

Number 3

**AMPHETAMINE-TYPE
STIMULANTS
A GLOBAL REVIEW**

*Prepared by UNDCP at the request
of the Commission on Narcotic Drugs*

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Introduction

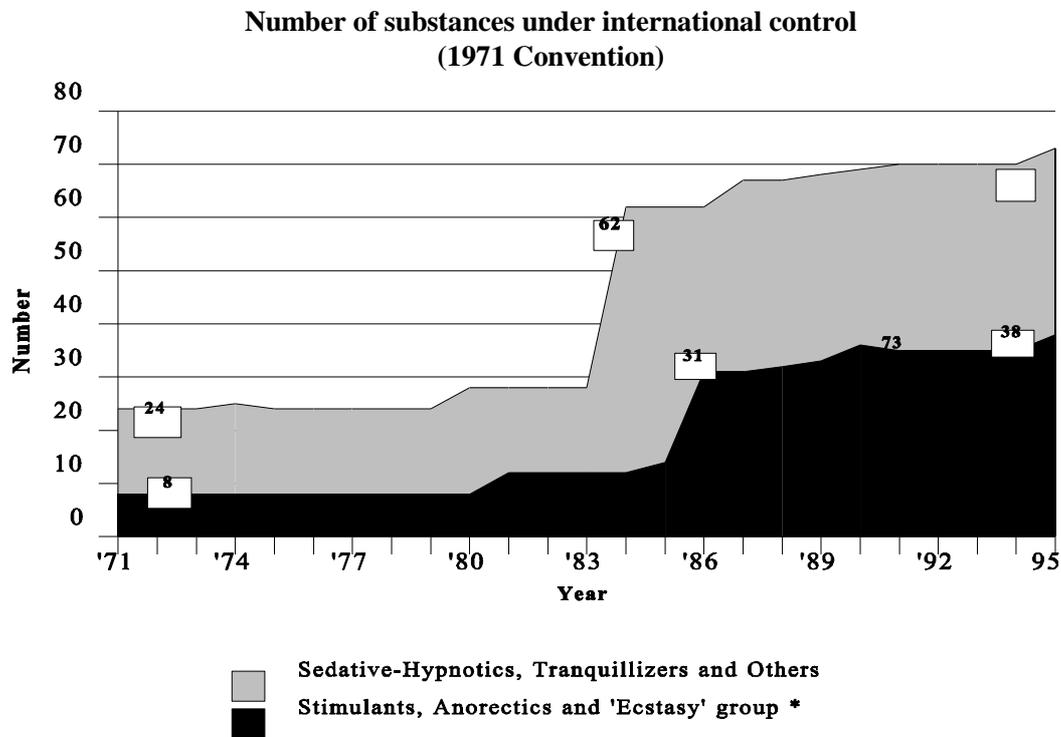
In the ever-widening discourse on substance abuse, it is frequently asserted that the key problem of the future will be associated with what are commonly known as synthetic drugs. The present paper is an attempt to assess the validity of this proposition. The subject is too vast and intricate to cover in a single review, but guidance for achieving a manageable focus can be found in two areas: the level of international consensus in defining a critical area and the nature of the substances themselves. With regard to defining the key area, the Economic and Social Council, reflecting the common concerns of many States Members of the United Nations, adopted resolution 1995/20 calling for a thorough study of psychotropic substances, particularly stimulants and their precursors. Even the category «stimulants», however, is a very wide one, covering a large range of substances whose principal pharmacological effect is to stimulate the central nervous system of the body. There is some pragmatic justification, detailed in [Table 1](#), in narrowing this category down to a group of substances that are similar, not only in their pharmacological effect but also in chemical structure: the amphetamine-type stimulants (abbreviated, throughout this review, as ATS).

Historically, the demand for ATS as medicines was satisfied by the licit pharmaceutical industry. Amphetamine, for instance, was synthesized in 1887 but only marketed (as *Benzedrine*⁷, in the form of an inhaler to relieve nasal congestion) in 1932. Probably as a result of its instrumental use during the Second World War, the post-war generation witnessed a proliferation of ATS being prescribed and abused, followed by isolated national control measures. By the 1970s, however, the therapeutic usefulness of these substances was recognized to be limited, but actual abuse had grown. Control measures, national and international, consequently became more stringent. Decline in licit pharmaceutical manufacture followed. Demand, however, did not show commensurate decline, and clandestine manufacture gradually became the major source of supply for some of these substances. Two factors supported this increase in illicit manufacture: the number and simplicity of synthetic routes to manufacture the end product and the easy access to a variety of potential starting materials.

While it is clear that there is sufficient basis to justify an international review, the utility of such a review will depend on resolving a number of fundamental questions at the outset. What are the magnitudes, in absolute and relative terms, of the problem as compared to the principal plant-based drugs of abuse? Is the provenance of the ATS problem limited to certain countries, or can it be deemed a global one? With what comparable phenomenon do we have a basis for comparison? International drug control has traditionally been dominated by the three plant-based drugs: opium, cocaine and cannabis. This factor sometimes over shadows other issues and may even prevent, or at any rate delay, the recognition of a new problem when it appears. The phenomenon of synthetic drugs, and of ATS within the category, could be a test case here. While it may be true that the illicit market for synthetic drugs merely complements the much larger illicit market for the plant-based drugs, it is clear that the driving forces, dynamism and potential for diversification of the former have not been sufficiently investigated. A good deal of work has been done in the area, but it has usually covered individual segments of the problem: the licit pharmaceutical industry, illicit markets for particular synthetic drugs, the precursors needed to produce the substances, the epidemiology of particular substances. These studies and reviews will be referenced in relevant chapters of the paper. What should be noted here is that the individual

segments they represent need to be integrated horizontally into a composite assessment: the present paper attempts to do this.

There is much evidence that the problem associated with synthetic psychotropic substances has been growing over the last two decades. Since the Convention on Psychotropic Substances of 1971 entered into force, there has been a three fold increase in the number of substances put under international control. No comparable increase was recorded for the number of narcotic drugs under the purview of the Single Convention on Narcotic Drugs of 1961. [Figure 1](#) illustrates the trend for two categories of substances. If the stimulants, anorectics and the 'ecstasy' group are taken together, as they are in the context of this review, then the number of ATS scheduled increased nearly five fold between 1971 and 1995. The sedative-hypnotic and tranquillizer category shows a four fold increase, primarily due to the scheduling of the benzodiazepines, which doubled the number of substances in the category in 1984.



*Note: In this figure, all ring-substituted amphetamine derivatives have been put in the same category ('ecstasy' group).

Figure 1

The scheduling of psychotropic substances under the 1971 Convention is based upon an assessment of the relationship between two variables: the therapeutic usefulness and the public health risk caused by abuse in a number of countries. The four schedules use a sliding scale of the two variables: Schedule I implies high public health risk and low therapeutic utility; Schedule IV the opposite - lower public health risk and higher therapeutic utility. Most of the ATS being discussed in this paper fall under Schedules I and II (except amfepramone, pemoline and phentermine, which are all in Schedule IV); this shows that there has been a general decline in

their therapeutic application and an increase in their abuse, confirming the historical trend noted above.

The nature of control regimes, national as well as international, is germane to this discussion. First principles of drug control seem to be perfectly clear: to ensure that drugs are available only for medical and scientific purposes, but not for uses that compromise individual and public health. There is, unfortunately, a grey area between these two propositions, and the technological innovation that is characteristic of our age appears to thrive within it. The ATS provide something of a paradigm to illustrate this. The synthesis of a psychoactive substance may offer therapeutic utility but also, very often, a potential for abuse. If the potential is realized, it becomes necessary to put the substance under control. Technological innovation in the grey area then drives the abuse by finding ways of circumventing the control. Breaking the law, or circumventing it, are two quite different propositions. The nature of the law will obviously determine, at least to some extent, whether loopholes will be found for circumvention: it can anticipate innovation, thereby closing the possible loopholes, or it can be simply reactive, setting in place some mechanism for modifications as and when the need arises. It will be argued, later in this paper, that the 1971 Convention is reactive in nature, and the evolution, development and scheduling of the ATS together provide the best documentary evidence. The application of a lengthy and laborious scheduling process, particularly if it applies to clandestinely manufactured drugs, would appear to imply that illicit markets will always stay ahead of the capacity to control them.

The notion of a grey area is also appropriate for the subject matter of this paper because the group of ATS appears to straddle the bipolar spaces of the licit and the illicit. Legitimate pharmaceutical preparations and therapeutic use of the substances coexist with abuse, linked via the grey zone of overuse/misuse. Most of the substances covered in this paper have, or were previously believed to have, some therapeutic value. Their considerable psychoactive properties, however, made some of them subject to abuse. If indeed there is an evolutionary path from licit to illicit use, as past experience suggests, then there is a need to investigate the validity of this notion, either to identify potential drugs of abuse or to assist policy development in countries which might wish to anticipate this shift. To give the investigation of illicit markets a perspective and a measure of magnitude, they are contrasted with the licit pharmaceutical market, wherein most of the substances originated and from which they were either diverted or copied in illicit markets. In order, thus, to arrive at a balanced view of the problem, this review looks at both the licit and the illicit markets, as well as the grey area between them.

The bipolarity suggests another double-edged quality to the substances under investigation. If the licit side of the equation is considered, there is powerful evidence of what can only be called a success story. On the global aggregate, manufacture and consumption appear to be tractable and seem to be coming down. Part one will detail this broad picture and show that, for most of the substances in question, the control system actually works. A switchback failure appears, however, when one considers the burgeoning of clandestine synthesis, illicit markets and widespread abuse on the other side of the equation. This, for all the limitations in the available evidence, will be covered in Part two. The need to establish a composite picture of the problem necessitates an intermediate step: the investigation of diversions from licit trade, medical prescribing practices and parallel markets. While it is clear that some of these subjects

are closer to the technical competence of other international agencies, the problems they pose will be highlighted, for the sake of consistency, in appropriate chapters of Parts one and two.

The ‘ecstasy’ group of substances are covered in this review because they are chemically related to the amphetamine molecule, though they have somewhat different pharmacological properties. In addition to stimulating the central nervous system, they also have hallucinogenic and/or entactogenic effects. This poses a problem of classification, frequently identified in the literature, because they can be considered stimulants or hallucinogens or entactogens. What is known about their consumption indeed suggests that they are used, or abused, precisely because they combine these effects. Further compounding the analytical problem is the fact that they do not have any officially recognized therapeutic value. Yet the extent of their illicit consumption appears to be growing rapidly. Probably driven by early experimentation and the present proliferation of technical know-how about them on the new information highway, consumption of the ‘ecstasy’ group may well overtake the other most frequently abused ATS, amphetamine and methamphetamine. If it does, and perhaps even if present levels of consumption are sustained, there is heuristic value in reviewing what is known about the ‘ecstasy’ group because it points so clearly to the lacunae that may appear in the regime of international control.

The question of precursors will also be addressed in this review. As noted above, the burgeoning illicit manufacture of the ATS is supported by the number and simplicity of synthetic routes to manufacture them and the easy access to an enormous variety of starting materials. Shadowing the situation of the stimulant end-products, there appear to have been major shifts in the clandestine use of precursors over the last two decades. As with the psychotropic substances, national and international responses to the control of precursors have also taken the form of a substance-by-substance approach, which, as noted above, is unlikely to keep pace with the perpetually innovative capacity of illicit markets.

Finally, it should be noted that the subject-matter covered here was ultimately determined by the resolution of the Economic and Social Council, which provided the mandate to undertake the review. Subsequent consultations with some Members States and with the INCB Secretariat established that the review would have to cover the substances listed in bold type¹ in Table 1 and integrate the various areas within which they are customarily studied: supply and demand for the substances and the precursors on both the licit and the illicit sides of the equation. This choice, covering such a diverse subject-matter, obviously dictated the sources of information and data that would have to be used. The review therefore draws upon official sources, a large corpus of grey literature and the even more copious body of scientific literature on individual dimensions of the problem.

Table 1: Categories of Central Nervous System Stimulants *

¹ In this table, and throughout part one, the chemical spelling (INN, international non-proprietary name) is used to distinguish individual optical isomers of a substance (e.g. *α*amphetamine, *α*examphetamine, *α*evamphetamine). In all other cases, where this distinction is not necessary, the generic spelling, *amphetamine* is used.

A. Stimulants under international control (Status 1996)	
1. with no currently accepted medical use	
<i>Amphetamine-type substances (1971, Schedule I)</i> - Cathinone - METHCATHINONE (EPHEDRONE) - 4-Methylaminorex - TENAMFETAMINE (MDA) - N-ETHYL-TENAMFETAMINE (MDE) - MDMA and - other ring-substituted amphetamine derivatives	<i>Others such as</i> - Cocaine: occurring naturally in coca leaves (1961, Schedule I) - Coca leaf (1961, Schedule I)
2. with currently accepted medical use	
<i>Amphetamine-type substances (1971, Schedule II)</i> - AMFETAMINE and its optical isomers: DEXAMFETAMINE LEVAMFETAMINE - METAMFETAMINE RACEMATE + opt. isomers: METAMFETAMINE LEVOMETHAMPHETAMINE - FENETYLLINE - METHYLPHENIDATE - PHENMETRAZINE <i>Schedule III</i> - Cathine <i>Schedule IV</i> - Aminorex - AMFEPRAMONE (DIETHYLPROPION) - Benzfetamine - Etilamfetamine - Fencamfamin - Fenproporex - Mazindol - Mefenorex - MESOCARB - PEMOLINE - Phendimetrazine - PHENTERMINE - Pipradrol - Pyrovalerone	<i>Others (1988, Table I)</i> - Ephedrine - Pseudoephedrine (both used in the clandestine manufacture of methamphetamine and methcathinone)
B. Stimulants not subject to international control (Status 1996)	
<i>Amphetamine-type substances such as</i> - Amfetaminil 6 psychostimulant - Clobenzorex 6 anorectic - Dexfenfluramine 6 anorectic - Fencamine 6 psychostimulant - Fenfluramine 6 anorectic - Furfenorex 6 anorectic - Metamfepramone 6 psychostimulant, anorectic - Propylhexedrine 6 nasal decongestant, anorectic - Selegiline 6 antidepressant, antiparkinsonian	<i>Others (pure substances, herbal products) such as</i> - Caffeine (present in coffee, tea, cocoa, cola nuts, maté tea, guarana paste, and in many products like chocolate, soft & energy drinks) - Nicotine (present in tobacco) - Herbal stimulants, such as - Betel nuts - Ephedra plant (ephedrine and pseudoephedrine, the main active ingredients, are controlled as precursors) - Khat plant (cathinone and cathine as the primary and secondary active ingredients are controlled)

*Note: **BOLD BLOCK LETTERS** indicate ATS covered by the study.

The year in brackets indicates under which of the three United Nations Conventions the individual substances are scheduled (Status 1996):

(1961): *Single Convention on Narcotic Drugs*

(1971): *Convention on Psychotropic Substances*

(1988): *Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances*

THE LICIT SIDE OF THE EQUATION: THE AMPHETAMINE-TYPE STIMULANTS (ATS) AS MEDICINE

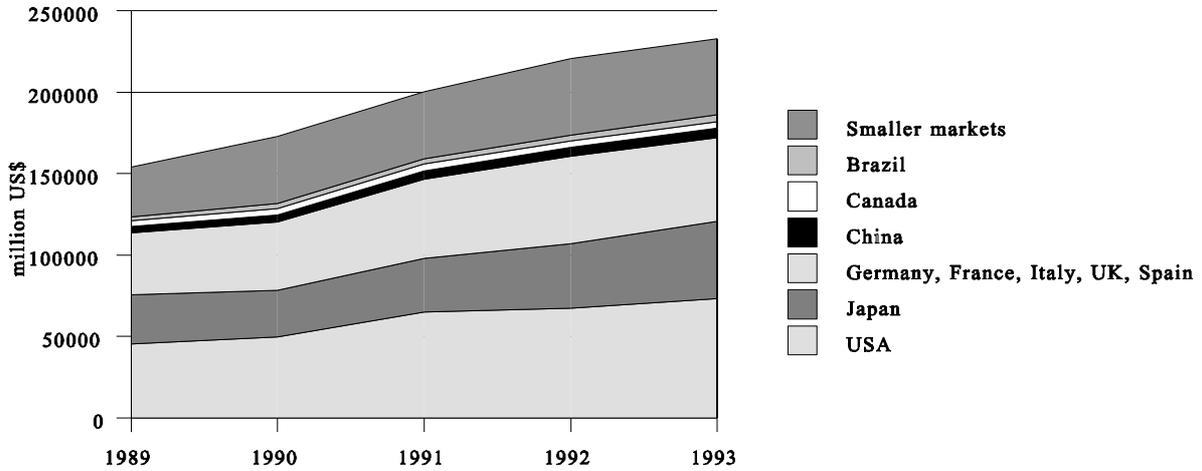
The ATS were previously considered to be an important group of medicines. Several major reviews of their licit use [DEA, 1973; Smith et al., 1979; NIDA, 1980; INCB, 1990] show that what was, from the 1930s, a wide range of therapeutic applications, has been shrinking steadily through the last two decades. They are now, in most countries, prescribed for a mere handful of medical indications. Yet the downward trend must be seen in the light of two negative factors, already noted in the Introduction: the localized epidemics deriving from misuse of licit pharmaceuticals, and the displacement effect of controls, sometimes driving manufacture and distribution into illicit markets. These apparently contradictory phenomena demand a detailed review of the historical evolution of the present situation, in order to avoid past mistakes, to develop a more informed forecasting capacity, and to ensure better control regimes in the future. Part one thus seeks to verify and complement previous assessments, as well as to synthesize, in the form of a review, the diverse information germane to the issue.

Controls, national and international, are instituted to ensure the availability of psychotropic substances for therapeutic use and to limit their non-medical use and consequent risk to public health. Therapeutic utility and public health risk are therefore the two variables that are examined in Part one, together with the other principal factors involved. In the context of the ATS, the relative positions of the two variables have been changing through this century. Part one thus discusses (I) the economic significance of ATS, (II) their relative importance within the larger group of psychotropic substances, (III) trends in their manufacture and trade and (IV) their changing therapeutic significance. Presented below is a synthesis of the main arguments. They are, in each case, substantiated by selected series of data and illustrated with figures. The period covered by the data goes back to the mid-1970s, when the 1971 Convention entered into force, and further back where feasible.

I. The economic significance of ATS in the pharmaceutical industry

The **world pharmaceutical market** was valued at US\$ 233 billion in 1993. Though large in absolute terms, distribution is skewed and the market shows a very strong concentration of manufacture and sales in a few industrialized countries. The only two developing countries which figure in the list of the 10 most important pharmaceutical markets are China and Brazil. The markets in the United States of America and Japan together account for 52% of global sales; the five largest European markets (Germany, France, Italy, the United Kingdom of Great Britain and Northern Ireland and Spain) take the share up to 71%; these, together with Canada, China and Brazil account for 80% of global sales. The rest of the 175 countries in the world share the remaining 20% (see [Figure 2](#)).

Global pharmaceutical sales
The largest 10 markets (in million US\$)



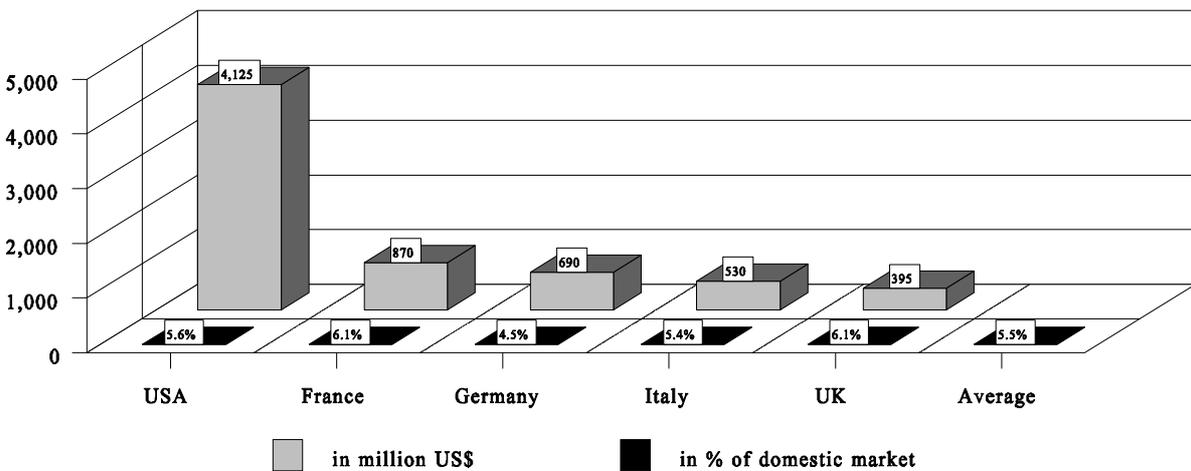
Sources: MSI, *World Drug Market Manual*, London, 1994

Figure 2

Understanding this broad spectrum of the pharmaceutical industry is important in order to set a frame of reference for the subsequent discussion of the manufacture and trade of ATS. Information is available on central nervous system (CNS) active drug sales in five of the world's six largest markets, which account for 51% of global licit drug sales. In these five countries the share of CNS active drug sales amounted to an average 5.5% of domestic pharmaceutical sales (see Figure 3). On the assumption of a similar pattern in the rest of the world, **global CNS active drug sales** can be expected to range from \$10 billion to \$14 billion, i.e. 4.5% - 6% of the global pharmaceutical market.

