countries were Denmark (31 kg), Sweden (20 kg), Norway (18 kg) and France (11 kg).

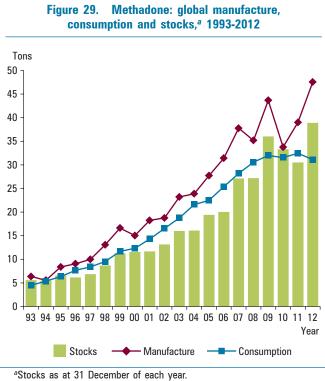
85. Global consumption of ketobemidone, which occurs mostly in the Scandinavian countries, amounted to 69 kg in 2012 (corresponding to 1.4 million S-DDD). Denmark (41 per cent of the global total), Sweden (31 per cent) and Norway (24 per cent) remained the main consumer countries of ketobemidone. Global stocks of ketobemidone stood at 209 kg in 2012. Germany continued to hold the largest stocks (79 per cent of the global total).

Methadone

86. Global manufacture of methadone has increased steadily over the past 20 years. Global manufacture increased to 47.6 tons in 2012 (see figure 29). The two countries accounting for most of the global manufacture in 2012 were the United States (25.1 tons, or 53 per cent of global manufacture) and Switzerland (14.1 tons, or 30 per cent). Five other countries reported manufacture of methadone in 2012 in quantities of more than 1 ton: China (2.3 tons), India (1.8 tons), Germany (1.2 tons), the United Kingdom (1.1 tons) and Slovakia (1 ton).

87. Global exports of methadone amounted to 17.1 tons in 2012. Switzerland remained the main exporting country (10.9 tons), followed by India (1.6 tons), the United Kingdom (1 ton) and Slovakia (1 ton). The largest imports of methadone were reported by Canada (2.2 tons) and the United Kingdom (2.1 tons). Three other countries reported imports of more than 1 ton: Italy (1.9 tons),³⁰ France (1.4 tons) and Switzerland (1.3 tons). Tables 3 and 4 of annex IV provide further details on exports and imports, respectively, of methadone.

88. The sharp upward trend in consumption of methadone is attributable to its growing use in the treatment of opioid addiction, although it is also used in several countries for the treatment of pain. Global consumption of methadone stabilized after 2008 and amounted to 31.1 tons in 2012. The United States remained the main consumer country (49 per cent of the global total), followed by Canada (6 per cent) and China (6 per cent). More details on the consumption of methadone can be found in table XII. Global stocks of methadone increased to 39 tons in 2012. The countries holding the largest stocks remained the United States (33 per cent of global stocks) and Switzerland (31 per cent).



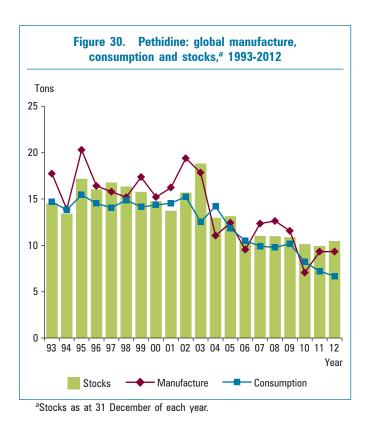
Pethidine

89. Global manufacture of pethidine followed a declining trend during most of the last 20 years, reaching a low of 7 tons in 2010. The decline is attributable to pethidine's low potency, short duration of action and unique toxicity, as compared to other available opioid analgesics. It is still being used for very specific indications. Several countries have put strict limits on its use but some physicians continue to use it as a strong first-line opioid. In 2012, global manufacture increased to 9.3 tons (see figure 30). The United States continued to be the main manufacturing country in 2012, with 2.8 tons, or 30 per cent of global manufacture, followed by Spain (2.7 tons, or 29 per cent) and Germany (1.3 tons, or 14 per cent). In 2012, global exports of pethidine decreased slightly to 4.9 tons. Spain remained the principal exporting country in 2012, accounting for 43 per cent of global exports. The main importer of pethidine in 2012 was Germany (726 kg), followed by South Africa (539 kg) and the United Kingdom (509 kg). Tables 3 and 4 of annex IV provide further details on exports and imports, respectively, of pethidine.

²⁹This figure is based on data submitted by the importing countries; it is being clarified with the Government.

³⁰This figure is based on data submitted by the exporting countries; it is being clarified with the Government.

90. Pethidine consumption amounted to 6.7 tons in 2012 (corresponding to 16.7 million S-DDD). The United States and China were the main consumer countries, accounting for 25 per cent and 23 per cent, respectively, of global consumption. Global stocks of pethidine totalled 10 tons in 2012. The largest stocks were held by the United States (34 per cent of global stocks), Germany (20 per cent) and Spain (6 per cent).