CNS drug sales in five major markets

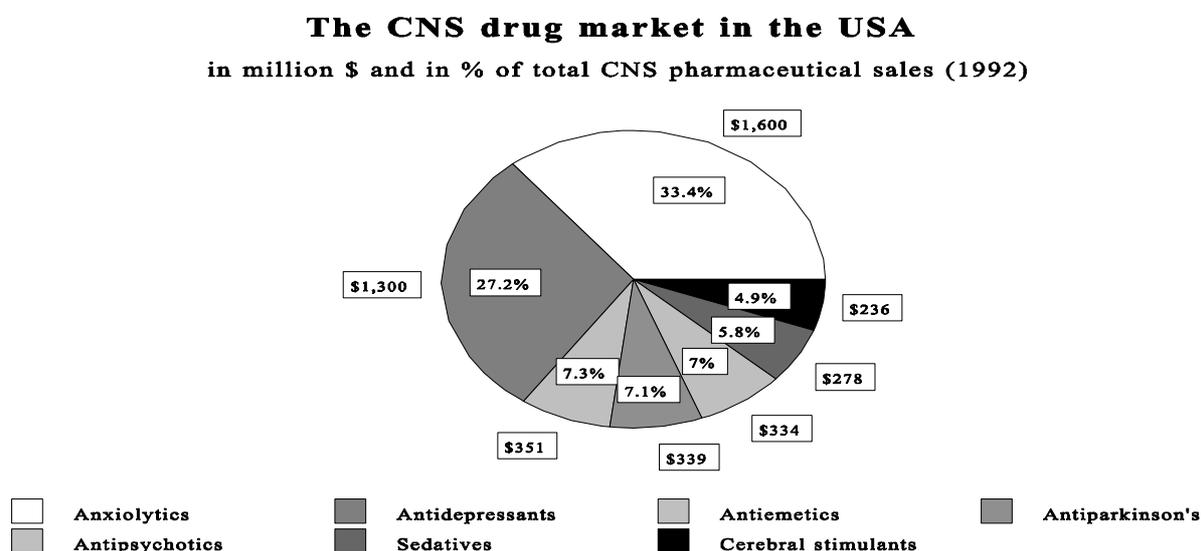
in million US\$ and in % of domestic pharmaceutical market (1993)



Sources: Menio Biomedical Associates, quoted in Scrip's 1995 *Yearbook*, Vol. 1, p. 156; IMS, *World Drug Manual* 1994.

Figure 3

The **CNS active drug market in the United States**, the largest of the five, is composed of the seven pharmaceutical categories shown in [Figure 4](#). While these categories do not correspond exactly with those of the CNS active substances under international control, one of the closest matches is precisely between the ATS considered in this study and the pharmaceutical category of the cerebral stimulants (\$236 million), which account for about 5% of the United States CNS active drug market. The leading ATS found in the cerebral stimulants category are methylphenidate, comprising 24% of the cerebral stimulants market, and pemoline and methamphetamine HCl, together comprising 21% of the cerebral stimulants market. While there are several other ATS in this category, no sales figures are available. What is available, however, is sufficient to estimate the size of the **market for ATS in the United States**: it would appear to be in the range of \$107 million to \$148 million, probably closer to the upper figure, which would be slightly less than 3% of the CNS active drug market, or 0.2% of the overall pharmaceutical market. Evidence from other countries [*cf.* Schwabe and Paffrath, 1994; *Scrip*, 1995] indicates that the proportion of ATS within the CNS drug category is even smaller.



Source: *Theta Corporation, Central Nervous System Pharmaceuticals, Report No. 343, April 1993.*

Figure 4

It is clear from the foregoing that the ATS have become marginal to the mainstream pharmaceutical industry in terms of market share. Major industry studies [*Theta*, 1993] indeed establish that there are hardly any new amphetamine-type molecules at present in an advanced stage of development for therapeutic application. Markets for other psychoactive drugs, however, have been growing strongly in recent years at a 17% annual rate of growth, from \$2 billion in 1986 to \$4.4 billion in 1991. This growth was led by the antidepressants, with sales that grew at a 42% annual rate during the same period [DiMasi and Lasagna, 1995].

With regard to ATS, a few specific therapeutic applications contrast with the general trend described above. As will be seen in Chapter IV, the market for a few drugs for the treatment of **attention-deficit disorder** and of **obesity** seems to be stable or, in some cases, expanding. In specific countries and/or regions there is considerable potential for further expansion. The best

examples are the various forms of overeating/overweight disorders, first of all obesity, affecting some 25-30% of the total population of the industrialized world and an increasing population segment in many developing countries. The total market of anorectic agents is estimated to be worth about US\$30 billion p.a. [*Scrip*, 1992], equivalent to more than 10% of the global pharmaceutical market. It is one of the most significant areas of potential growth. Several factors, however, limit more precise analysis: (a) the complex nature of this product group, ranging from non-pharmaceutical therapies such as low-calorie foods, drinks and meal replacements through a range of herbal products (often also containing chemical pharmaceuticals) and ending with a broad range of anorectic pharmaceuticals and other more advanced drugs; (b) the complementary nature of the various treatment modalities and therapies, compounded by easy availability in many countries of products with ATS constituents; (c) lax prescribing practices; and (d) the existence of considerable parallel markets. Estimates (i.e. US\$ 50 million p.a.) for the anorectic pharmaceuticals within this market have to be interpreted, therefore, with great caution.

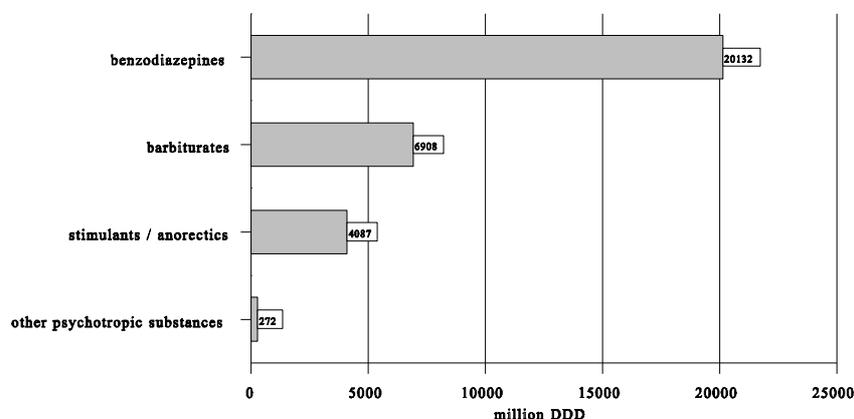
II. The relative significance of ATS among psychotropic substances

Moving from the broad categories of the pharmaceutical drugs as a whole, this chapter tries to assess the relative position of the ATS among the main categories of psychotropic substances, as well as licit global manufacturing volumes of the individual substances themselves. The changing therapeutic significance of the ATS is considered in detail in Chapter IV. However, a rough assessment of their therapeutic significance compared to other categories of psychotropic substances can be derived from the **number of substances under international control** and from the degree of control applying to individual substances. Between 1971 and 1995, the number of stimulants and anorectics under international control increased by 385%, which is less than the 433% increase in controlled sedative-hypnotics and tranquillizers. Comparing the degree of control, however, shows a quite different picture: as of 1995, a third of all controlled stimulants and anorectics (which include three-quarters of the medically used ATS covered in the present study) are listed under Schedule II; by contrast, 83% of the sedative-hypnotics and tranquillizers are under the less strict control regime of Schedule IV of the 1971 Convention. As noted above, the scheduling criteria of the 1971 Convention are based on a sliding scale of therapeutic usefulness and public health risk. The benzodiazepines are therefore considered to have a higher benefit-to-risk ratio, whereas the stimulants and anorectics carry a higher public health risk.

A comparison of the number of new drug approvals of different classes of psychoactive drugs in the United States largely shows a similar picture. Among the 45 psychoactive drugs approved in the period from 1963 to 1992, there were only two ATS, pemoline and bupropion (an antidepressant which is not under control). By contrast, and in the same period, 13 new benzodiazepines, 11 tricyclic antidepressants and 4 phenothiazines were approved [DiMasi and Lasagna, 1995].

The comparative purpose of this chapter is best served by using **licit global manufacturing volumes**, expressed in defined daily doses (DDD), as illustrated in Figures 5 and 6. The principal source for the following analysis is INCB data. In line with previous analyses [*cf.* INCB, 1990], these data establish the following crucial points: (a) the stimulants, which used to be the second largest group of psychotropic substances in licit manufacturing volume terms, have fallen to third place following widespread use of the benzodiazepines and their relative significance can be expected to decline further; (b) the ATS covered in the present study constitute an overwhelming share of the total category of the licit stimulants scheduled under the 1971 Convention; and (c) within the ATS group a considerable restructuring has occurred: some substances have become obsolete and virtually disappeared (fenetylline, phenmetrazine); a few new drugs, such as pemoline, have emerged; therapeutic applications have become increasingly refined; and the therapeutic uses have changed from direct to indirect, increasingly using conversions into safer medicines. The latter is particularly true for amphetamine and methamphetamine isomers and will be discussed below.

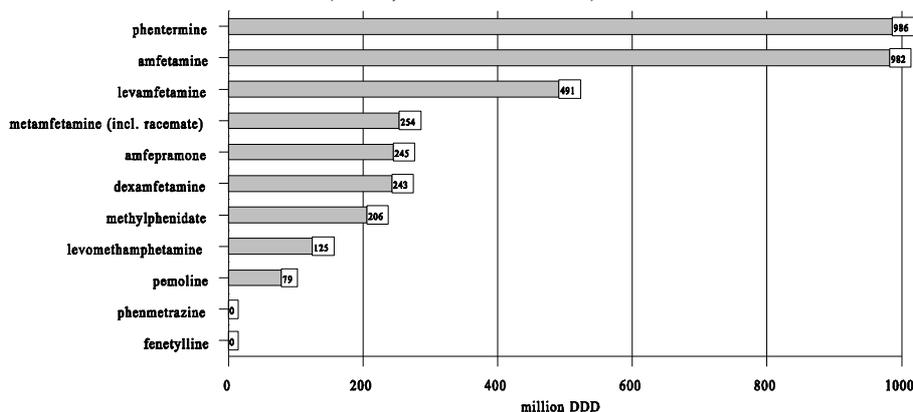
**Licit global manufacture of psychotropic substances
(1993, in million DDD)**



Source: INCB, *Psychotropic Substances, Statistics for 1993*, New York, 1995.

Figure 5

**Licit global manufacture of ATS
(1993, in million DDD)**



Source: INCB, *Psychotropic Substances, Statistics for 1993*, New York, 1995.

Figure 6

The evolutionary path of research for better and safer therapeutic application of ATS is similar to that of many other categories of drugs, the barbiturates being a typical example. Ever since the negative effects of the large-scale therapeutic applications of the various amphetamines were recognized, technological innovation in the pharmaceutical industry has been driven by the **need to find safer drugs** with more specific therapeutic application, thus avoiding the problems inherent in the amphetamine molecule. As happened with research on the barbiturates and opiates, there was a long-standing hope among researchers that by altering the core amphetamine molecule, the useful effects could be retained, indeed made more specific, while the addictive potential could be eliminated or reduced. The result has been a range of new generation drugs which were either simple structural modifications or more complex constructions (fenetylline,

mesocarb, amfetaminil etc.) where the core amphetamine molecule is partly **packaged** by chemically combining it with other structural entities. Practically all the amphetamine-type drugs that have been developed since the 1950s are the results of these efforts. Yet many of these products are reconverted by the human body into the core amphetamine/methamphetamine molecule and therefore have a similar addictive potential. There is now a growing body of evidence to show that some of these newer generation drugs, while indeed more specific and safer in therapeutic application, still carry considerable potential for abuse if frequently used on a large scale. It is also ironical that many of these drugs may be potential candidates for future scheduling; some of them have indeed been subject to pre-review or review by the Expert Committee on Drug Dependence of the World Health Organization (WHO).

Another effort to improve the risk-to-benefit profile of ATS has been a gradual move towards manufacturing and marketing **pure optical isomers** instead of the racemates. With individual isomers usually displaying quantitatively and/or qualitatively different activity profiles, it is possible to produce the specific isomer which is more beneficial in the desired direction and less potent in its side effects. The introduction of dexamphetamine (*Dexedrine*) with a two to four times higher CNS stimulant activity than the racemic amphetamine (*Benzedrine*) in 1935 in the United Kingdom was the first step in this direction. This trend has continued since, for example with selegiline and dexfenfluramine. As a result, it is now common practice that both optical isomers may be in medical use in addition to the racemic mixture. There is no other category of substances among the narcotic drugs and psychotropic substances where this issue is so significant, from both the therapeutic as well as the control point of view. It is all the more unfortunate, then, that the 1971 Convention and many national laws do not provide a simple tool to address this technical problem.

In spite of the increase in specificity and in the benefit-to-risk ratio of the classical ATS, their place on the pharmaceutical market has been gradually taken by various other drug groups with more specific therapeutic applications, the main one being the various antidepressants. This overall trend, which, again, has a parallel in the gradual replacement of barbiturates by various benzodiazepines, continues. It may be expected that with the appearance of more specific, non-amphetamine medicines for the three areas of medical indication where amphetamines are used today (attention-deficit disorder, narcolepsy and obesity; see below), the downward trend in the use of licit amphetamine-type substances will continue and may perhaps eventually eliminate the few ATS remaining on the licit pharmaceutical market, or at least discourage their prescription. While this process obviously follows its own laws and has to be regarded as a positive one, the potential will always exist for a licit-to-illicit shift in manufacturing and consumption. Past experience also shows that professional bodies can play a very significant role in this development by balancing prescribing practices, consumer preferences and commercial interests, thus accelerating a process which is usually a lengthy one.

III. Global manufacture and trade of licit ATS

INCB reports regularly present statistics and detailed analyses of **global manufacture and trade** of ATS. A number of trends relevant to the purposes of the present study emerge from these data. Among the ATS covered, two broad groups can be identified. The first group (see Figures 7 - 12)², comprising amphetamine (all isomers), phenmetrazine, fenetylline and pemoline, shows a clear downward trend in terms of manufacturing volumes, or, more precisely, the amount remaining after conversion into other pharmaceuticals, which is the crucial indicator for the availability of a particular substance. From initially high levels at the time when the 1971 Convention entered into force, the amphetamine isomers and phenmetrazine showed a rapid decline to levels that have stayed remarkably consistent over two decades. The global manufacturing volume of levamfetamine (Figure 9), which appears to be an exception, is in fact a confirmation of what was noted earlier: many of the ATS covered by this study are no longer used directly in medicine but rather as intermediates in the manufacture of other pharmaceuticals. Levamfetamine, which is almost entirely converted (racemized) into amphetamine is, thus, probably the best example of a >virtual= drug which still has to be reported to INCB under the special reporting requirements of the 1971 Convention. Phenmetrazine, by contrast, is the best example of another trend in the licit ATS market, i.e. it has become a drug of essentially theoretical interest, which can be expected to disappear from the pharmaceutical market. INCB data also show that global stocks and international trade of amphetamine-type substances are declining. With regard to the latter, it is important to stress the steadily converging figures of reported global exports and imports, which thus indicate a gradual improvement in the international control situation, leaving less space for diversion.

Licit global manufacture (vs. amount remaining after conversion)

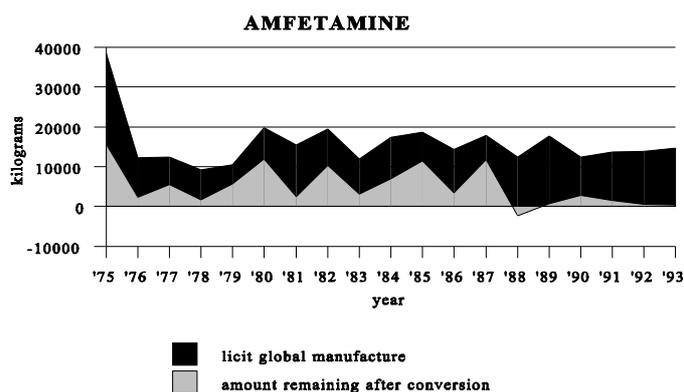


Figure 7

² It should be noted that all figures on manufacturing volumes are presented in the same format but have different scales and reflect different magnitudes.

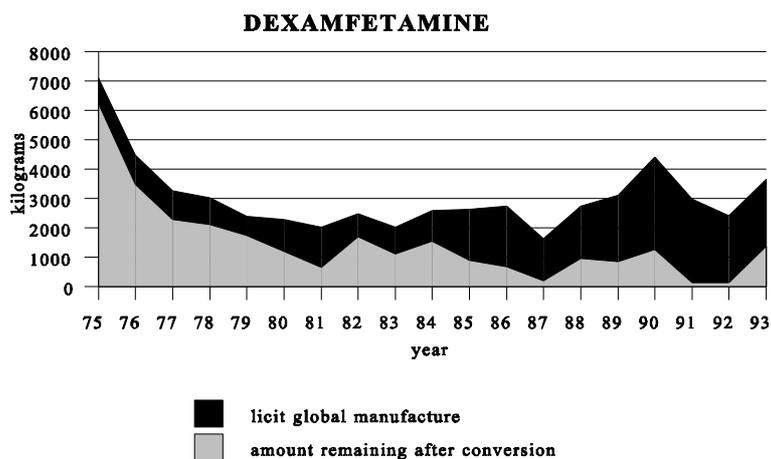
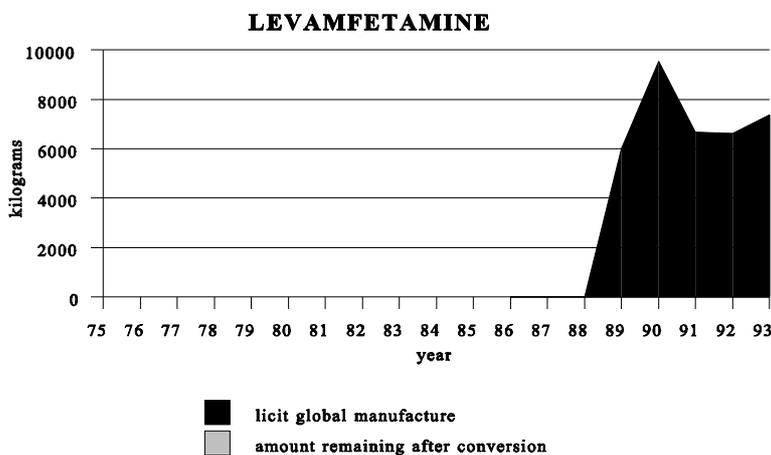
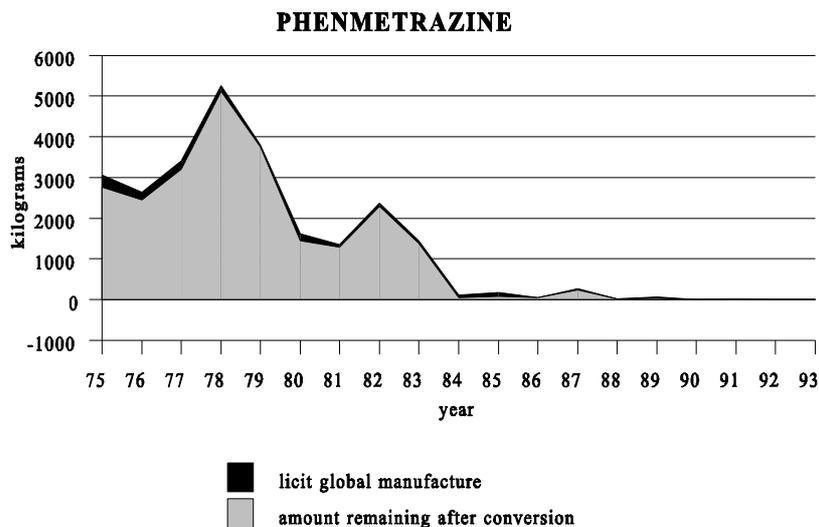


Figure 8



Note: Levamfetamine has been under international control since 1986

Figure 9

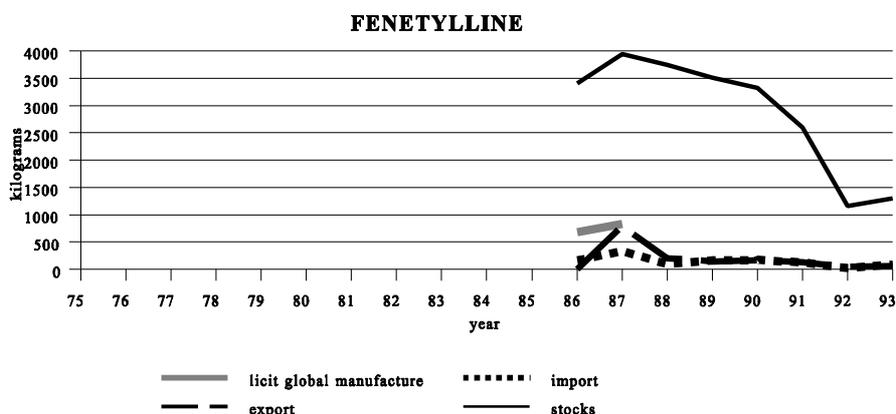


Source: INCB, *Psychotropic Substances, Statistics* (E/INCB Series).

Figure 10

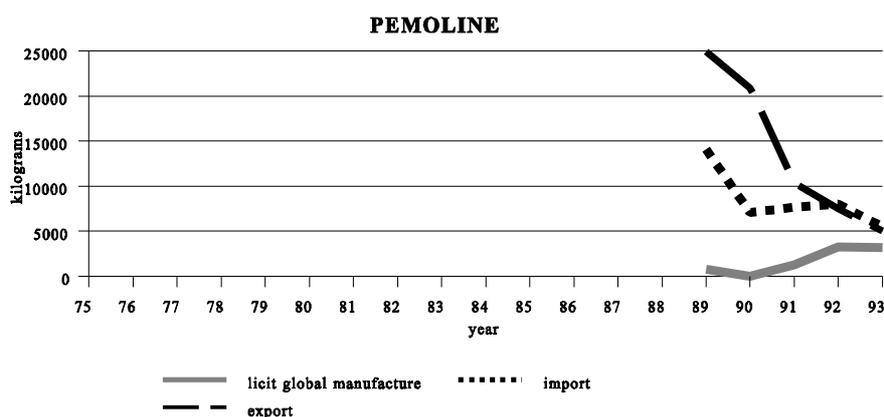
A downward trend also appears for fenetylline and pemoline but obviously comes later, after they were scheduled in 1986 and 1989, respectively. In both cases, the downward convergence of the indicators (manufacture, export, import and/or stocks) is a clear sign of an improving situation and also confirms that control measures, accompanied by appropriate implementation efforts, can lead rapidly to positive changes on the licit pharmaceutical market. Both substances, however, remain targets of relatively frequent diversion attempts.

Licit global manufacture, trade and manufacturers' stocks



Note: Fenetylline has been under international control since 1986. No licit manufacture has been reported since 1987.

Figure 11



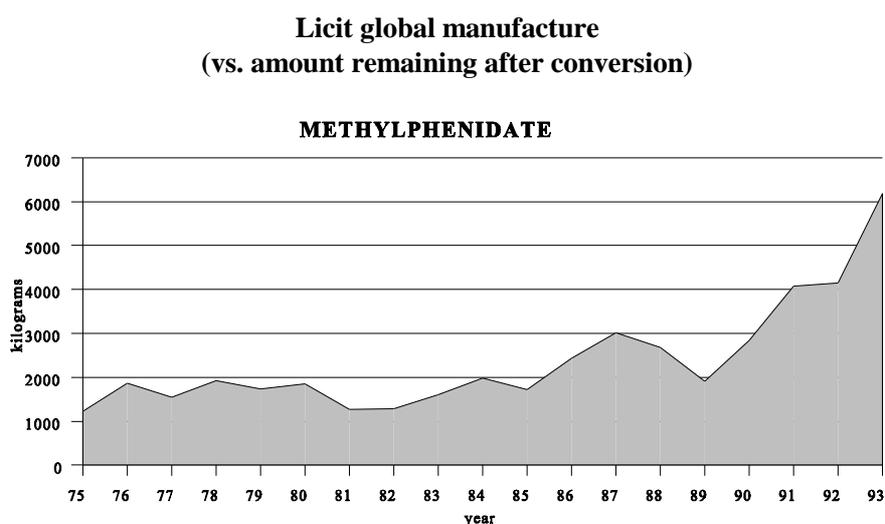
Note: Pemoline has been under international control since 1989. No information on stocks of Schedule IV substance available.

Source: INCB, *Psychotropic Substances, Statistics* (E/INCB Series).

Figure 12

The second group, consisting of methylphenidate, amfepramone, phentermine and methamphetamine isomers, shows more fluctuation but with a recent upward trend (see [Figures](#)

13 - 17). Direct consumption or conversion into other psychotropic substances and into non-psychotropic drugs appear to be behind the increases in licit global manufacture of these substances. While increasing consumption is the main cause for the upward trend of methylphenidate, amfepramone and phentermine, the demand for various conversion products seems to drive licit manufacture of methamphetamine isomers. Levomethamphetamine (Figure 17) is the only exception to this trend, since it is increasingly converted into selegiline, an antiparkinsons drug, but also used directly as a nasal inhaler, particularly in the United States.



Note: Methylphenidate is not converted into other pharmaceuticals.

Figure 13

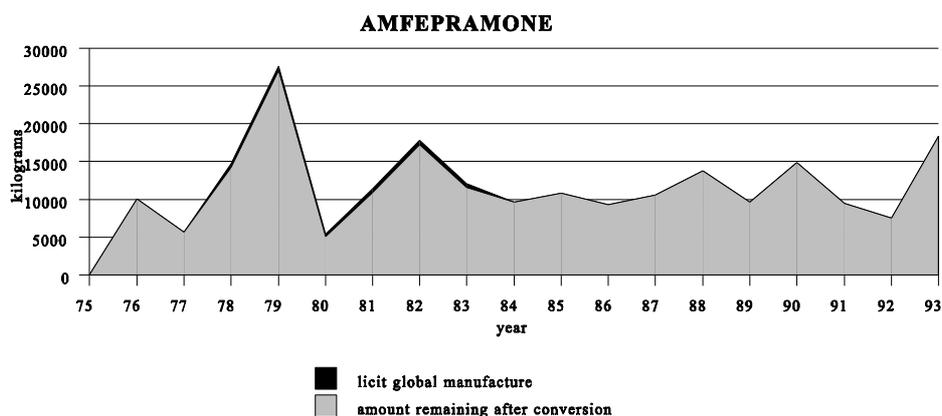
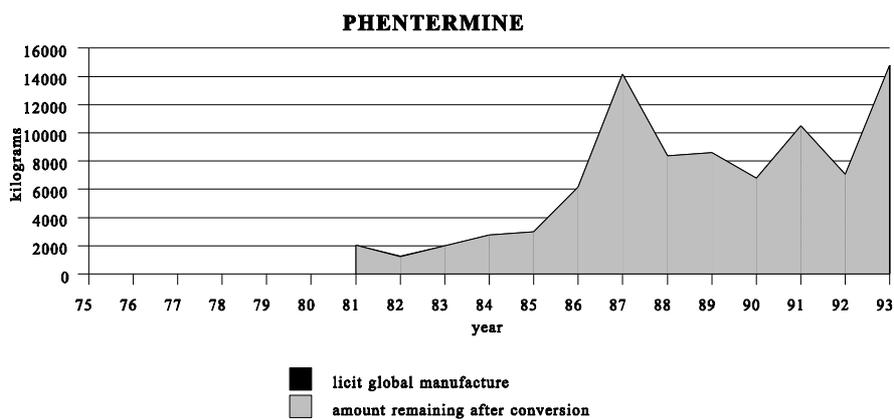
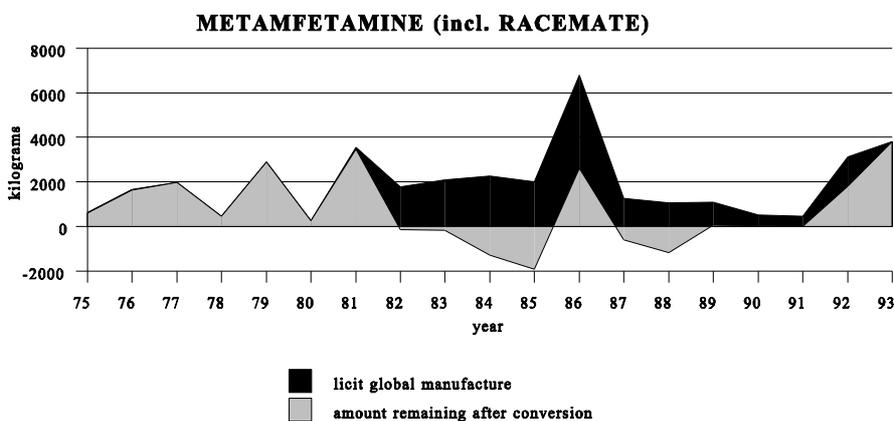


Figure 14



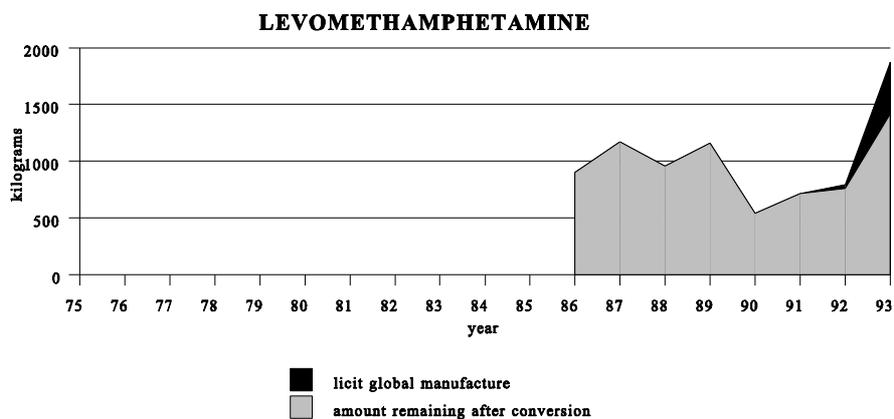
Note: Phentermine has been under international control since 1981.

Figure 15



Note: Metamphetamine racemate has been under international control since 1988.

Figure 16



Note: Levomethamphetamine has been under international control since 1986.

Note: Some important manufacturing countries have not yet started to report on Schedule IV substances (such as amfepramone and phentermine).
 Source: INCB, *Psychotropic Substances, Statistics* (E/INCB Series).

Figure 17

As noted above, any analysis that tries to aggregate global manufacturing of the ATS is complicated by the complex pattern of industrial **conversions** (see [Table 2](#)) of the substances originally manufactured into three further subcategories:

- (a) Into the optical isomers of the original substances;
- (b) Into other, usually stimulant-type psychotropic substances that may or may not fall under the same control requirements as the original substance (for instance, benzphetamine, fenproporex and mefenorex);
- (c) Into other psychoactive substances that are not under the purview of the 1971 Convention (for instance, clobenzorex, prenylamine and selegiline).

While the 1971 Convention foresees reporting quantities of psychotropic substances used for the manufacture of substances which are not under its purview (i.e. for conversions referred to under (c) above), the reporting of quantities used for conversion into other psychotropic substances, including optical isomers of the original substance, is only voluntary. This, of course, complicates global monitoring and aggregation of quantities of ATS manufactured licitly.

Even if exact global licit manufacturing volumes of ATS and their conversion products were known, the reverse aspect of this interrelationship would still require consideration. Although many of the conversion products are structurally different from the original amphetamines and may be indicated for different medical conditions, many of them are readily metabolized by the human body back into amphetamine or methamphetamine, and they thus have to be regarded as pharmacological equivalents of the parent molecule. The consequences for regulatory control will be discussed in the context of [Figure 22](#) below.

Data on **licit manufacture and trade** at the **country level** allow the identification of the countries and regions where these substances still play a significant role, either as therapeutic drugs or as starting materials for the licit pharmaceutical industry. Since statistics and comments on recent trends are provided annually by INCB, this discussion seeks only to summarize the present situation.

While the manufacture of ATS is largely dominated by western European countries and the United States, **international trade** in these substances is far more diverse. Using the **number and diversity of importing countries** as a criterion, at least two groups of substances can be distinguished. The first group covers substances where total imports are dominated by a small number of countries accounting for the majority of the global total. This group comprises amphetamine, metamphetamine and their isomers, i.e. the parent substances of the synthetic stimulants, which are used mainly as starting materials in the licit pharmaceutical industry of a few European countries and the United States. Large-scale industrial conversions include the manufacture of benzphetamine (an anorectic) from metamphetamine, of selegiline (used as antiparkinson agent) from levomethamphetamine and of clobenzorex and fenproporex (both of which are anorectics) from amphetamine and dexamphetamine (see [Table 2](#)).

Table 2: Licit use of controlled amphetamine-type substances in the manufacture of other pharmaceuticals

Starting material (optical isomer)	Product			Therapeutic category /Use of product	Conversion cases reported (1990-1993) ^{b/}	
	1971 Convention		isomer that is usually used ^{a/}			
	Sche- -dule	optical isomer ^{a/}				
AMFETAMINE (")	amfetaminil	-	-	psychostimulant	-	Germany
	clobenzorex	-	-	anorectic	(+)	Switzerland
	dexamfetamine	II	(+)	psychostimulant	(+)	France
	<i>fenalcomine</i> ^{c/}	-	-	coronary vasodilator	-	-
	fenetylline	II	-	psychostimulant	-	Bulgaria [Dimova and Dinkov, 1994]
	fenproporex	IV	(")	anorectic	(")	France, Switzerland
	mefenorex	IV	-	anorectic	-	- [Sittig, 1988]
	mesocarb	IV	-	psychostimulant	-	Bulgaria [Dimova and Dinkov, 1994]
	phenatine	-	-	psychostimulant	-	- [Merck Index, 1989]
	prenylamine	-	-	coronary vasodilator	-	Germany
	racefemine	-	-	antispasmodic	(")	- [Merck Index, 1989]
	sydnophen	-	-	psychostimulant, antidepressant	-	Bulgaria [Dimova and Dinkov, 1994]
DEXAMFETAMINE (+)	clobenzorex	-	-	anorectic	(+)	France
	<i>dextrofemine</i>	-	-	antispasmodic	(+)	-
	fenproporex	IV	(")	anorectic	(")	Switzerland
LEVAMFETAMINE (-)	amfetamine	II	(")	psychostimulant	(")	France
LEVOMETHAMPHET- AMINE (-)	selegiline	-	-	antiparkinsons, MAO-B inhibitor	(-)	France, Germany, Ireland, Israel, USA
METAMFETAMINE RACEMATE (")	levomethamph. + metamfetamine	II	(-)	nasal inhalant	(-)	United States
		II	(+)	antihypotensive, sympathomimetic	(+)	
	famprofazone	-	-	analgesic, antipyretic	-	Germany
	<i>fencamine</i>	-	-	psychostimulant	-	-
	<i>furfenorex</i>	-	-	anorectic	(")	-
METAMFETAMINE (+)	benzfetamine	IV	-	anorectic	(+)	United States
	propylhexedrine	-	-	nasal decongestant, anorectic	-	- [Schröder, 1976]
PHENMETRAZINE ^{d/}	<i>fenbutrazate</i>	-	-	anorectic	-	-
	morazone	-	-	analgesic, antipyretic	-	Germany
	<i>phendimetrazine</i>	IV	(+)	anorectic	(+)	-
MDA ^{d/}	protokylol	-	-	bronchodilator, β-sympathomimetic	-	-
PMA ^{d/}	fenoterol	-	-	antiasthmatic, bronchodilator	-	France
	<i>formoterol</i>	-	-	bronchodilator, β-sympathomimetic	(")	-

^{a/} A dash indicates that the optical isomer is not specified.

^{b/} The cases mentioned were reported to INCB [INCB, 1993a and 1995a]. Other sources are indicated separately.

^{c/} Italics indicate substances which can be manufactured from the respective starting material. However, no reference on the chemical synthesis has been found.

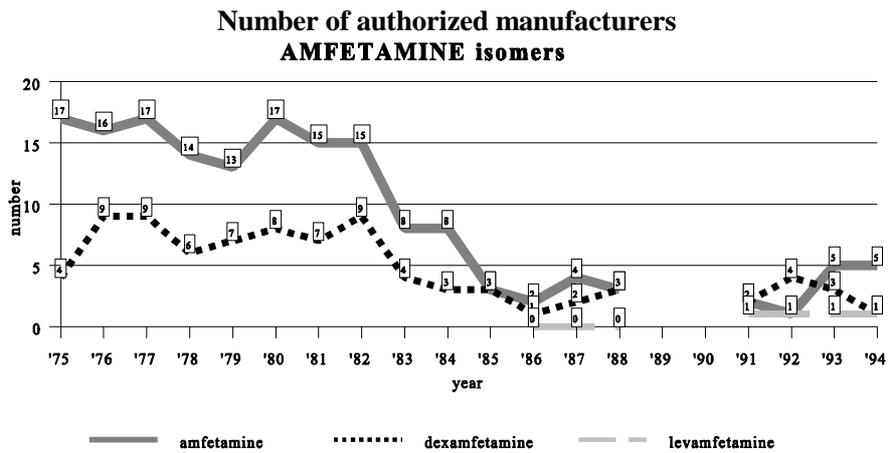
^{d/} The optical isomers of phenmetrazine, MDA and PMA are not specified in the 1971 Convention.

The second group covers substances that are characterized by a larger number of countries with licit imports. Other characteristics of this group, which comprises the Schedule II substance methylphenidate as well as the Schedule IV substances amfepramone, pemoline and phentermine, are frequent re-exports and the relative importance of some Latin American countries such as Argentina, Brazil, Chile, Mexico and Panama, as well as that of China, India and South Africa, in their manufacture, trade and/or use.

The conversion of amphetamine and methamphetamine isomers into other pharmaceutical products implies very little direct therapeutic use of the parent substances. Yet in view of the global availability of the many structurally and pharmacologically related conversion products, there is still controversy about their relative safety, therapeutic usefulness and metabolic re-conversion into amphetamine or methamphetamine. With regard to substances of the second group, the relatively high consumption figures in certain parts of the world are of some concern (see Chapter IV). The diversity of the global market and inadequate reporting on Schedule IV substances from some important manufacturing countries contribute to the intractability of global manufacture and trade, particularly in regard to amfepramone, pemoline and phentermine. Diversion, of which attempts are known for pemoline from Latin America [INCB, 1995a] and for phentermine from the Far East, may, in such circumstances, be facilitated.

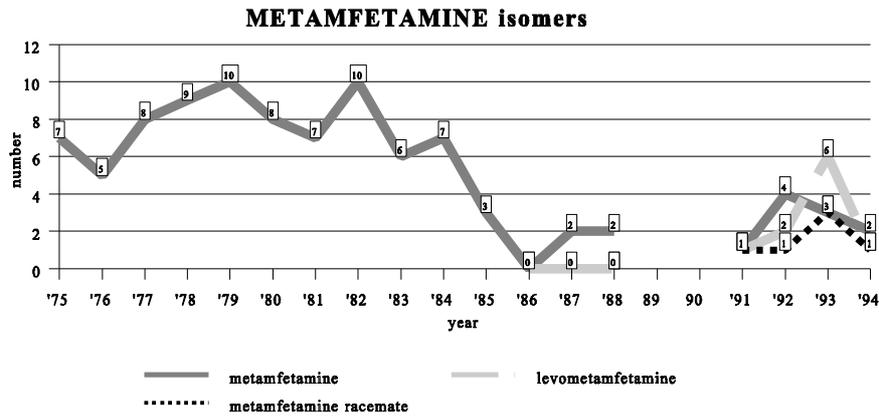
Another factor which complicates global monitoring is the frequent re-exports associated with the **concentration of manufacturing and/or processing sites** of international companies in very few countries. This is known, for example, in Ireland, where large-scale conversion of imported levomethamphetamine into selegiline takes place, and in Switzerland, which has always been the major supplier for global methylphenidate requirement, but which recently emerged as a processing site, tableting methylphenidate raw material manufactured elsewhere. A complex re-exporting activity follows such manufacturing and processing, the products being either the remaining substances themselves or the various preparations or a conversion product, i.e. even a different (psychotropic or non-psychotropic) pharmaceutical drug. As a consequence of this, figures of reported manufacture and/or imports need not necessarily reflect the actual scientific and medical requirements of the country in question. While all this is normal and perfectly legitimate industrial practice, it obviously complicates accurate international monitoring of the movement of the multiplicity of end-products. When a particular country which re-exports is not a party to the 1971 Convention, it is not bound to report the information, although it may do so voluntarily. The monitoring chain could thus be broken.

The **number of authorized manufacturers** of ATS, which reflects, to some extent, the interest of the pharmaceutical industry, has also declined considerably on the global aggregate (see [Figures 18 - 21](#)). The picture presented in the figures is a complex one, but a few specific points may serve to make the pattern clear. The crucial variable to interpret the number of authorized manufacturers is the point in time that the substance in question was scheduled and/or when major manufacturing countries acceded to the 1971 Convention. At the time when the individual substances were scheduled, a large number of authorized manufacturers was usually reported. For the substances scheduled in 1971, there was then a significant downward trend, which lasted up to the mid-1980s. Since then, and apart from some fluctuation, the situation has stabilized at a low level of a mere handful of manufacturers for each substance worldwide.



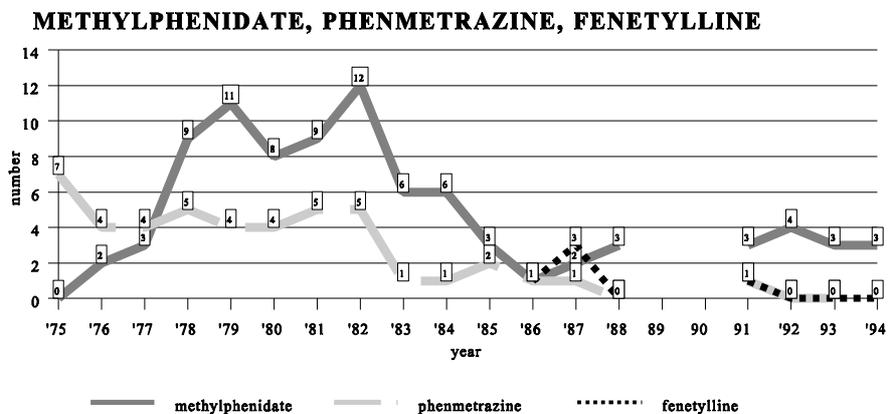
Note: Amphetamine and dexamphetamine have been under international control since 1971, levamphetamine since 1986

Figure 18



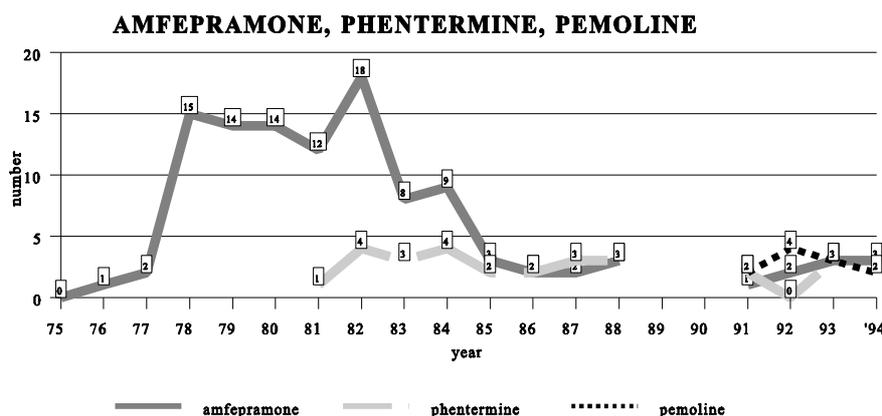
Note: Metamphetamine has been under international control since 1971, levomethamphetamine since 1986; Metamphetamine racemate since 1988.