Tilidine

91. Global manufacture of tilidine has fluctuated from year to year; it amounted to 39.3 tons in 2012, when Germany was again the main manufacturer, accounting for almost all of the total manufacture. Total exports of tilidine increased sharply from 8 tons in 2011 to 20 tons in 2012. Germany continued to be the principal exporting country in 2012, accounting for 98 per cent of global exports, followed by Belgium (2 per cent). Those two countries were also the main importers in 2012.

92. Consumption of tilidine reached a record level of 59.1 tons in 2012 (corresponding to 296 million S-DDD). Most tilidine has been consumed in Germany, which accounted for 96 per cent of the world total in 2012. In 2012, the countries with the highest consumption of tilidine, in terms of defined daily doses for statistical purposes consumed per million inhabitants per day, were Germany (9,499 S-DDD), Belgium (2,662 S-DDD) and Luxembourg (1,201 S-DDD). Global stocks of tilidine stood at 35.4 tons

in 2012, almost all being held by Germany (98 per cent) and Belgium (2 per cent).

Trimeperidine

93. Global manufacture of trimeperidine has fluctuated from year to year; in 2012 it decreased from 309 kg to 105 kg. The Russian Federation and Ukraine were the only manufacturers in 2012, accounting for 59 per cent and 41 per cent of total manufacture, respectively. India was again the leading exporting country of trimeperidine in 2012 (128 kg), followed by Ukraine (12 kg), the Russian Federation (5 kg) and Latvia (3 kg). Most of the global consumption of trimeperidine in 2012 (311 kg, corresponding to 1.6 million S-DDD) occurred in the Russian Federation (70 per cent), Kazakhstan (10 per cent), Ukraine (8 per cent), Belarus (6 per cent) and Uzbekistan (2 per cent).

94. The countries with the highest consumption of trimeperidine, expressed in defined daily doses for statistical purposes per million inhabitants per day, were Belarus (27 S-DDD), Kazakhstan (27 S-DDD), the Russian Federation (19 S-DDD), Latvia (18 S-DDD) and the Republic of Moldova (11 S-DDD). In 2012, global stocks decreased to 308 kg, with the Russian Federation reporting the largest share (78 per cent of the global total).

Opioid analgesics controlled under the 1971 Convention

95. Buprenorphine and pentazocine are opioid analgesics that are controlled under the 1971 Convention. Brief information on these opioids is included in the present publication; more detailed comments on statistics on buprenorphine and pentazocine can be found in the INCB technical report on psychotropic substances.³¹

Buprenorphine

96. Buprenorphine is an opioid used as an analgesic and in detoxification and substitution treatment for opioid dependence. Since the late 1990s, global manufacture of buprenorphine has increased steadily, reaching a peak of 7.3 tons in 2012 (see figure 31); manufacture was reported by nine countries, including the United

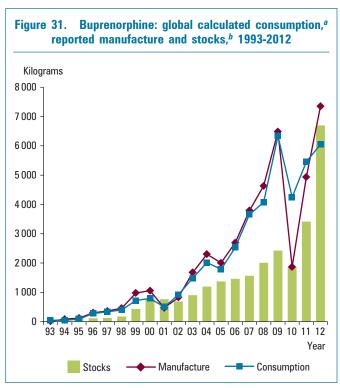
³¹Psychotropic Substances: Statistics for 2012—Assessments of Annual Medical and Scientific Requirements for Substances in Schedules II, III and IV of the Convention on Psychotropic Substances of 1971 (United Nations publication, Sales No. T.14.XI.3).

English — Comments Part two Deuxième partie Segunda parte

Kingdom (4,608 kg), the Czech Republic (749 kg), Belgium (655 kg) and Switzerland (453 kg). The volume of trade in buprenorphine amounted to 7.2 tons in 2012. The main exporters were, in descending order, the United Kingdom, Belgium, Germany and the Czech Republic. The United States, Germany, France and the United Kingdom, in descending order, were the main importing countries of buprenorphine in 2012.

Pentazocine

97. Pentazocine is an opioid analgesic with properties and uses similar to those of morphine. In 2012, global manufacture of pentazocine dropped to 685 kg, from a peak of 8.5 tons in 2009. India was the main manufacturer in 2009 and 2010. In 2011 and 2012, India did not submit data on manufacture of pentazocine, and the drop can be attributed to this. If India is excluded, most pentazocine (512 kg) is manufactured by the United States. In the absence of data from India, the world's leading exporters of pentazocine in 2012 were Italy, Switzerland, Portugal and Slovenia. The United States, Nigeria and Pakistan were the main importers in 2012.



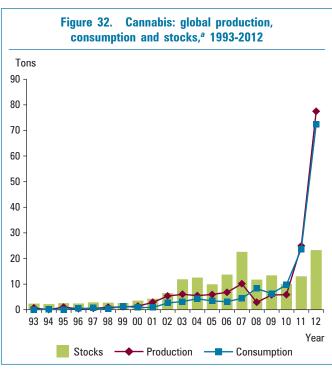
^aUntil 2009, approximate calculated global consumption, determined on the basis of statistical data submitted by Governments.