Figure 19



Note: Methylphenidate and phenmetrazine have been under international control since 1971, fenetylline since 1986.

Figure 20



Note: Amfepramone has been under international drug control since 1971, phentermine since 1981, pemoline since 1989

Figure 21

Note: This covers only those manufacturers which have actually manufactured and/or converted ATS. For 1989 and 1990 no data are available.

Source: UNDCP, *Manufacture of Narcotic Drugs and Psychotropic Substances under International Control* (ST/NAR.4).

All of the above may well be an indication of declining interest among established manufacturers. It certainly implies, however, a **concentration of the licit manufacture** of ATS in fewer hands, which would, *ipso facto*, make manufacture and trade easier to monitor, at both national and international levels. This could be counteracted by indications that the manufacture of certain stimulants is shifting geographically to countries which did not previously manufacture them. If the regulatory and reporting apparatus in these countries is not sufficiently developed, a decline in the number of authorized manufacturers need not necessarily imply an actual decline in manufacturing volumes, or even a market that is easier to monitor. In addition, such concentration does not automatically mean better control. Experience has shown that non-compliance with the treaties, or with national laws and regulations, by one single major manufacturer or exporter is sufficient to offset the entire monitoring process. Only global adherence and compliance, better assessments of real therapeutic requirements, accompanied by vigilance of consumption patterns and therapeutic uses, can provide a sound basis for lasting improvement. A recent international conference clearly demonstrated the magnitude of this problem by identifying certain critical countries as well as problematic substances [INCB/UNDCP, 1995].

Another aspect which should be considered in the context of manufacture of ATS is, as mentioned before, their **metabolic conversion** in the human body. [Figure 22](#) illustrates these conversions. The industrial/chemical conversions, which were detailed in [Table 2](#) above, are also summarized in [Figure 22](#).

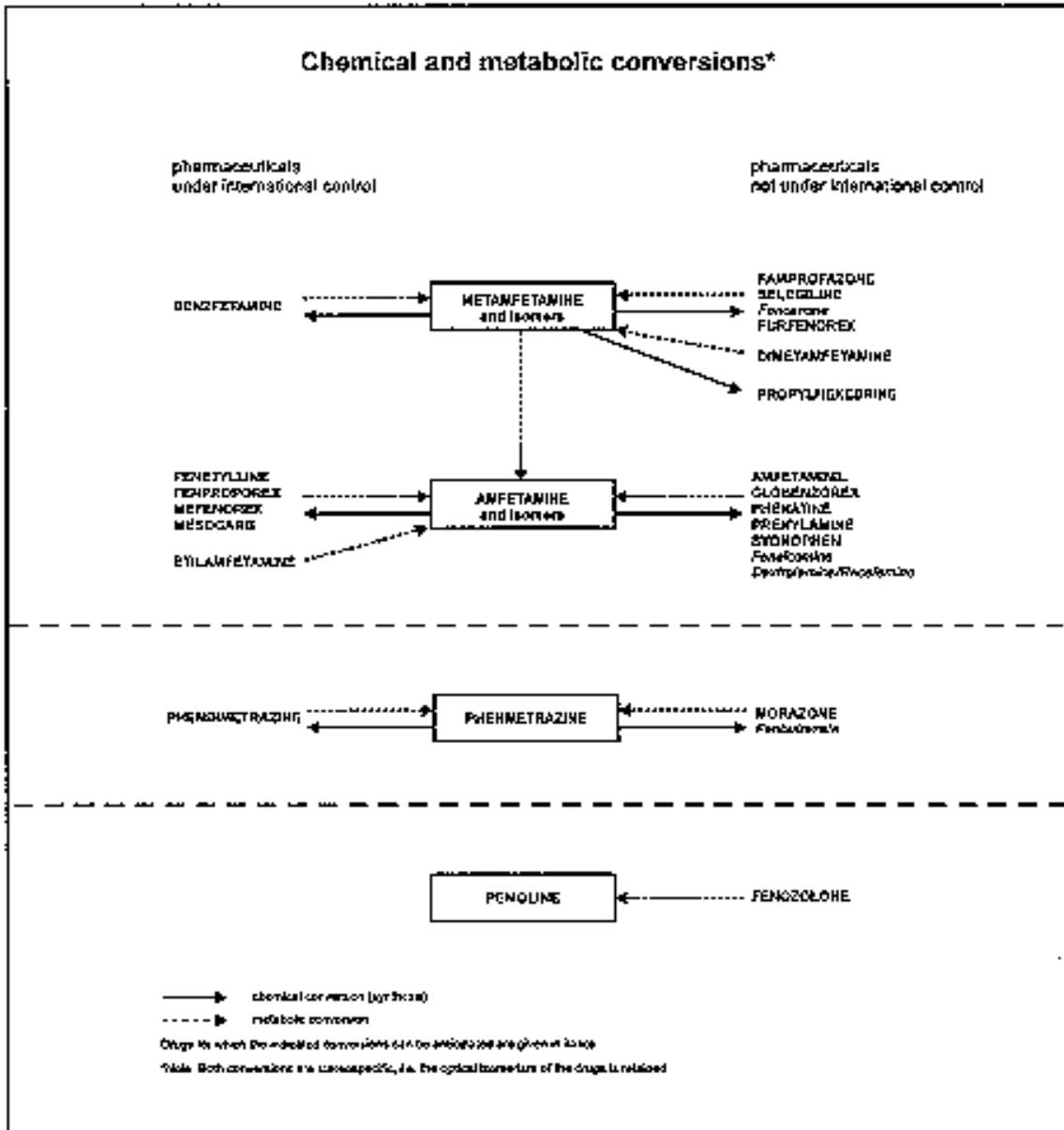


Figure 22

These chemical and pharmacological considerations have **direct consequences for regulatory control**. Figure 22 shows that seven of the ATS already under international control may be classified, in qualitative terms, as metabolic equivalents of amphetamine (etilamfetamine, fenetyliline, fenproporex, mafenorex, mesocarb), metamfetamine (benzfetamine) and phenmetrazine (phendimetrazine). The public health problems encountered with them can, to varying degrees, be attributed to the metabolic end-products amphetamine, methamphetamine and phenmetrazine. Yet most of the metabolic precursors have been placed under a less strict control regime, Schedule IV, thus leaving room for diversions and overconsumption. The figure also lists 16 further pharmaceutical drugs for which experimental data indicate a similar metabolic conversion into one of the psychotropic substances or where such conversion can reasonably be

expected on the basis of their chemical structure. Some of these substances are already under national control in a few countries, indicating isolated cases of concern which may subsequently lead to international review. It appears, though, that a group review of the "interconversion families" would probably better address these issues. Such an approach has, in fact, been proposed during the process of reviewing 28 amphetamine-type substances for eventual international control [Keup, 1986]. Past experience has shown that these substances do actually substitute for each other quite frequently, not only on the licit but on the illicit market as well. It is quite revealing in this respect to observe the gradual shifts during the past two decades in a few West African countries: first from the traditional natural stimulant cola nut to various synthetic stimulants and later from one ATS to another. Thus, there were shifts from aspirin/amphetamine mixtures to fenetylline, to pemoline, to mesocarb and to ephedrine preparations. Illicit markets appear to have responded efficiently to the controls instituted by the governments concerned. This was then followed by the next regulatory steps, national and international, almost always reacting to a situation rather than preventing the next, often foreseeable, shift to another substitute stimulant. While any regulation encompassing all possible stimulants is unlikely to be feasible, the present philosophy and practice seems to be a form of damage control, with limited possibilities for significant improvement. On the whole, therefore, the group of ATS appears to be an excellent case for testing new approaches to the issue of the scope of control.

IV. The therapeutic significance of ATS

The **perception of the therapeutic utility** of ATS has changed drastically over the last three decades. The spectrum of suggested therapeutic indications recommended earlier by the medical establishment or the manufacturer has been reduced from an enormous agglomeration of conditions³, for both mono- and combination preparations, into essentially three conditions: narcolepsy, attention-deficit disorder (ADD) and obesity.

All three of these indications are today outside the domain of the **main therapeutic applications of psychoactive drugs**: anxiety, depression, epilepsy, psychosis and sleeping disorders. As noted in Chapter I, within the growing psychoactive drug market, these drug application areas are constantly developing, with sales growing at annual rates of up to 42% (for the antidepressants). ATS, by contrast, seem to have become marginal to the pharmaceutical industry in terms of growth rates and market share. This is substantiated by a comparison of the median levels of consumption of groups of psychotropic substances, in defined daily doses per thousand inhabitants per day [INCB, 1996a]: tranquilizers take the lead with 20.1 DDD, followed by sedative-hypnotics with 7.4 DDD, and anti-epileptics with 2.9 DDD. Stimulants, by contrast, are consumed at a median level of 1.2 DDD per thousand inhabitants per day.

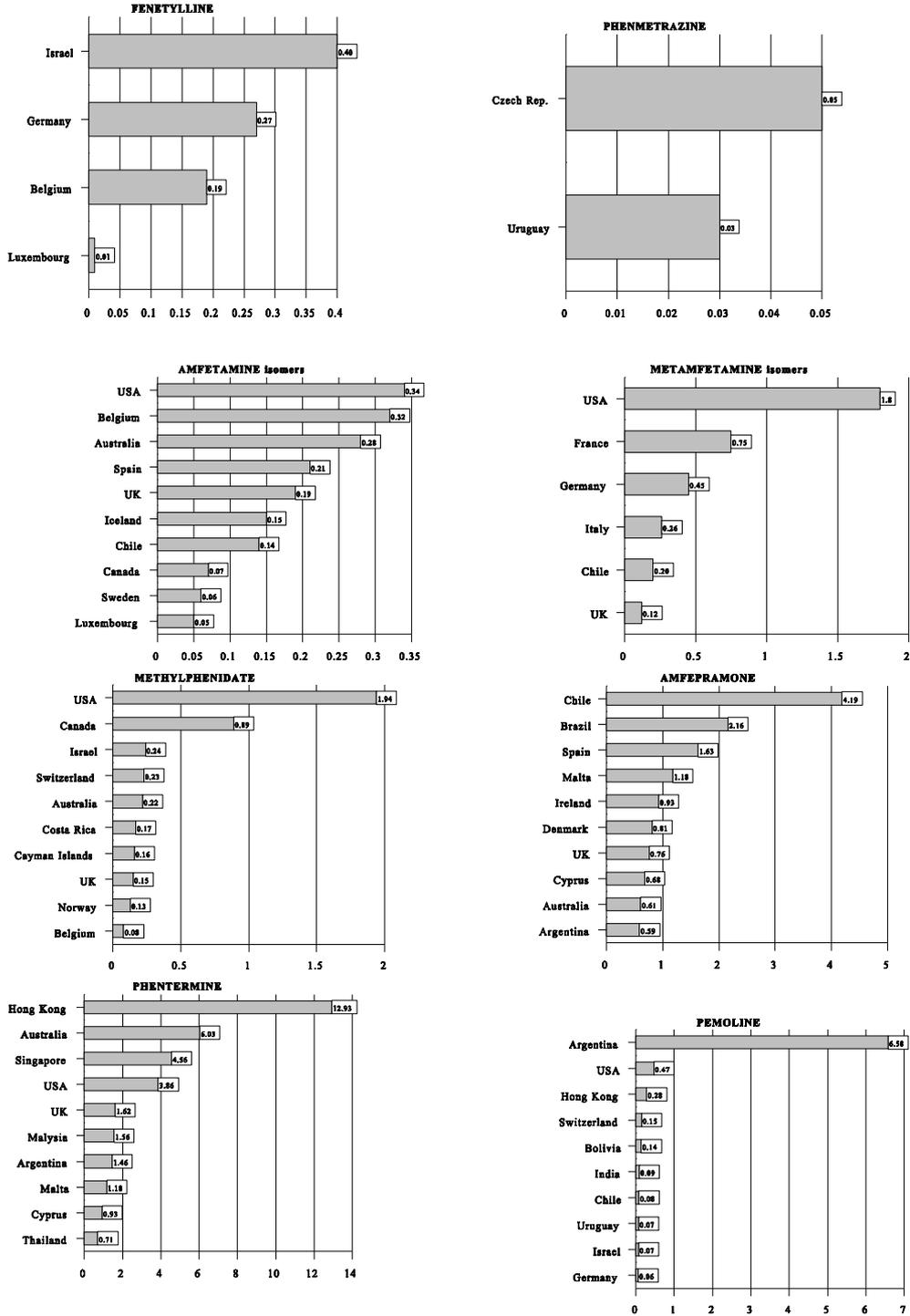
Figures 23 - 30 show the **medical use of ATS** in selected countries. At least three groups can be distinguished:

- (a) Substances with very low levels of medical use in a few countries (fenetylline, phenmetrazine). The figures confirm the conclusions made earlier on the basis of data on manufacture, that these substances are no more considered useful in therapy and may eventually disappear from the market;
- (b) Substances which are mainly used for conversion into other psychoactive substances and which are, to a much lesser extent, consumed themselves (amphetamine and methamphetamine isomers);
- (c) (c) Substances which are used in a few countries in amounts considerably above consumption levels in the rest of the world (amfepramone, methylphenidate, phentermine and pemoline).

³ By 1946, Bett [cited in NIDA 1980] had listed 39 clinical uses for these drugs, including the treatment of such diverse conditions as schizophrenia, infantile cerebral palsy, morphine and codeine addiction, Menieres syndrome, Anicotinism®, heart block, head injuries, depression, alcoholism, myasthenia gravis, disseminated sclerosis, migraine, dysmenorrhoea, restless legs, irritable colon, night blindness, caffeine mania and hypotension. In addition, up to the late 1960s, the US National Formulary (Physicians' Desk Reference, PDR, 1967) listed such ambiguous uses of ATS as for loss of interest and of the ability to concentrate, difficulty in thinking and communicating thoughts, improving mood and maintaining vitality, and also for weight control in pregnancy.

Medical use of ATS (n DDD per 1000 inhabitants per day)

Figures 23 to 30



Note: In these data, consumption means availability of the substances in a country and not necessarily actual use. Levels of consumption (in DDD per 1,000 inhabitants per day) are calculated on the basis of statistics on manufacture, trade, stocks and conversion into non-psychoactive provided by governments for the years 1992-1994. Incomplete data sets may distort the picture of actual consumption. For amphetamine isomers, France and Switzerland have been excluded because of unreasonably high calculations. Source: INCB

A small number of therapeutic indications for ATS does not, however, necessarily imply decreasing consumption of the substances themselves. There are reports that some 3% to 6% of school-age children in the United States require **attention deficit disorder** (ADD) medication [Safer and Krager, 1988], and an estimate that about 3% of children suffer from this condition worldwide [Cowart, 1988]. A recent review covering 30 countries found that 5% to 40% of children under psychiatric care were diagnosed as hyperkinetic or as conduct-disordered. Between 0.2% and 100% of these children received medication, reflecting considerably divergent prescribing practices, in different countries as well as among individual physicians. The most frequent drugs for the treatment of these behavioural disorders were stimulants, followed by antipsychotics and the antidepressant imipramine. The most frequently used stimulant drug was methylphenidate, followed by dexamfetamine. The use and choice of medication by country revealed no particular pattern [Simeon, et al. 1995]. In the United States, where methylphenidate consumption is steadily increasing, the use of dexamfetamine and pemoline for the treatment of ADD is also on the rise [INCB, 1996a].

Worldwide, the medical use of methylphenidate, the drug of first choice, has been increasing consistently since the beginning of the 1980s, both in terms of countries reporting use and in terms of the magnitude of consumption within different countries. The number of countries reporting medical use has doubled, and consumption in most of these countries has tripled since the early 1980s. In Germany, for example, though still at low levels, imports increased from two to six million 10 mg tablets between 1990 and 1994. The increase in the United States, however, which accounts for almost 90% of global methylphenidate consumption, was more than 600% in the same period. Other countries with strong increases in the use of methylphenidate are Canada, Switzerland, Australia and Israel [UNDCP/EGM, 1996]. The number of countries reporting the use of pemoline for the treatment of ADD is also increasing steadily [UNDCP/EGM, 1996].

Psychoactive drug medication in children, divergent prescribing practices, the absence of uncontested diagnostic criteria for ADD and reports of abuse of methylphenidate - all of these make the ADD/methylphenidate issue an illustrative example of problems that may arise in the difficult area of the treatment of mental disorders. According to INCB [INCB, 1996b], potential abusers are adolescents who illegally obtain the substances in tablet form from children undergoing treatment for ADD. Yet the vast majority of children who are given methylphenidate therapeutically do not appear to become dependent on the drug. The high prevalence of chronic use of methylphenidate by young people does, however, give some reason for concern [DEA, 1995e]. In view of the controversy surrounding the etiology, diagnosis and treatment of ADD, many questions remain open.

For the use of anorectics in the treatment of **obesity**, the situation is similar. Though estimates of incidence vary considerably depending upon diagnostic criteria used, the prevalence of obesity ranges from 30% to 50% or more of the middle-aged population of many countries. The health consequences, including increased mortality and morbidity from conditions such as coronary artery disease, hypertension and diabetes, and other indirect costs to society, are considerable. It was estimated, in the Framingham epidemiological study in 1983, that if everyone were at optimal weight, there would be 25% less coronary heart disease and 35% less congestive heart failure and brain infarction. This would save the German economy, for instance, 1% of the

GNP annually, equivalent to the annual cost imposed on that country by the effects of obesity on the incidence of cardiovascular disease alone [*Scrip*, 1992]

Amphetamine-type pharmaceutical drugs (starting with amphetamine itself) have been extensively used in the treatment of overweight for their anorectic effect. Their efficacy and safety has been repeatedly evaluated, safer drugs have been introduced, and new prescription guidelines issued in a number of countries. Yet, a recent market analysis concludes that the situation in terms of currently available drugs has changed little since the US Food and Drug Administration (FDA) conducted a large-scale survey in 1972 of eleven anorexigenic agents@ [*Scrip*, 1992]. It therefore seems reasonable to conclude that considerable amounts of ATS are being marketed for this particular area of application.

With obesity being a chronic condition, which is in fact increasingly considered to be a disease rather than a problem of will, treatment has to be long-term, ranging from several weeks to several months. In view of the required duration of treatment, and considering its potential for abuse, the continuing use of ATS in this area is subject to professional debate, with frequent revisions of guidelines and positions. One major revision proposed was the limitation of these substances to short-term use, i.e. to a maximum of 12 weeks. However, it is generally agreed that there is, thus far, no really effective pharmacological treatment for obesity, and that there is no place in treatment for drugs such as amphetamine and metamphetamine isomers, nor for phenmetrazine. Several studies indicate that there are great differences among various countries in the choice of treatment, its duration and the preferred drugs, but, as noted above, ATS still play a dominant role [e.g. Bray, 1993]. Despite considerable research efforts into anti-obesity drugs [Jack, 1996], progress in this area seems to be slow, with the situation in terms of currently available drugs having changed little over the past 25 years: amfepramone and phentermine are still in use, and except for dexfenfluramine, no basically new drug appears to have been introduced into medical practice recently.

In view of the continuing use of various anorectic agents, two trends are of concern. First, the on-going use of a broad spectrum of anorectic products, many containing ATS, in a large number of developed countries. Much of this flies in the face of professional opinion, articulated in many of these countries, that ATS have virtually no therapeutic value as anorectics.

The second trend of concern is the recent large-scale prescribing and use of several amphetamine-type anorectics in developing countries. This is particularly clear in Latin America, especially Argentina, Chile and Brazil. The most frequently used drugs in this region are pemoline and amfepramone (see Figures 23 - 30), but also mazindol and fenproporex [UNDCP/EGM, 1996]. The latter appears to be consumed in 18 countries worldwide, 13 of them in Latin American [UNDCP/EGM, 1996]. With both the popularity and the consumption of anorectics moving from developed into developing countries, there is a potential for history repeating itself in what happened some years ago in Europe, the United States and Japan. This development would be a potential threat, especially if it were to follow the same historical pattern: licit oversupply, followed by clandestine synthesis, with the clandestine products starting to substitute for licit pharmaceutical drugs. The next step, in view of this historical analogy, could then be a wave of abuse of clandestinely manufactured, structurally related 'designer drugs'. There is

already some evidence of such a development in the Far East, with unusually high levels of phentermine use in Hong Kong, Australia and Singapore.

The prevalence of **narcolepsy** (sudden attacks of daytime sleep, accompanied by insomnia), the third condition for which ATS are still in use, is estimated at 0.1% globally [Mitler, 1994]. As with obesity, narcolepsy requires long-term treatment. Since thus far there is no single medication for this disorder, the symptoms have to be treated separately. ATS are, to varying degrees, recognized as being effective in the treatment of daytime sleepiness [Mitler, 1994; Schütz, 1990]. The development of amphetamine psychosis, which is reported to occur in 0.5% of narcoleptic patients, sometimes even in cases of low-dosage treatment [Parkes, 1994], clearly indicates the limitations of these substances, particularly of amphetamine and methamphetamine.

As noted earlier, even for the three conditions, attention-deficit disorder, obesity and narcolepsy, the use of ATS is controversial. While some hyperactive children and obese people may well need medication to treat an organic disorder, many others could well be looking for ways to ease the competitive social pressure of modern society. Culturally bound notions of behavioural conformity and a *shapely* figure, as well as the pressure for better performance of certain kinds of mental and physical activities, seem to be germane to understanding this grey area on the edge of the proper, and licit, use of ATS.

Another area of continuing therapeutic use of ATS, though less visible, is in **nasal inhalers** as decongestants. The two principal substances used for this purpose are levomethamphetamine and propylhexedrine. Following large-scale misuse in a number of countries, compositions and dosages have been changed and substances with improved safety have been introduced to minimize the risk of abuse. Yet the easy availability (over-the-counter or on prescription), especially of levomethamphetamine in nasal inhalants, is considered by many reviewers to be a regulatory anomaly and remains an area of concern requiring continued vigilance.

A potentially controversial issue in the licit use of ATS is the prescription of oral amphetamine to dependent amphetamine users as a **maintenance therapy** [Fleming and Roberts, 1994; Pates, 1994, both in Fleming, 1995; Mattick and Darke, 1995]. Similarly, the use of amphetamine in heroin maintenance as well as of methylphenidate in cocaine maintenance have also been suggested. None of these therapies have, however, reached the status of an institutionalized approach.

A review, albeit incomplete, of the **aggregated number of preparations** containing any of the substances covered by the study in selected pharmaceutical markets, confirms the general trends noted above (see [Figure 31](#)). The number of preparations containing Schedule II substances (i.e. those with high abuse potential and limited therapeutic value) has declined steadily over the last three decades. In contrast, the number of preparations containing Schedule IV substances (i.e. those with more therapeutic value and limited abuse potential) has increased slightly. This is even more important since the number of Schedule II substances covered by this study is three times larger than the number of Schedule IV substances. In more general terms, the significance of the relative positions of the two kinds of preparations should be seen in the context of a stabilized market with gradually declining production levels.

**Aggregated number of preparations on selected* national pharmaceutical markets
(sorted according to Schedules of the 1971 Convention)**

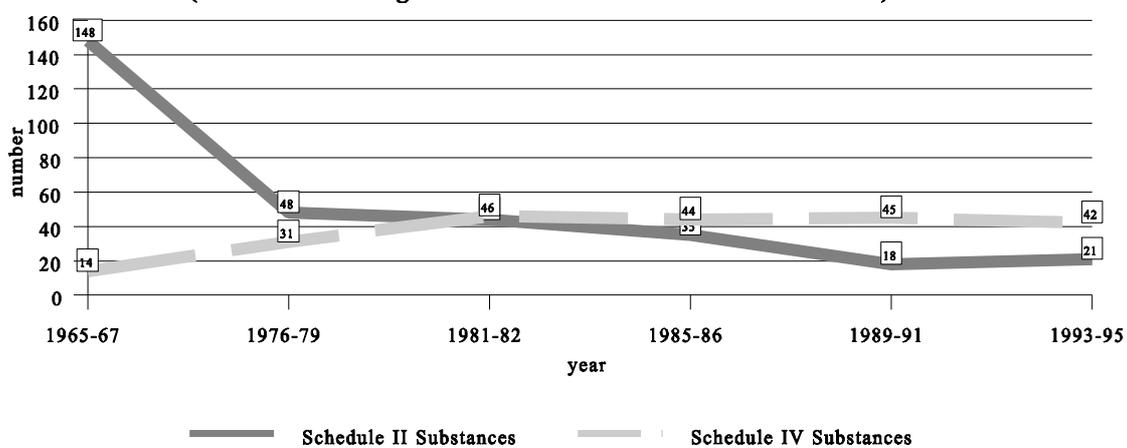


Figure 31

* France, Germany, Italy, Switzerland, United Kingdom, United States

Note: Combination preparations containing more than one of the substances covered by the study have been counted as one item only.

Sources: VIDAL (France), *Route Liste* (Germany), *L'Informatore Farmaceutico* (Italy), *Arzneimittel-Kompendium der Schweiz* (Switzerland), *British National Formulary* (UK), *Physicians' Desk Reference* (United States).

V. Conclusion

The therapeutic use of ATS has declined; this has been accompanied by commensurate declines in the volume of manufacture, international trade and aggregate consumption, especially of the substances in Schedule II of the 1971 Convention. The classical ATS have been gradually replaced by more specific drugs, initially of amphetamine-type and later by entirely new drug classes. Most of the parent substances, i.e amphetamine, methamphetamine and their isomers, have thus become almost ~~virtual~~ drugs and are used as intermediates in the manufacture of other pharmaceuticals rather than directly as medicines. This general trend is accompanied by the contracting interest of the pharmaceutical industry in manufacturing ATS and in developing new pharmaceuticals based on the amphetamine model. All of this is clearly a success story for international control. What is harder to estimate, however, is the relative extent to which control or declining therapeutic use were the driving forces. There can be little doubt, though, that control pressures have greatly contributed to the transformation of the licit amphetamine markets, as well as to the radical declines in manufacture and trading of such ATS as fenetylline and phenmetrazine. The same positive trend does not appear to apply to Schedule IV substances. This is chiefly on account of the frequently emphasized deficiencies of the mandatory control measures required for substances under Schedule IV of the 1971 Convention.

The few remaining therapeutic applications of ATS, for narcolepsy, ADD, obesity and nasal decongestion, are subject to on-going review by medical associations as well as by health and regulatory authorities. The high consumption of some licit ATS in a handful of countries, while perhaps small in comparison with other major drug abuse problems, still presents a potential risk. ADD and obesity are conditions whose prevalence is still open to much debate because they cover a wide range of diagnostic complications: psychosomatic, physiological, genetic and even cultural factors are each given different degrees of prominence in various assessments. Further complications arise with the complementary phenomena of over-the-counter availability in parallel markets and the possibility of self-medication for these conditions. This is particularly relevant in the context of the rapidly growing weight-control and ~~Asmart~~ food markets.

The reductions in aggregate volumes of manufacture and trade and the gradual concentration in fewer hands reflect the contracting interest of the pharmaceutical industry in manufacturing ATS and in developing new pharmaceutical drugs based on the amphetamine model. They have produced a more transparent market and could make, *ipso facto*, national and international monitoring simpler and more efficient. Past experience indicates, however, that these potentially positive trends have frequently been countered by a number of other factors, such as:

- (a) The marketing of new ATS as new generation substitutes for controlled ATS, despite their often foreseeable dependence potential. Today, there is a growing body of evidence to show that some of these drugs, while indeed more specific and safer in therapeutic application, still carry considerable potential for abuse if frequently used on a large scale;
- (b) The complicated industrial interconversions of various ATS. These, together with the present reporting obligations, cloud the situation and set limits to effective global monitoring. Some conversion products are under international control, others are not.

Scientific data indicate that many of the latter are potential problem drugs and candidates for future control;

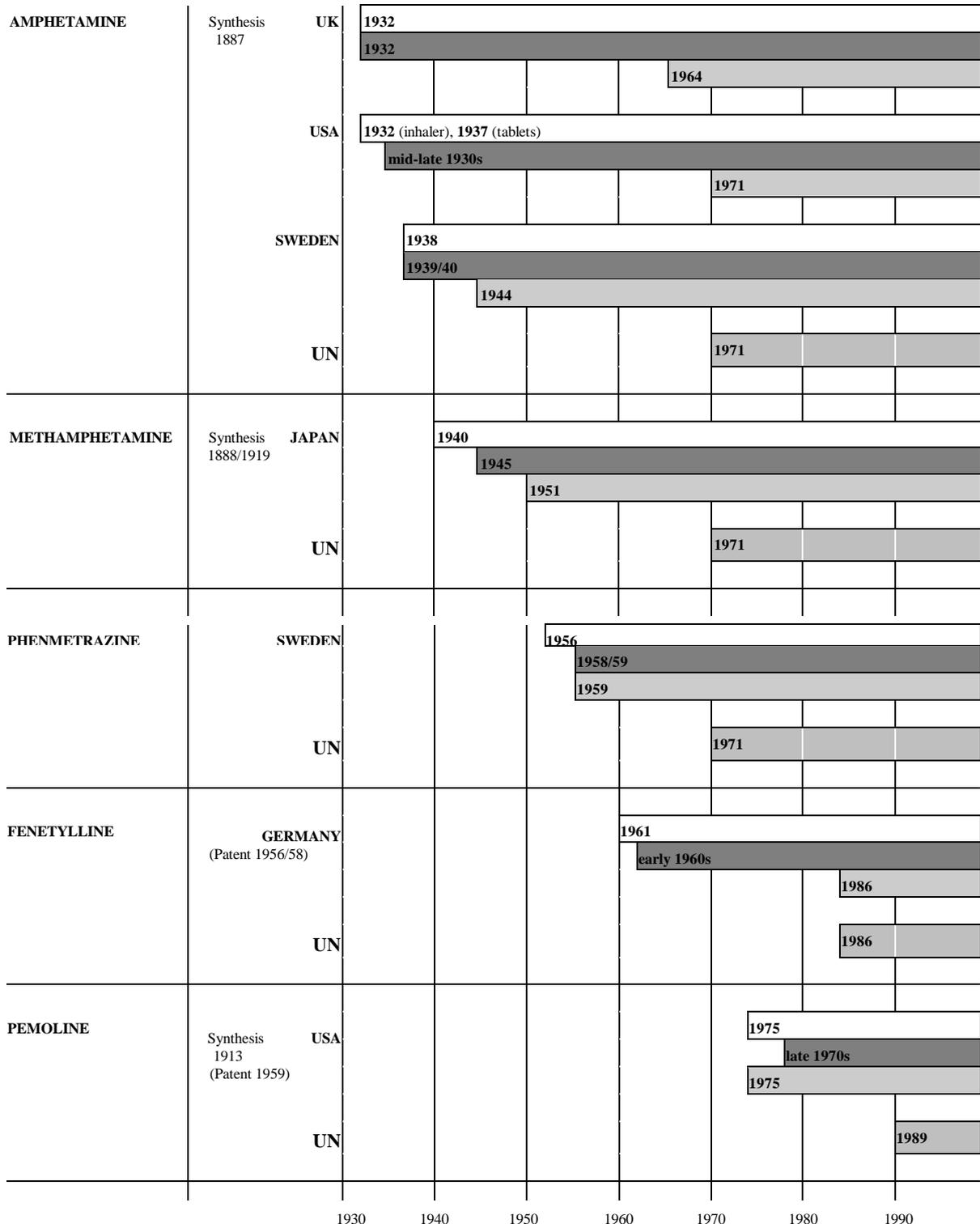
- (c) The complex trading pattern in the substances and their pharmaceutical preparations, including frequent re-exports, which complicate accurate international monitoring of the movement of the multiple end-products;
- (d) Geographic shifts in the manufacture, therapeutic use and sales of scheduled ATS to countries and regions where large-scale consumption was hitherto unknown. With some of these countries having limited regulatory capability and experience, there is a potential for history repeating itself: licit oversupply is followed first by clandestine synthesis, with the clandestine products substituting for licit pharmaceutical drugs, and eventually by clandestine manufacture and abuse of structurally related designer drugs;
- (e) The operation of commercial forces, particularly in a market with fewer patent protections. Since most licit ATS are no more protected by patents, new manufacturers can easily enter the market and offset the sensitive supply-demand balance.

An optimal supply-demand balance, foreseen as fundamental to the 1971 Convention, would require that (a) reliable national estimates of medical and scientific requirements are available for all controlled ATS and are universally reported to INCB, (b) all manufacturing and exporting countries are not only parties to the 1971 Convention but comply fully with the treaty requirements, and (c) effective national distribution and regulatory monitoring systems are in place and consumption is directed by sound medical prescribing practice. While some of these conditions are sometimes met, they do not prevail universally. Under such circumstances, voluntary compliance with treaty provisions and appropriate Economic and Social Council resolutions becomes the last resort to secure a balance between licit supply and medical requirements.

The conversion problem and the handling of stereo isomers are two technical areas not adequately addressed by the 1971 Convention. The lengthy substance-by-substance approach to scheduling and weak regulatory controls for Schedule IV substances tend to exacerbate the problem. Many of these technical limitations are reflected in national regulatory regimes and practices. It is, however, difficult to estimate the extent to which inadequate adherence, improper compliance or technical deficiencies in the 1971 Convention contribute to lacunae in the present international drug control system.

A review of past control approaches to the problem virtually dictates the further conclusion that regulatory and control efforts have tended to react to the problem rather than anticipate it. This is especially true for an institutionalized international response, which came 10-20 years after the appearance of problems with the first handful of substances (see [Table 3](#)).

Table 3: Licit ATS: evolution of the problem



marketing
 reports on abuse (pemoline: reports on diversion)
 national control
 international control (UN)

Given the continuing downward trend in the licit consumption of ATS, which may perhaps eventually eliminate the few remaining substances on the licit pharmaceutical market, their retention under the various control regimes and/or their eventual rescheduling would then become more of a preventive control measure.

The historical evolution of the ATS problem in this century points to three principal problem areas:

- (a) The demand for specific ATS has often been driven by lax medical practice and over-prescribing;
- (b) The illicit demand thus created has often been met by a combination of the above with diversions of some ATS (e.g. fenetylline, pemoline) from licit pharmaceutical trade, compounded by the existence of parallel markets outside regulatory control in a number of developing countries;
- (c) The establishment of controls on a market where demand exists has often encouraged a shift into clandestine synthesis of what were originally licit pharmaceuticals, followed by successive generations of entirely new derivatives (Adesigner amphetamines®), a typical characteristic of synthetic drug markets, of which this is a prototype. An analysis of the chemical and pharmacological properties of the entire group of licit amphetamine-type medicines indicates that there are still potentially attractive compounds among the presently controlled amphetamines, as targets for future clandestine entrepreneurs.

In view of the potential for the problem to worsen, for instance by moving into new geographical areas, it seems that the only effective prevention will come from a combination of more careful vigilance, more detailed scientific review, better information for the user public, improved prescribing practices, more responsible pharmaceutical marketing, more rigorous regulatory measures and better compliance with existing control systems. There is, indeed, a considerable corpus of practical solutions and proposed measures, both national and international, which has been developed in the recent past [UNDCP/WHO, 1993; ICPO/INTERPOL, 1994; INCB, 1994a; INCB/UNDCP, 1995; UNDCP, 1995a]; this knowledge appears to be a sufficient basis to make control regimes more effective.

THE ILLICIT SIDE OF THE EQUATION: MANUFACTURE, TRAFFICKING AND ABUSE OF AMPHETAMINE-TYPE STIMULANTS (ATS)

Part one established that the licit manufacture and consumption of ATS declined over the last two decades. Illicit manufacture, trafficking and abuse, by contrast, grew over the same period. While it is clear that the two phenomena are often related, the specific nature of the relationship needs to be investigated. This implies, among other things, careful consideration of the grey area between the licit and the illicit sides of the equation, at least in so far as the limited evidence can sustain. It also implies the necessity of establishing some measure of the extent and the trends of illicit manufacture, trafficking and abuse of ATS. Part two therefore tries to estimate some of the magnitudes and detail them in terms of trends pertaining to the main substances, the geographical distribution of manufacture and abuse, the significance of precursors, the forces that drive the illicit market for synthetic drugs and the impact of consumption.

One caveat concerning the nature of information upon which this analysis is based needs to be made at the outset. Data on illicit markets and abuse is *ipso facto* fragmentary, full of gaps and sometimes flatly contradictory. The clandestine nature of the activity virtually dictates this. Some generalization is still possible, although the conclusions are limited by the weight the evidence can carry. In the chapters that follow, the extent of manufacture of ATS is extrapolated from the number and size of illicit laboratories detected; patterns of trafficking are extrapolated from seizures; and estimates of consumption are derived from data which is seldom clearly representative of the whole population in a given area. Specific questions of interpretation will be raised, where relevant, in the chapters that follow, but the limitations of data on the illicit side of the equation [investigated in detail in UNDCP, 1994] should be kept in mind throughout this discussion.

The **historical development of the ATS problem** has been covered, from different perspectives and geographical areas, in several reviews [for instance, Smith et al., 1979; NIDA, 1980; Pickering and Stimson, 1994] and need only be summarized here. Amphetamine was synthesized in 1887; methamphetamine, about which there are different claims, in 1888 [NPAJ, 1995a] or 1919 [Merck Index, 1989]. Medical use began to grow in the 1930s when, as noted in Part one, the amphetamines were prescribed for a wide range of medical conditions. The perception of a panacea for many ailments, over-the-counter availability and lax prescribing practices all contributed to the early localized epidemics in countries as diverse as the United States, Japan and Sweden. Instrumental use of these stimulants, as a way of keeping alert and awake for the better performance of an occupational task, was probably legitimated by widespread use in the military during the Second World War and in a number of later military conflicts. But while occupational use began to stretch beyond soldiers to other groups such as truck drivers, students and sportsmen, other kinds of users also emerged: the recreational and compulsive users who used the drug as a mood enhancer.

As early as the 1970s, analyses that found similarities between the amphetamine **epidemics** in Japan, Sweden and the United States began to appear [Ellinwood, 1974; summarized in NIDA, 1980]. The epidemics started among *avant garde* sections of society, spread through the middle classes and came to rest among the marginal sections of society. All three countries had cultures that emphasized individual productivity and achievement, and the epidemics coincided with periods of intense social change: Japan in the post-war decade; Sweden

in the decade before the war and again in the late 1950s; and the United States in successive waves from the 1960s onwards.

The same review noted above [Ellinwood, 1974; cited in NIDA, 1980] found six sequential factors in the progression of the epidemics: (a) an initial oversupply of ATS that finds its way into both licit and illicit markets, (b) the >inoculation= of large sections of the population through medical, occupational or recreational use, (c) widespread dissemination of knowledge and at times proselytizing about the experience, (d) development of a subcultural core of abusers who maintain an illicit market for the drugs; (e) increasing use of the intravenous route for administration and (f) multiplication of >kitchen= or >garage= laboratories to compensate for national controls on licit supply.

Later work from other parts of the world where amphetamine problems appeared [for instance, Australia: Hall and Hando, 1993; the United Kingdom: Advisory Committee on Drug Dependence, 1970, and Klee, 1992] noted several other factors which contributed to the spread of amphetamine epidemics. These factors can be synthesized into three principal **characteristics of illicit ATS**: (a) they tend to be cheaper than cocaine, the other main stimulant available in illicit markets, and have a longer stimulant effect, (b) compared to cocaine, they have a relatively benign image of the harm they do to the user, and (c) they can be produced locally, close to areas of consumption, since they are not dependent on specific botanical raw materials like coca leaf and opium poppy.

Turning to the supply side, the **clandestine manufacture of ATS** seems to date back to the early 1960s and developed as licit markets were brought under control. By the mid-1970s, annual detections of clandestine laboratories began to appear in significant numbers. A new, and in some senses qualitatively different, phenomenon has been the development of substances such as methcathinone, the >ecstasy= group and the rapidly growing number of new >designer drugs=, all of which did not start with legal manufacture and consumption but basically evolved in illicit markets.

Methcathinone was first patented in Germany in 1928. It was used in the Soviet Union in the late 1930s and 1940s for the treatment of depression [McGivney, 1994]. This was eventually discontinued, but by the early 1980s there was a flourishing clandestine manufacture of methcathinone, known in the area as >ephedrone= [Sheu, 1993; Glennon et al., 1995]. In the United States, commercial interest in the molecule dates back to 1957 [Calkins et al., 1995], when it was tested as an anorectic. Because of severe side effects and its high CNS potency (one and half times greater than that of methamphetamine), testing was discontinued and methcathinone was never marketed. It was only rediscovered in the clandestine sector in 1989, and the first illicit laboratory was detected in Michigan in 1991 [McGivney, 1994; DEA, 1994a]. By late 1993 methcathinone abuse had reached epidemic proportions in Michigan and was spreading to other states [Glastris, 1993; *Narcotics Control Digest*, November 23, 1994]. After having been brought under emergency scheduling in the United States in 1992 [*Narcotics Control Digest*, 14 September 1994], methcathinone became subject to international control in 1995.

There has been a similar development with the **substances of the >ecstasy= group**. MDA was first synthesized by German chemists in 1910. MDMA was discovered three years later in Germany and patented by a pharmaceutical company in 1914 [ISDD, 1993]. It was intended for

use as an anorectic but, because of its side effects, never marketed. The various substances of the 'ecstasy' group were rediscovered in the United States in the mid-1960s [Shulgin and Shulgin, 1992] and began to be reported in a growing literature. By 1968, MDA started to reach the streets on the West Coast of the United States, prompting the authorities to bring the substance under control in 1970, while MDMA remained outside the control mechanism for another 15 years. During the 1970s, some psychiatrists used MDMA to encourage loquacity among their patients [Beck, 1993], as well as to encourage empathy and dissipate hostility and anger [ISDD, 1993]. By the early 1980s, the use of MDMA spread among students and some affluent sections of American society [Dowling et al., 1987]. It was put under national control in the United States in 1985 [Saunders, 1994] and under international control a year later. In the United Kingdom, MDMA had already been subject to control since 1977, when a generic definition was introduced into the United Kingdom Misuse of Drug Act, covering most amphetamine-like compounds. The most rapid spread of MDMA and other substances of the 'ecstasy' group, however, only started after they had become subject to control, driven partly by an increasingly innovative clandestine sector. In tandem with this, clandestine operators began to develop related 'designer drugs' which were pharmacologically similar but different enough in chemical structure to stay one step ahead of national and international controls [Ziporyn, 1986].

Today, ATS abuse is a multifaceted phenomenon. Different phases of the historically observed shift from the licit to the illicit sector appear to coexist, though with geographical differences. While many less developed countries may be on the edge of a wave of abuse of ATS, evolving from licit oversupply, the abuse of these substances in most developed countries is largely dissociated from licit use; illicit demand has evolved or increased in spite of decreasing licit consumption. A good example of this dissociation is the evolution of the two waves of methamphetamine abuse in Japan in the early 1950s and since the 1970s: while the first epidemic originated in massive licit oversupply in the aftermath of the Second World War [Konuma; Fukui et al., both in Cho and Segal, 1994], the second epidemic started almost 15 years after the first one had been curtailed and despite the fact that licit methamphetamine use had virtually disappeared.