^bStocks as at 31 December of each year; data are provided on a voluntary basis and may therefore be incomplete.

Cannabis

98. Prior to 2000, the United States was the only country to report the use of cannabis solely for scientific purposes. Since then, some countries have started to use cannabis and/or cannabis extracts³² for medical purposes, in addition to scientific research. Global licit production of cannabis reached a record high of 77 tons in 2012, up from 23 tons in 2011 (see figure 32). The principal producers in 2012 remained Canada, the United Kingdom and Israel, accounting for 75 per cent, 18 per cent and 5 per cent of global production, respectively. While cannabis produced in Canada is used for medical purposes in that country, cannabis produced in the United Kingdom is used mainly for the manufacture of cannabis extracts for medicinal preparations, part of which is exported to other countries. In addition, Sri Lanka has regularly released seized cannabis for use for licit purposes (in Ayurvedic medicine).

³²In statistical reports to INCB, data on cannabis extracts are expressed in terms of cannabis, using the conversion factors published by INCB in the list of narcotic drugs under international control ("Yellow List").





99. Global consumption of cannabis amounted to 72 tons in 2012. Canada remained the main consumer country (58 tons), followed by the United Kingdom (8.8 tons), Israel (4 tons), Germany (470 kg) and the Netherlands (162 kg). The countries reporting significant cannabis stocks in 2011 were the United Kingdom (20.8 tons),³³ Canada (1.2 tons) and the United States (499 kg). The United States reported the cultivation, manufacture and consumption of cannabis for research purposes only. The amount indicated by the United States federal authorities does not include the amounts cultivated, manufactured and consumed in states that have "medical cannabis" programmes.

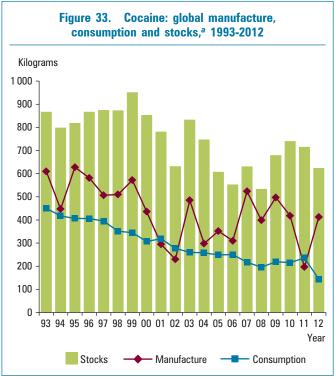
Coca leaf and cocaine

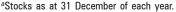
Coca leaf

100. Peru has been the only country exporting coca leaf for the global market since 2000. The United States has been the leading importing country, accounting for almost 100 per cent of global imports. Imports by the United States declined from 175 tons in 2001 to 90 tons in 2011, but rose again to 157 tons in 2012. Coca leaf is used in the United States for the extraction of flavouring agents and the manufacture of cocaine as a by-product. Such use in the United States fluctuated in the period 1993-2012, following a general downward trend until 2008 and then gradually increasing again to more than 150 tons in 2012. In Peru, the amount of coca leaf used for the manufacture of cocaine totalled 83 tons, a slight decline from the annual average of about 90 tons used in 2009 and 2010 but a considerable increase from the 30 tons registered in 2011. In recent years, small quantities of coca leaf have been used in Italy, the Netherlands and Switzerland for the extraction of flavouring agents and in France for use in homeopathic medicines. Stocks of coca leaf held in the United States account for the majority of global stocks. In 2012, stocks held in that country amounted to about 732 tons, or 99.9 per cent of the world total. Since its reaccession in 2012 to the 1961 Convention, Bolivia (Plurinational State of) has not provided the Board with information on its licit cultivation, manufacturing and consumption of coca leaf.

Cocaine

101. Global licit manufacture of cocaine continued to follow a slow declining trend with considerable fluctuations during the period 1993-2012. After reaching a record low of 197 kg in 2011 (see figure 33), cocaine manufacture rose again to 412 kg, approximately the same level as in 2010. The main manufacturing countries in 2012 were Peru (359 kg) and the United States (41 kg). Peru remained the leading exporting country in 2012, accounting for 220 kg, or 65.9 per cent of global exports, but its dominance of the previous years (e.g., 79 per cent in 2011) was considerably reduced. Exports from Peru in 2012 continued to be destined mainly for the United Kingdom, where imported cocaine is purified and partly re-exported. Consumption of cocaine has followed a declining trend, from more than 500 kg in 1992 to 143 kg in 2012. In 2012, the United States remained the main consumer country of cocaine (39 kg, or 27 per cent of global consumption), followed by Canada (21 kg), Belgium (10 kg), the United Kingdom (10 kg) and Australia (8.9 kg). In 2012, global stocks of cocaine stood at 624 kg. The countries holding the largest stocks were the United Kingdom (371 kg), the Russian Federation (49 kg), the United States (48 kg) and Canada (27 kg).





³³This figure was calculated by INCB using available data series; it is being clarified with the Government.