This summary of the historical evolution and present characteristics of the ATS problem lays the ground for an assessment of the present incidence of the ATS problem in aggregated global terms. The following chapters thus review (VI) the grey areas of over-prescribing, diversion from licit trade, parallel markets and doping, (VII) illicit manufacture, (VIII) precursors, (IX) trafficking, (X) the economic incentives for manufacture, trafficking and consumption, (XI) the extent of abuse, (XII) the impact of consumption, and (XIII) the salient points that emerge from this global review.

VI. Prescription drug misuse and diversions from licit trade

The misuse and abuse of prescription drugs is a complex and vexatious issue [NIDA, 1993; Wilford et al., 1994] which is beyond the ambit of the present paper. The central policy question that it raises - how to make drugs easily available for medical use while limiting access for purposes of abuse - is, however, relevant in the historical context of many psychotropic drugs. In the past few years, sedative-hypnotics and tranquilizers, especially benzodiazepines, have been the prescription drugs of particular concern, as reflected in a number of reviews [INCB, 1994b; Harlow, 1991; de Burgh et al., 1995; Woods et al., 1995]. By contrast, no similar studies of the pattern and extent of medically inappropriate use of ATS are available. The issue of abuse of a variety of prescription drugs due to self-medication and/or overprescription illustrates, however, the grey area which exists between licit and illicit markets in this field and which has long been overshadowed by concern about the abuse of the plant-based drugs. Today, the abuse of prescription drugs is recognized as one significant facet of the drug problem. The number of publications and conferences dealing with the triangular relationship between doctors, patients and the law and with the development of models and guidelines to improve prescribing practices and to avoid misuse of these drugs, all reflect a change in the perception of prescription drug abuse. This chapter summarizes some aspects of the use of prescription ATS and also considers the question of diversions from licit pharmaceutical trade.

The high prevalence of **licit psychoactive drug use** with, for example, 11% of French adults regularly taking psychoactive medicines [Nau, 1994] and, as noted in Part one, a considerable proportion of school-age children in the United States receiving medication for attention-deficit disorder, is an issue of concern. On the one hand, long-term use of psychoactive drugs may lead to drug dependence, with discernible withdrawal symptoms experienced after termination of the medication. On the other hand, because psychoactive drugs are prescribed mainly for individuals experiencing emotional problems, there remains a certain risk that the individual, given access, may misuse or abuse the prescription drug [the Availability-proneness theory of Smart, 1980, cited in Harlow, 1991] and that doctors, albeit unintentionally, may promote this kind of non-medical use [Wesson and Smith, 1990]. Apart from this misuse of prescribed psychoactive drugs by the patient, which is beyond the ambit of this review, there is the equally problematic area of unauthorized use of prescription drugs without any therapeutic indication. The latter often includes other criminal activities such as prescription frauds, thefts of prescription pads or the drugs themselves, or diversions from licit trade, at all levels of the distribution chain. The abuse of methylphenidate by adolescents who illegally obtain the drug from children undergoing ADD treatment (see Chapter IV), as well as the fact that the drug ranks among the 10 most frequently stolen pharmaceuticals in the United States, [DEA, 1995e] are good examples of the potential problems associated with the widespread licit use of psychoactive drugs.

The extent of unauthorized use of prescription psychotropic drugs by persons other than patients to whom they were prescribed is not known. However, since several publications emphasize the link between high prescription figures and abuse [Schwabe and Paffrath, 1994; Sadusk, 1968, cited in Bayer, 1973; Ghodse and Khan, 1988], data on legitimately dispensed prescriptions, and especially their changes over time, can serve as a basis for a rough estimate of the availability of these drugs from medical prescriptions for illicit purposes. With regard to ATS, the **incidence of prescribing** has decreased significantly over the past 30-40 years. For example,

amphetamines represented 2% of all prescriptions dispensed in the mid-1950s in the United Kingdom, and can be estimated to have declined to less than 0.1% today. While they accounted for 13.9% of all psychoactive prescriptions in 1965, this figure dropped to 6.1% in 1971 and 0.5% in 1979 [INCB, 1990]. For the United States, a similar series of prescription data are available.

Between 1976 and 1979 an estimated yearly average of 3.5 million prescriptions for amphetamine (including its isomers) were dispensed; this figure dropped by more than 80% to about 640,000 between 1983 and 1985. The decline of methamphetamine prescriptions in the same period was more than 65%, from 368,000 to 128,000 [Davis et al., 1991]. This decline in the number of annually dispensed prescriptions, which is in line with the downward trend in the global manufacturing volumes of these substances, thus reflects a decrease in the availability of licit ATS for illicit purposes.

The **impact of legislative restrictions** on the availability of amphetamine-type substances and subsequently on their licit and illicit consumption is well documented [de Alarcón, 1972; Bayer, 1973; Adams and Kopstein, 1993; Haislip, 1993]. Today, the situation is still an ambivalent one, and two examples illustrate the positive and negative sides of the coin. With regard to the former, the United States manufacture of amphetamine and methamphetamine dropped from an estimated 80 tonnes (8 billion 10-mg tablets) in 1962 to 35 tonnes by 1970 and, as a consequence of stringent manufacturing quotas, to less than 5 tonnes by the end of that decade. Over the 1991-1993 period, the average annual United States manufacture of both substances (including their isomers) was 1.5 tonnes; imports raised this annual average to 2.6 tonnes. On the global scale, the annual average over the same 1991-1993 period was 28 tonnes (see Figures 7 - 9 and 16 - 17 in Part one). Thus, global manufacture of amphetamine and methamphetamine today is less than half of United States manufacture in 1962.

The negative side of the coin was already illustrated in part one: the relatively high levels of consumption in some countries, particularly of methylphenidate, and the Schedule IV substances, amfepramone, phentermine and pemoline. Given the historical pattern that amphetamine epidemics often seem to originate with oversupply that travels through licit markets into illicit ones and is then sustained by the latter, these areas command vigilance. They should also be considered in light of the general problem, discussed briefly in part one, about insufficient regulatory requirements for substances under Schedule IV of the 1971 Convention. INCB data on licit consumption levels show that for Schedule III and IV substances, 10 countries have more than 3 DDD per 1,000 inhabitants per day, compared to only one country for Schedule II stimulants above that level [INCB, 1996a]. The global median of consumer countries, as a measure of salience for assessing these data, is 1.14 DDD for Schedule III and IV substances and 0.16 DDD for Schedule II substances. The fact that the consumption level in some countries is so much higher than the global median indicates that current prescribing practices could still be a source of oversupply of ATS, particularly Schedule III and IV ones.

In recognition of the impact of lax prescribing practices on non-medical use and of potential leakage of ATS, particularly Schedule IV ones, from licit sources into the illicit market, a number of countries are amending their legislation. The measures taken recently include the prescription requirement for some anorectic drugs such as amfepramone and phentermine, in Chile [*WHO Pharmaceuticals Newsletter*, 1992/3], certain restrictions on combination preparations of anorectic drugs with each other or with other psychoactive substances, in Brazil [*WHO Pharmaceuticals Newsletter*, 1994/10] and in Italy [*Scrip*, 1993/1820, May 14], and the

prohibition of the manufacture, use, storage and trade of amphetamine and methamphetamine isomers and of fenetylline, as well as the withdrawal of mesocarb, in Bulgaria [*WHO Pharmaceuticals Newsletter*, 1992/7].

These measures are all aimed at minimizing the risk of indiscriminate and inappropriate use. By lowering the overall availability of these substances, the incidence of their diversion at all levels of the distribution chain, from the bulk manufacturer down to the household medicine cabinet, may be reduced significantly. This is particularly relevant in view of the fact that the diversion of legitimately manufactured controlled substances has traditionally been an important source of supply for the illicit market.

In historical perspective, ATS are one of the earliest and best examples of large-scale **diversions from licit trade**. There were times in the 1960s when it was estimated that 90% of legal supply went into the illicit market [NIDA, 1980]. In 1970, there was evidence for more than 50%, or 13 tonnes, of amphetamine and methamphetamine manufactured licitly in the United States being unaccountable by total legal prescription, wholesale, and retail sales [DEA, 1973], and it was assumed that most of the surplus reached the illicit market. By 1977, estimated diversion of amphetamine was down to 10% of authorized United States manufacture [Durrin, 1979, in Smith et al., 1979]. Thus, with the tightening of national and international controls, including stringent manufacturing quotas in several countries, diversions of amphetamine and methamphetamine steadily decreased and virtually ceased in the early 1980s.

A similar development can be seen for other Schedule II substances, for example fenetylline, where actual diversions of up to several hundred kilograms ceased a few years after its international scheduling in 1986. Diversions, or attempted diversions, of Schedule IV substances, by contrast, tell a quite different story. Between 1988 and 1994, for example, attempts to divert more than 25 tonnes of pemoline (equivalent to more than 0.5 billion DDD at 40mg each) were prevented. This is particularly significant because the figure is three times larger than total reported licit pemoline manufacture (some 8 tonnes) over the same period (see [Figure 12](#)). The differences could be explained partially by accumulated stocks, but it seems to be more likely that ineffective controls and loopholes in legislation in some important manufacturing countries play a major role in allowing for these large-scale diversions [*Scrip*, 1993/1805, March 23].

Insufficient awareness of regulations governing the use of psychotropic substances in veterinary medicine has also contributed to attempted diversions of some of these substances, particularly pemoline. Since a recent study conducted by INCB has shown that at present not a single ATS is used for legitimate veterinary purposes (i.e. excluding their illicit use in the doping of animals), large-scale orders of these substances to meet alleged veterinary requirements remain dubious [INCB, 1996b].

In contrast to the pattern for clandestinely manufactured ATS, where illicit trafficking is confined to particular regions or even to the country level, diversions of these substances from licit trade are interregional in character. International trafficking usually moves from developed countries, where manufacture of the bulk material of most ATS is concentrated, into less developed ones [INCB, 1980], sometimes via another developing country, where tableting takes place. The illicit consignments of pemoline, for example, usually originate in Europe and are

destined for West Africa and the Middle East. So far, there has been only one documented diversion of pemoline involving a pharmaceutical company in the Far East in the manufacture of this substance [INCB, 1995b]. In addition to diversion from international trade, significant quantities of psychotropic substances are diverted from domestic distribution channels and then either sold for local abuse or smuggled into countries of final consumption [INCB, 1996b].

All of the above is yet another facet of what is often called the **balloon effect**. Instituting more stringent controls on traditional ATS like amphetamine and methamphetamine (Schedule II) than on other drugs of the same group, such as pemoline (Schedule IV), leads to a shift in large-scale diversions from the former group of substances to the latter. There is, for example, concern that once international trade in pemoline has been controlled in all manufacturing countries, traffickers will attempt to divert other stimulants, including some not under control of the 1971 Convention, into the illicit traffic in West Africa [INCB, 1996b]. Large-scale diversion attempts in 1995 involved ephedrine, a stimulant drug which is merely controlled as a precursor under the less stringent regime of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. Yet, since the methods and routes of diversion of ephedrine preparations are often the same as those for psychotropic substances, it is assumed that they are diverted for abuse as stimulants [INCB, 1996b]. Moreover, the strengthening or better implementation of controls in an increasing number of countries results in a diversification of illicit trafficking, as reflected in the increasing number of transit countries.

Another area of concern in recent years has been the proliferation and expansion of **parallel distribution systems**, usually called **parallel markets**, in countries lacking an adequately regulated pharmaceutical distribution system and sufficient medical care. Such markets work outside legal or formal frameworks authorized by law for the distribution of psychoactive drugs. They are supplied through informal/illegal international trade, including diversion at different levels of the distribution chain. Other characteristics are the absence of any quality control and frequent shipments of substandard or entirely fake products originating from illegal or unauthorized manufacturers. Narcotic drugs or psychotropic substances and their preparations usually enter this **parallel trade** through false documentation and go on to local street markets. Apart from being a health hazard and undermining the credibility of the legal health care system, such parallel distribution systems also facilitate misuse or abuse.

Parallel markets for pemoline and mesocarb have been observed in recent years in a number of West African countries, where these drugs are frequently available on local street markets, at low prices, either as the original brand products or as various imitations thereof. The latter often contain substitutes for the active substance, such as caffeine, theophylline and ephedrine, which are not under national control in the countries concerned. Very often, a number of substitute products for the same stimulant are distributed in the same market.

The implications of parallel markets are multiple and far-reaching, and governments, international and national professional bodies are equally concerned about the consequences. The relationship with the subject of the present study is obvious, and since there are several parallels, including, for example, the criminal nature of the supply side activities in both areas, they should be addressed together, within the overall context of drug control. In view of these ramifications, WHO and UNDCP, with the involvement of INCB and the International Federation of

Pharmaceutical Manufacturers Association (IFPMA) have addressed these issues in recent years, both at the policy as well as at the operational level [WHO/IFPMA, 1992; UNDCP/WHO, 1993].

While the existence of parallel markets reflects the failure to establish a basic system of checks and balances between the prevention of public health risk and ensuring the availability of psychotropic substances for licit requirements, as envisaged in the 1971 Convention, there is an ongoing discussion in many countries on how to further improve prescribing practices and refine control mechanisms for proper dispensing of prescriptions. There have been various attempts to reduce both drug diversion and pharmaceutical cost [Wilford, 1991]. Some authors, however, in view of shortages of psychotropic substances for approved medical indications (methylphenidate in 1986 and dexamfetamine in 1990, both in the United States), are of the opinion that current controls and manufacturing quotas are already too restrictive [Cole et al., 1993].

Doping is another related aspect of the misuse of licit pharmaceutical drugs, which was brought to the attention of the Commission on Narcotic Drugs as early as 1965 [CND, 1965]. Often seen in the history of the licit ATS, doping still seems to be a common feature, reflected, for instance, in the most recent case of mesocarb at the 1992 Olympic Games in Barcelona [Ventura et al., 1993]. The use of doping agents in sport is obviously aimed at enhancing the physical performance of athletes. However, since ATS suppress the sensation of fatigue but do not constitute a supply of energy, their use may well lead to complete exhaustion and even death. It was, in fact, a fatal doping case involving amphetamines during the 1960 Olympic Games in Rome that led ultimately to the creation of the Medical Commission of the International Olympic Committee (IOC) in 1967 [IOC, 1996].

The doping list issued by this Commission presently [IOC, 1996] consists of five prohibited classes of substances (narcotics, stimulants, anabolic agents, diuretics, and peptide and glycoprotein hormones and their analogues) and five classes of drugs subject to certain restrictions (alcohol, marijuana, local anaesthetics, corticosteroids, and beta-blockers). Prohibited substances in the class of stimulants include, for example, ecstasy-type and amphetamine-type substances, ephedrines (ephedrine, pseudoephedrine, norephedrine and norpseudoephedrine), as well as cocaine. Unlike the substance-by-substance scheduling concept of the international drug control conventions, the doping definition of the IOC Medical Commission is based on the banning of pharmacological classes of agents. This concept was developed in anticipation of the emergence of new drugs especially designed for doping purposes. It also addresses the substitutive nature of many such drugs, including ATS, by covering the whole group of related substances, thus preventing a shift from a controlled drug to another drug that is not controlled but is equally suitable for doping purposes.

Between 1986 and 1988, stimulants were the second most frequently detected agents in doping cases (25%-35%), following anabolic steroids (55%-65%). In absolute figures for 1988, anabolic steroids and stimulants accounted for 791 and 420 doping cases, respectively, while the figure for all the other doping classes together was 142. Similarly, 25% of all 51 doping cases recorded at the Olympic Games between 1968 (the year of the introduction of controls) and 1992, involved stimulants, namely amphetamines and ephedrines. Today, there are signs that drug use in sports is spreading from professional athletes to amateurs and even to people using these substances in leisure time sports [UNDCP/EGM, 1996]. The initiation of a global project by

WHO, with support from UNDCP in 1992, to assist countries in their efforts to prevent this potentially harmful use of substances and to reduce health and social problems related to it, well reflects contemporary concern over drug use in sports [Husch, 1995].

VII. Illicit manufacture of ATS

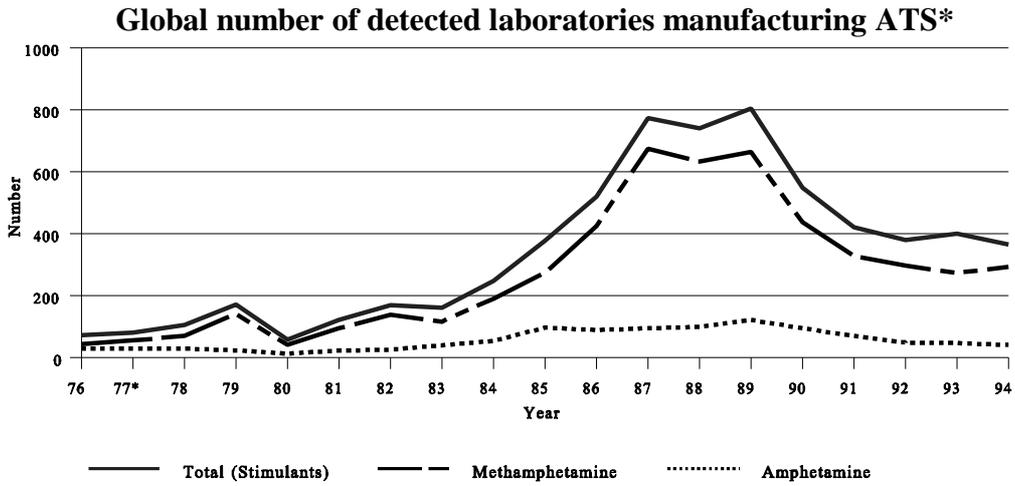
With better controls for licit manufacture in place, the clandestine sector has emerged as the main source of supply for illicit markets of ATS since the mid-1970s. A number of specific characteristics of manufacturing ATS appear to have supported this development.

One characteristic is the **simple synthesis** of many ATS, which enabled a large number of clandestine laboratory operators to start activities in this field [U.S. Congress, 1986]. This is particularly the case for methamphetamine and methcathinone, less so for the substances of the 'ecstasy' group, which require more know-how. The level of sophistication differs considerably, ranging from kitchen-laboratories to high-tech laboratories with the latest pharmaceutical equipment. A number of Dutch [Saunders, 1994] and United States= laboratories producing 'ecstasy'-type substances [*Narcotics Control Digest*, 12 June 1992] fall in the second category, while most methamphetamine and methcathinone laboratories fall in the first category.

Compared with plant-based drugs, the clandestine laboratories manufacturing ATS are characterized by **greater flexibility**, not only with regard to the level of sophistication but also the use of precursors and the necessary quantities to be processed. Since economies of scale tend to play less of a role, even small quantities can be profitably manufactured by choosing the appropriate technique. The flexibility has also enabled clandestine operators to misuse the premises of licit enterprises for illicit manufacture, particularly in transition countries.

Another general characteristic of the illicit manufacture of ATS is the **location**, which - in contrast to plant-based drugs - tends to be relatively close to the respective markets and thus reduces the subsequent trafficking risks. This is particularly true for methcathinone and methamphetamine, slightly less so for amphetamine and the 'ecstasy' group. For the latter two, notably 'ecstasy', more centralized manufacture for a larger regional market (e.g. Europe) is very common.

The main indicator for estimating the extent of global illicit manufacture is data on the detection and **seizure of clandestine laboratories**. There is enough evidence in these data to substantiate the general argument of this paper that declines in the licit manufacture of the ATS should be seen in the light of proportionally greater increases in illicit manufacture. From the mid-1970s, a clear global trend, illustrated in [Figure 32](#), is discernable. The number of detected laboratories producing ATS increased steadily, peaking in the late 1980s, then declined through this decade, though it is at levels that are still substantially higher than in the mid-1970s. The decline in the 1990s is primarily on account of fewer detections in the United States, because clandestine manufacture appears to have shifted to Mexico [DEA, 1995d]. It should also be noted that fewer detections do not necessarily imply less manufacture, which could well be concentrated in fewer but larger laboratories.

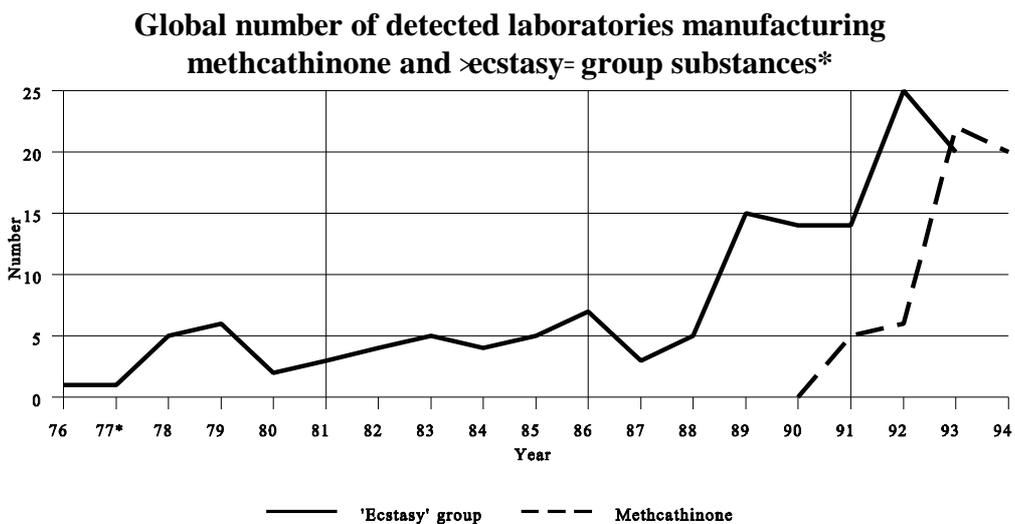


* Estimate for 1977.

Source UNDCP ARQ Data.

Figure 32

Recent increases in the illicit manufacture of the 'ecstasy' group and methcathinone have been more significant than for other ATS. Figure 33 shows the steady rise for the 'ecstasy' group since the late 1980s. The rapidity of the rise is more important than the actual number of detections, which still only account for 4% of all ATS laboratories detected. Methcathinone shows an even more recent and rapid increase. Its illicit manufacture was confined to the former Soviet Union till the beginning of this decade, following which it has become steadily more popular in the United States, where methcathinone laboratories now constitute some 3% of all ATS laboratories detected.

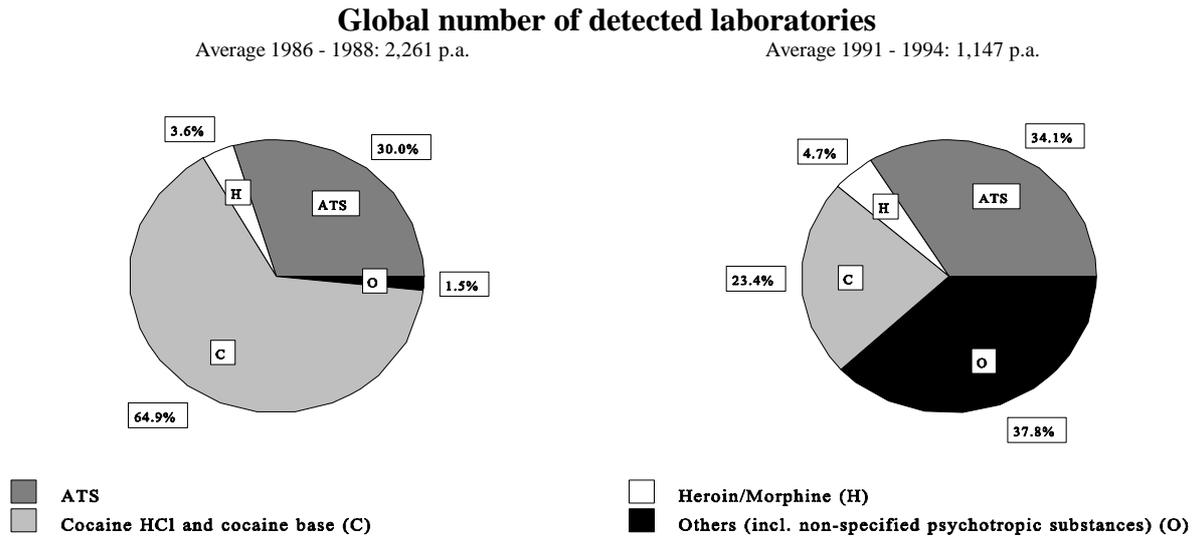


* Estimate for 1977.

Source: UNDCP ARQ Data.

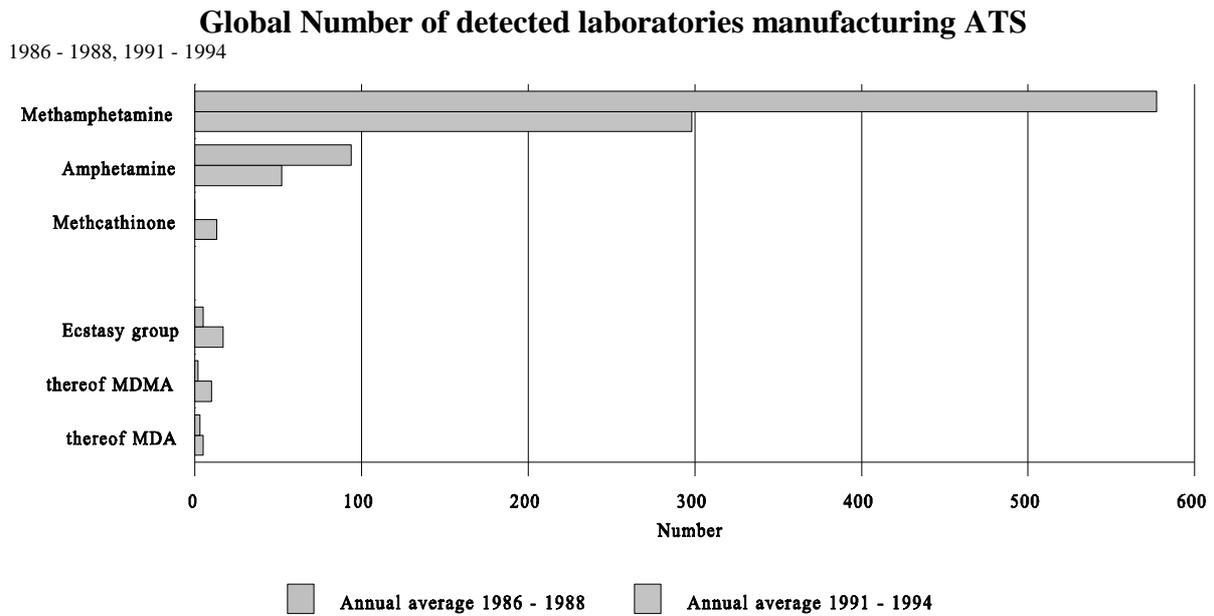
Figure 33

Figure 34 puts these data into a wider perspective, showing the laboratories in the **total number of clandestine laboratories** detected worldwide. Annual averages of detections are compared over two periods, 1986-1988 and 1991-1994. In the latter period, ATS detections surpass detections of both heroin and cocaine laboratories and constitute a third of all detections. Figure 35 covers the same time-scale but differentiates between the ATS and substantiates what was argued above: relative to amphetamine and methamphetamine, the illicit manufacture of the 'ecstasy' group and methcathinone is increasing.



Source: UNDCP ARQ Data.

Figure 34



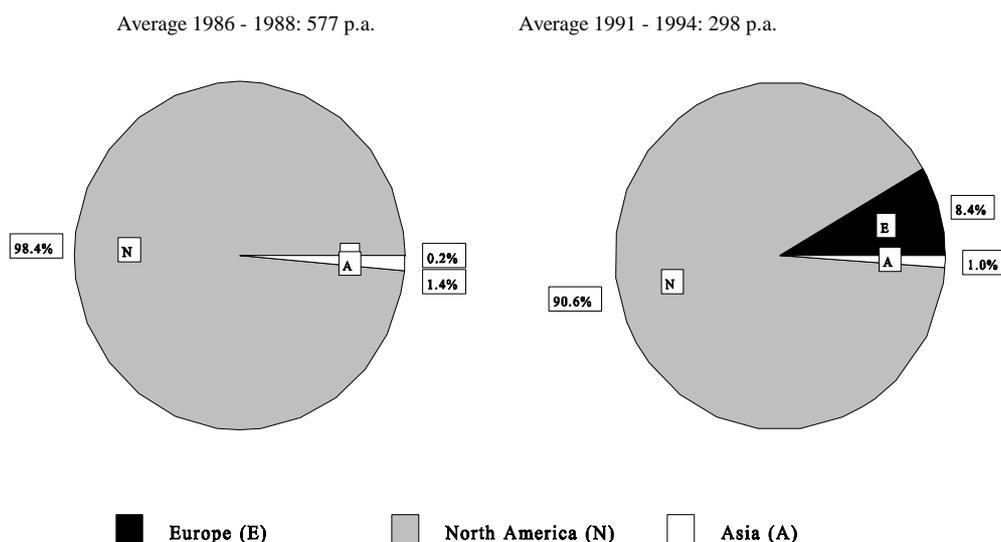
Source: UNDCP ARQ Data.

Figure 35

The next level of analysis tries to establish **regional patterns of illicit manufacture** for the main substances. Comparisons are made over the same periods, 1986-1988 and 1991-1994, with an annual average of the number of laboratories detected for each period. Figure 36 shows the regional breakdown for **methamphetamine**. From an overwhelming concentration in North America, the present decade shows the emergence of methamphetamine in Europe. Methamphetamine manufacture in Europe seems to be concentrated in a few east European countries, notably the Czech Republic. Some reports on methamphetamine manufacture also mention the Commonwealth of Independent States (CIS) [DEA, 1995a]. There is one difficulty with European data, which stems from the different reporting practices of individual countries: Germany, for instance, reports detections of amphetamine and methamphetamine laboratories together; the United Kingdom reports seizures of laboratories manufacturing amphetamines. As there have not been any reports suggesting significant methamphetamine trafficking or consumption in these countries, the above-mentioned laboratory detections were assumed to be amphetamine laboratories.

Global number of detected laboratories manufacturing methamphetamine

Regional breakdown



Source: UNDCP ARQ Data.

Figure 36

The most important centre for clandestine methamphetamine manufacture is still North America, particularly California and northern Mexico. Large-scale manufacture in this region is closely linked to recently acquired abilities of local drug cartels to organize quasi-legal ephedrine and pseudoephedrine imports, directly into Mexico or via neighbouring countries [UNDCP, 1995b], with the substances then diverted and used for either domestic manufacture or manufacture across the border in the United States [DEA, 1994c]. In 1993 about 80% of all methamphetamine laboratories detected in the United States were detected in California, most of them in southern California close to the Mexican border [*Narcotics Control Digest*, August 31, 1994]. Many of the laboratories were set up in rural areas to produce for only short periods of time to avoid detection [DEA, 1994b]. By contrast, a decade earlier the manufacture of methamphetamine was still a cottage industry, with laboratories set up primarily in homes or

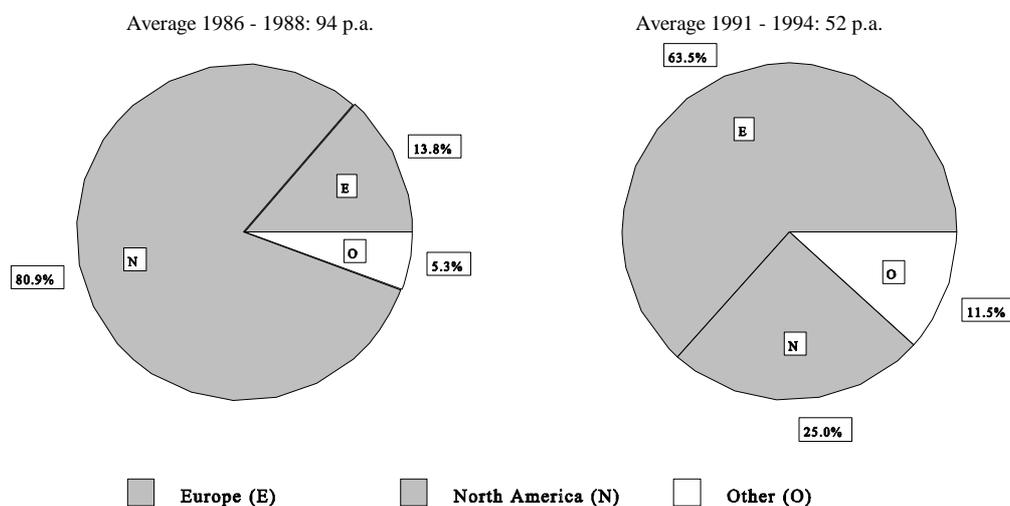
apartments and Texas was the main centre [*Narcotics Control Digest*, December 11, 1985]. This change in the nature of the clandestine laboratories may well explain the declining trend noted in [Figure 32](#).

The lack of reported seizures of methamphetamine laboratories for Asia opens up several avenues of interpretation (*cf.* Chapters VIII and IX). There have been frequent reports from national authorities and other organizations about the manufacture of methamphetamine shifting from the Republic of Korea and the Philippines to China and Thailand. Several of these reports have also suggested that substantial supplies of the main precursor, ephedrine, may originate in China [Republic of Korea, 1994; NPAJ, 1995; ICPO/Interpol, 1994 and 1996; UNDCP/HONLEA, 1994; NNICE, 1995; INCB, 1996b and 1996c; UNDCP/EGM, 1996].

[Figure 37](#) shows the picture for **clandestine amphetamine laboratories**: the North American share declined from over three quarters to one quarter; the European share increased from little more than a tenth to three fifths, underlining the increasing importance of Europe as the main manufacturer of amphetamine. Most of the North American segment is accounted for by the United States and the largest components of the European segment are the United Kingdom, Germany, the Netherlands and Poland. In the other category, which is 11.5% in this decade, a substantial part of detections have taken place in Australia.

Global number of detected laboratories manufacturing amphetamine

Regional breakdown



Source: UNDCP ARQ Data.

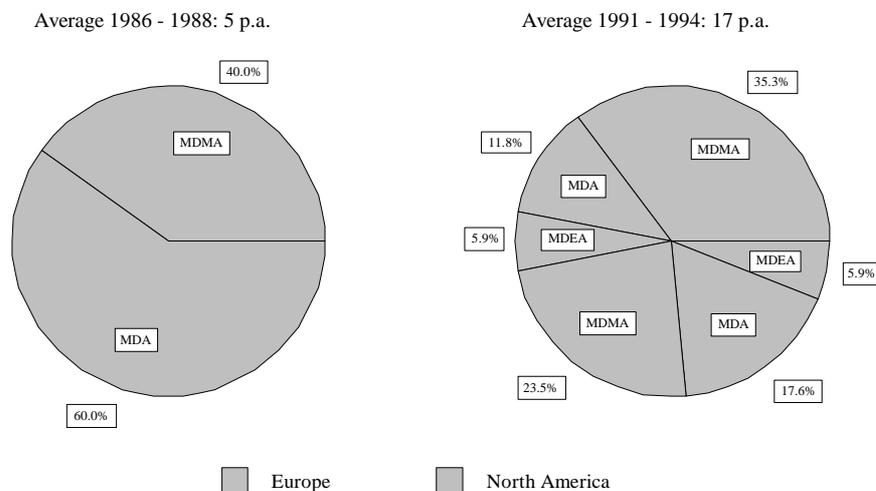
Figure 37

The European figures need some additional interpretation. German detections may not necessarily reflect high manufacturing volumes because most of these reports cover small laboratories often producing only for the requirements of the operators [BKA, 1995]. By contrast, the small number of detections in the Netherlands may not necessarily imply low illicit

production levels. Many European countries, including the United Kingdom, France, Germany and the Nordic countries, have reported for years that 70%-80% of their illegally imported amphetamine originated in the Netherlands. Illicit manufacture in Poland has assumed some significance as well [DEA, 1995c]. Analysis of amphetamine seized in Germany, for which the origin could be determined, showed that 55% of it was manufactured in the Netherlands, 21% in Germany, 18% in Poland and the remaining 6% in other parts of Europe [BKA, 1995]. Data from Sweden suggest that almost half of the supply of amphetamine originates in eastern Europe [NCIU, 1995], while in the late 1980s about 80% originated in the Netherlands.

Figure 38 shows the regional breakdown of **laboratory detections for the 'ecstasy' group** of substances. The most striking phenomenon here is the strong increase of illicit manufacture in Europe, which has moved up from virtually nothing in the earlier period to more than half of the total in this decade. Globally, the share of MDMA within the 'ecstasy' group seems to have increased from some 40% to about 60% while the share of MDA declined. One caveat should be made here. Since the clear identification of the various substances within the 'ecstasy' group requires expensive and sophisticated equipment, the distinctions are often based on rudimentary rule-of-thumb identification techniques rather than on proper chemical analysis.

Global number of detected laboratories manufacturing 'ecstasy'
Regional breakdown



Source: UNDCP ARQ Data.

Figure 38

VIII. Precursors of ATS

One of the essential conditions for the clandestine manufacture of any synthetic substance is access to a chemical that serves as the key building block for the synthesis. This starting material, the precursor, has to fulfill a few **basic conditions**:

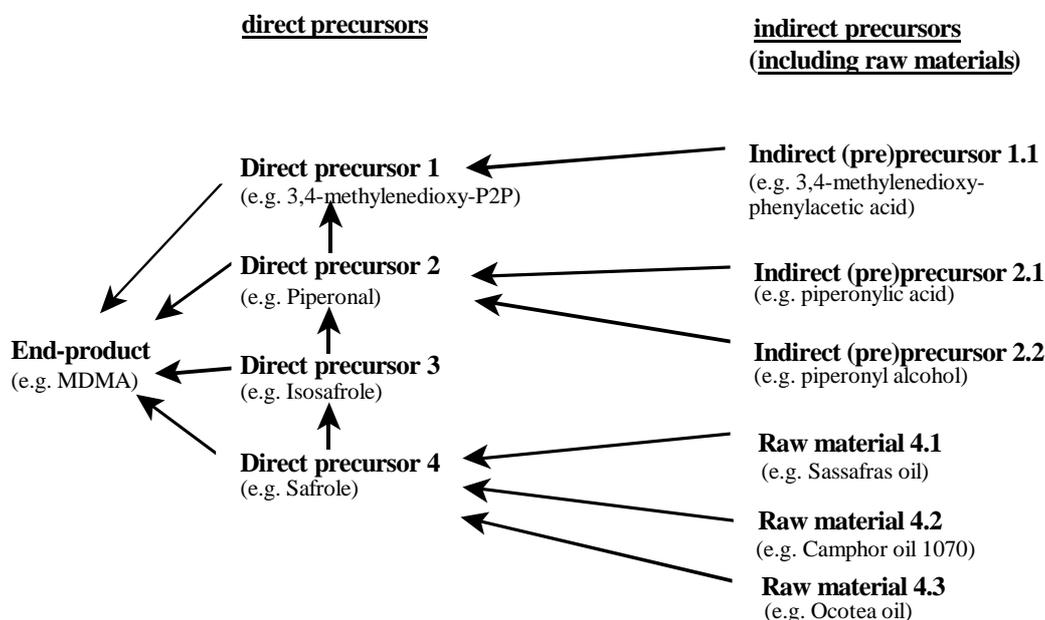
- (a) It has to have in its chemical structure some essential parts of the final molecule, so that it is possible to build the amphetamine-type substance through a relatively **simple process**, in a few steps, requiring few and easily available additional chemicals and relatively simple technology;
- (b) The starting material should be **cheap** and **easily available**. While the preceding criterion does have some technological limits in terms of convertibility and feasibility, price and accessibility seem to be very elastic [*cf.* Remberg et al., 1994 for general background];
- (c) The chemical structure of the precursor should provide for some **flexibility** in the synthesis. The number of alternates that are available on legitimate chemical markets for a given precursor, the number of end-products that can easily be made from that precursor, as well as the number of synthetic pathways that exist, or are possible, from a given precursor to a given amphetamine-type substance, all contribute to the attraction of a starting material to clandestine operators. Using the «ecstasy» group as an example, [Figure 39](#) tries to illustrate this versatility.

The qualitative and quantitative relationship between starting material and end-product is one of the principal **differences between plant-based drugs and ATS**. In the case of cocaine and morphine/heroin, one single starting material (disregarding poppy straw, which is not yet a significant heroin raw material, and codeine, the use of which is localized) yields one end-product. For ATS, this relationship is a cascade in both directions: one key precursor may have a number of pre-precursor «ancestors» and may serve as starting material for several ATS end-products; conversely, any end-product may have several alternate precursors within a broader synthetic concept; and finally, synthetic pathways from a given precursor to a given end-product are numerous (see [Figure 39](#)).

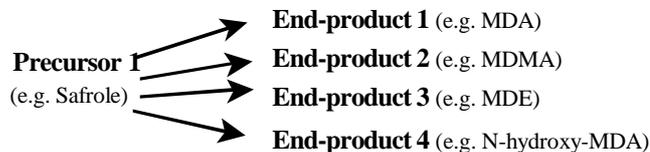
In comparing the **illicit manufacturing process** for ATS with that of cocaine and heroin, a few significant differences are readily apparent (see [Figure 40](#)): (a) The relative quantities of chemical precursors required to produce a synthetic drug tend to be considerably less than the quantities of botanical raw material needed to produce a comparable amount of a plant-based narcotic drug. In view of the option of small-scale manufacture of ATS using clandestine «kitchen» technology, these quantities may even fall below the threshold of the amounts for which monitoring and record keeping are mandatory; (b) The immediate precursors of the synthetic drugs are comparable, in terms of the processing stage, to the intermediate products coca paste and morphine; (c) All intermediates of the production process of plant-based drugs

Versatility of ATS syntheses

a) Several precursors for one end-product



b) One precursor for several end-products



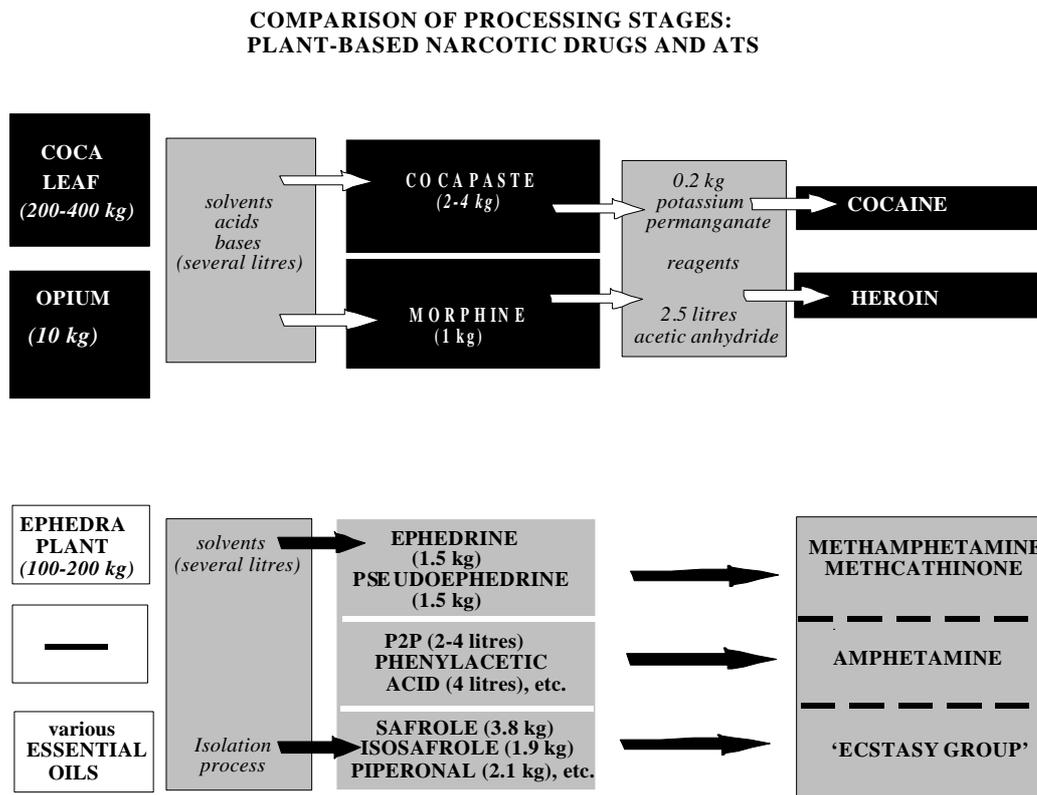
c) Several alternate pathways from one precursor to one end-product



Figure 39

can be, and indeed are, available in illicit markets. With synthetic drugs, only the end-product of the clandestine synthesis appears on illicit markets; (d) The nature of the manufacturing process differs considerably: while the whole process of manufacturing cocaine and heroin is essentially an extraction, i.e. the end-products (cocaine and morphine) are present in the reaction mixture from the very beginning, the ATS end-products are only constructed during the synthetic process; (e) A different degree of control applies to the precursors involved (see [Figure 40](#)): while in the case of plant-based drugs, raw materials, intermediates and end-products are subject to the same control regime (the 1961 Convention), the ATS and their precursors are a heterogenous

group. The starting materials are mainly licit substances, with the provisions of the 1988 Convention applying only in the case of suspicious orders and/or diversion. The end-products, by contrast, are subject to the 1971 Convention. This has a considerable impact on the effectiveness of control, which is discussed below.



Note: The quantities of precursors given are necessary to produce one kilogram of end-product.

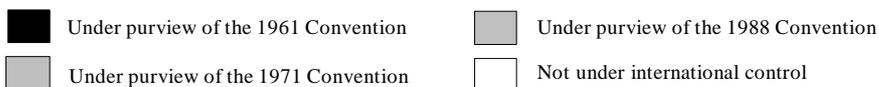


Figure 40

The **principle of controlling materials**, natural or synthetic, which serve either as sources for extraction (raw materials) or as precursors in the synthetic processing of a narcotic drug or a psychotropic substance is not new and has been part of national and international drug control strategies and instruments since the 1920s. Specific precursors of ATS were placed under control by a few countries such as Japan (1955), the Soviet Union (in the mid-1970s) and the

United States (1980). It appears that the most scientifically comprehensive approach was developed in Japan during the methamphetamine epidemic of the 1950s, when the most critical precursors (e.g., P2P, phenylacetic acid, ephedrine and pseudoephedrine) were placed under regulatory control. National controls of specific ATS precursors, however, were essentially determined by the nature of illicit drug problems in the particular country.

The **nature and degree of control** has shown considerable variation, both in historical terms, as well as among different countries at any given time. Some countries have simply placed the precursors of prime concern under the strictest control regime applying to end-products (e.g., acetic anhydride together with morphine and heroin); others under a less strict control; and still others, under a specific/separate control regime. The case of ephedrine illustrates the dilemma arising from different levels of control: ephedrine, which itself has significant CNS stimulant activity, is a major precursor of methamphetamine and methcathinone and is presently controlled as such, under the 1988 Convention. Recently, however, in view of growing abuse of ephedrine as a stimulant, the WHO Expert Committee on Drug Dependence recommended that it be considered for eventual control under the 1971 Convention [WHO, 1995]. A good example of early awareness of the need for controlling precursor chemicals is reflected in the schedules and scheduling criteria of the 1961 Convention. Based on the *convertibility rule*, as provided for in article 3, paragraph 3 (iii), many chemical compounds that can be used to easily synthesize other drugs are included as narcotic drugs in Schedule I.

As an increasing number of countries recognized the importance of controlling starting materials in the 1970s and 1980s, the result was the development of **article 12** and the selection of substances listed in Tables I and II of the **1988 Convention**. With regard to precursors of ATS, eight substances are under purview of this Convention today: three substances (P2P, ephedrine and pseudoephedrine) were originally scheduled in Table I and four more were added in 1992 (safrole, isosafrole, piperonal and 3,4-methylenedioxy-P2P). Phenylacetic acid, the only ATS precursor in Table II, was also scheduled in 1988 (see [Table 4](#)). These eight substances together constitute over one-third of the chemicals listed in Tables I and II.

The **scope of precursor control** is much broader in several countries, particularly those most seriously affected by the illicit manufacture and/or abuse of drugs, natural or synthetic. A recent report lists 94 chemicals (beyond the 22 listed in Tables I and II of the 1988 Convention) that are presently controlled in various countries [INCB, 1996c]; of these, 20 are precursors of the ATS group. Some countries have gone one step further by issuing warning lists of non-controlled alternate and pre-precursor chemicals, or by establishing close cooperation between their enforcement authority and their chemical industry.

Table 4: Precursor chemicals controlled under the 1988 Convention (Status 1996)

TABLE I of the 1988 Convention	
Precursor chemicals (resulting amphetamine-type end-products)	
N-Acetyl anthranilic acid	
EPHEDRINE	(MA, Me-Ca + others?)
Ergometrine	
Ergotamine	
ISOSAFROLE	(Ecstasy= group)
Lysergic acid	
3,4-METHYLENEDIOXY-P2P	(Ecstasy= group)
P2P (1-phenyl-2-propanone)	(Amphetamine, MA)
PIPERONAL	(Ecstasy= group)
PSEUDOEPHEDRINE	(MA, Me-Ca + others?)
SAFROLE	(Ecstasy= group)

TABLE II of the 1988 Convention	
Precursor chemicals (resulting amphetamine-type end-products)	
Acetic anhydride	
Acetone	
Anthranilic acid	
Ethyl ether	
Hydrochloric acid	
Methyl ethyl ketone	
PHENYLACETIC ACID	(Amphetamine, MA + others?)
Piperidine	
Potassium permanganate	(Me-Ca)
Sulphuric acid	
Toluene	

Note: Precursors used in the clandestine manufacture of ATS are highlighted.
 Ecstasy= group = MDA, MDMA, MDE, N-hydroxy-MDA etc. ...
 MA = Methamphetamine
 Me-Ca = Methcathinone
 For the manufacture of ATS, several solvents and acids are also necessary.

The 1988 Convention provides, for the first time, the possibility of **gathering global time-series data on clandestine manufacture and precursor trafficking**. Though it came into force only in 1990, a few countries began reporting voluntarily on precursor seizures to INCB from 1989 onwards. Today, more than two-thirds of the parties to the 1988 Convention, and over one half of all countries and territories, report on seizures and diversion methods of substances in Tables I and II. While most countries known to have significant clandestine manufacture on their territory provide annual reports, this is not always regular, and some major precursor manufacturing and exporting States are not yet parties to the 1988 Convention and therefore not bound to report. Bilateral or multilateral agreements that have been established between certain precursor exporting and importing countries are, to some extent, useful in verifying the legitimacy of individual transactions. The flexibility of the precursor field, however, requires close cooperation on the global level in order to investigate patterns of past diversions so as to prevent future ones.

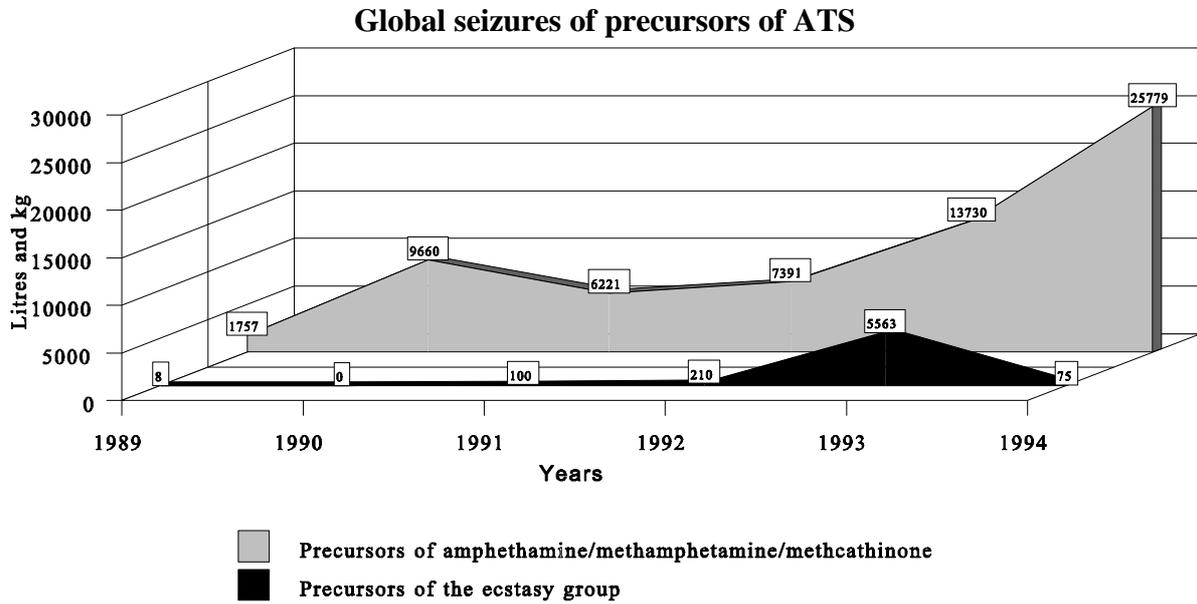
On the basis of the data systematically collected by INCB for the last six years, it is possible to highlight a few **salient points**: (a) The relatively small quantities of the different precursors seized do not correspond to the widespread availability of the related end-products on illicit markets. This applies particularly to the 'ecstasy' group of substances, where abuse, especially in western European countries, is growing, while precursor seizures have not been reported in large quantities; (b) The total number of countries reporting seizures of precursor

chemicals has decreased steadily since peaking in 1992. This includes a growing number of countries which reported seizures of precursors in previous years and where illicit manufacture of drugs has been known to take place; (c) The only exception is ephedrine, where the number of countries reporting seizures in 1994 is greater than in 1993, thus reflecting the impact of the increased global vigilance over this particular precursor of methamphetamine and methcathinone.

It is important to note that the quantities of seizures reported by Member States only reflect actual quantities seized in international traffic. Quantities of chemical precursors that are prevented from being diverted from international trade (the so-called **Attempted or Prevented diversions**) as well as quantities that are diverted from national distribution channels, i.e. within a country (**Domestic or Internal diversions**) are not covered. Both, however, are significant. Attempted diversions reflect effective enforcement and implementation of precursor control, but they are also an indicator of the scale of clandestine manufacture. Domestic diversions, by contrast, actually add to the problem. Weak national regulations in countries with a chemical industry or abundant natural raw materials (e.g. the *Ephedra* plant) may undermine efforts to control the availability of potential starting materials for illicit purposes. In the Asian region, for example, internal diversion and subsequent smuggling into neighboring countries remains the principal source of ephedrine for clandestine manufacture of methamphetamine [UNDCP/EGM, 1996].

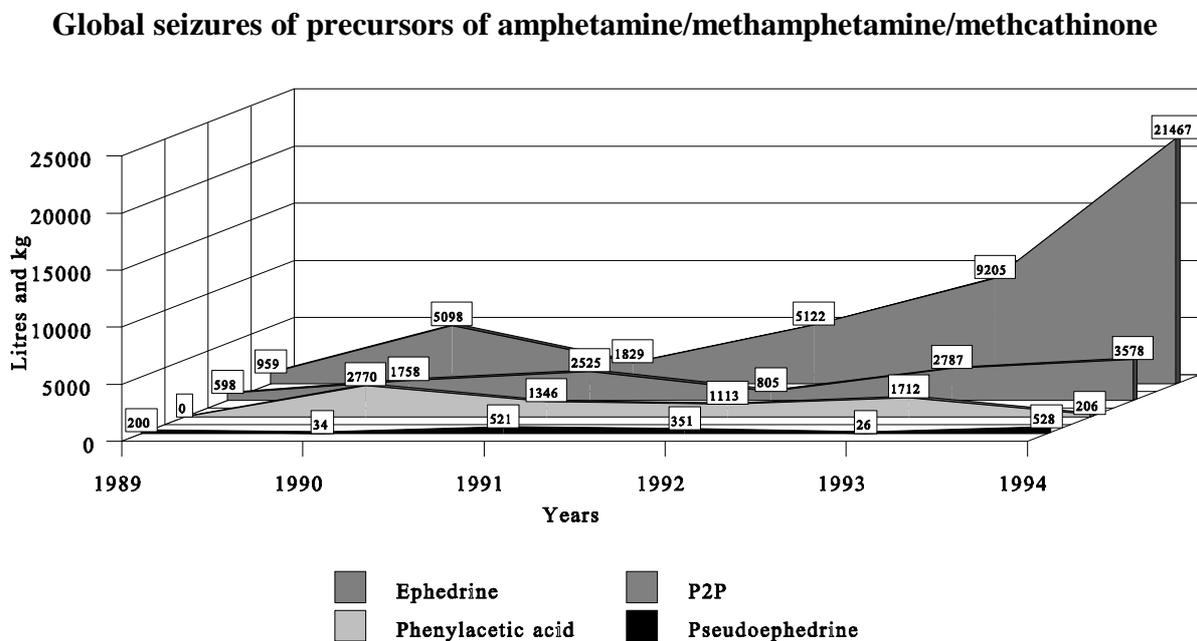
In 1994, more than 80% of all reported **diversion attempts** of substances in Table I involved ephedrine and pseudoephedrine [INCB, 1996c]. Other precursors of ATS prevented from being diverted were P2P, isosafrole and 3,4-methylenedioxy-P2P. The quantities involved were significant. From 1992 to 1994, suspicious orders for a total of 210 tonnes of P2P and 3,4-methylenedioxy-P2P were canceled in Germany alone [UNDCP/EGM, 1996], which is more than 50 times larger than total global seizures (3.8 tonnes) in the same period. The quantities of ephedrine and pseudoephedrine involved in prevented diversion cases identified recently totalled 95 tonnes [INCB, 1996b], an amount that is four times larger than the quantity reported as actually diverted in 1994.

Figures 41 and 42 present **aggregate seizure figures of precursors of ATS** over 1989-1994. Fluctuations in these figures, particularly in those of precursors of the 'ecstasy' group, should be seen in light of what was noted above: the short period of time the 1988 Convention has been in force; the later scheduling, only in 1992, of the 'ecstasy'-precursors; the limited global adherence to, and compliance with, the 1988 Convention; and the small number of countries reporting seizures.



Source: INCB, *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances* (E/INCB/1996/4).

Figure 41



Source: INCB, *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances* (E/INCB/1996/4).

Figure 42

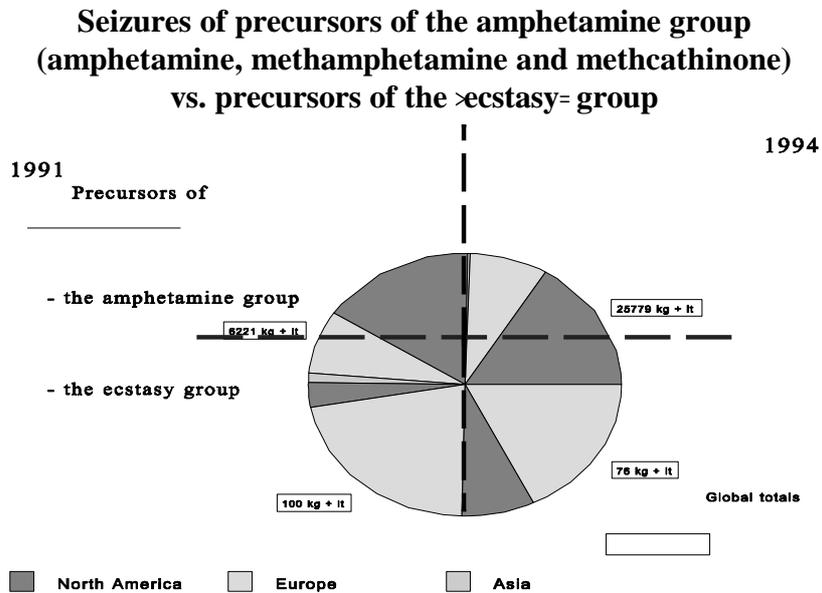
The following trends are nonetheless discernable from Figures 41 and 42:

- (a) The total seizure volumes have fluctuated between 2,000 and more than 25,000 kilograms (and litres), with the precursors of amphetamine, methamphetamine and methcathinone comprising the major share, partly as a result of their earlier scheduling;
- (b) P2P and phenylacetic acid, both of which have long been the most common precursors of amphetamine and methamphetamine, are still in use, though clearly being outweighed by ephedrine, and account for a sixth of global seizures of the four substances;
- (c) Ephedrine emerges as the most significant precursor of the ATS covered by this study, accounting for most of the aggregate seizures, having risen from less than 1,000 kilograms to more than 20,000 kilograms;
- (d) Several sources indicate that pseudoephedrine, although not yet visible in the aggregate figures, is partly replacing ephedrine in many countries [INCB, 1996b], because in practice it is less strictly controlled. A new development in this respect is the cultivation of species of the *Ephedra* plant, rich in pseudoephedrine, in China [Hutchinson and Andrews, 1995];
- (e) Total seizures of precursors of the 'ecstasy' group (isosafrole, safrole, piperonal and 3,4-methylenedioxy-P2P) are still very small and contrast sharply with the continuing widespread availability of the related end-products on illicit markets. These factors may contribute to this situation: the focus of law enforcement on ephedrine and pseudoephedrine, probably as a result of their earlier scheduling; the decreasing number of countries reporting seizures of precursors to INCB in 1994 (this applies particularly to several western European countries, which have traditionally been associated with abuse and clandestine manufacture of 'ecstasy'-type substances); and the possibility that precursor traffickers may be reacting to the implementation of national control measures by resorting to smuggling.

Figure 43 compares the **relative shares of different geographical regions in the aggregate seizure volumes** of two categories of precursors: those of the amphetamine group (amphetamine, methamphetamine and methcathinone) and of the 'ecstasy' group. The emerging regional pattern fits largely with the data on illicit manufacture and trafficking of the corresponding end-products, although with a major limitation regarding the magnitudes involved. Precursors of both groups are essentially seized in North America and in Europe, although the relative quantities seized are inverted: with regard to the amphetamine group, North America accounted for 66% of global seizures in 1994 and Europe for 32%; by contrast, seizures of precursors of the 'ecstasy' group were dominated by European countries (71% in 1994) and, to a much lesser extent, by North America (29%).

The discrepancy between the magnitudes of seizures of precursors and end-products is particularly large in Asia, the third region with reports on large-scale illicit trafficking of ATS. Though increasing amounts of ephedrine are reportedly being seized in China and Taiwan Province of China [INCB, 1996b], the total quantity of precursors seized in Asia still amounts to only about 1% of global seizures in 1994. This adds to the quandary to be discussed in the

context of Figures 64 and 65 in Chapter IX. Seizures of precursors of ATS in African countries are negligible. In 1994, however, Belgian authorities seized the equipment for an 'ecstasy' laboratory with an estimated production capacity of some 12 million tablets per day, which was apparently destined for Kenya [INCB, 1996c].



Note: Each quarter of the pie represents the total global seizure of precursors of the amphetamine or the 'ecstasy' group in 1991 and 1994, respectively. Precursors of the 'ecstasy' group were placed under international control in 1992.

Source: INCB, *Precursors and Chemicals Frequently Used in the Illicit Manufacture of Narcotic Drugs and Psychotropic Substances* (E/INCB/1996/4).

Figure 43

The figures of actual and attempted diversion of precursors of ATS have to be set in the context of their **licit manufacturing volumes** in order to assess the salience of the problem. The number of countries known to manufacture ephedrine regularly is small, being limited to only five: China, the Czech Republic, Germany, India and Japan. In addition, sporadic use of the *Ephedra* plant for the licit manufacture of ephedrine is known from some central Asian CIS countries such as Kyrgyzstan or Kazakstan [INCB, 1996b; UNDCP/EGM, 1996]. Despite the small number of ephedrine manufacturing countries, information on the licit manufacturing volumes is limited. The most comprehensive source of data on licit precursor chemicals is the UNCTAD Trade Analysis and Information System [UNCTAD, 1995], which provides figures on global licit imports (sales figures, in million US\$) and does not, therefore, include quantities manufactured for domestic use. Information from individual countries suggests, however, that domestic use may account for up to half of the quantities manufactured [UNDCP/EGM, 1996]. Using UNCTAD data⁴, the following trends emerge for ephedrine/pseudoephedrine and phenylacetic acid, the only Table I

⁴ For the conversion of value into volume, constant prices of US\$ 65 per kilogram for ephedrine/pseudoephedrine, and of US\$ 4.75 per kilogram for phenylacetic acid have been used.

and II precursor chemicals included in the data set. From 1992 to 1994, global licit imports of ephedrine/pseudoephedrine rose only slightly, to just over 1,000 tonnes in 1994. In the same period, however, worldwide seizures of these two substances more than tripled, to almost 22 tonnes, and prevented diversion cases identified recently totalled 95 tonnes. For phenylacetic acid, licit global imports have been more or less stable over the 1992-1994 period, at approximately 1,500 tonnes annually. Seizures amounted on average to one tonne per year over the same period. The dramatic decline in 1994 of phenylacetic acid seizures, as in most precursor seizures other than those involving ephedrine and pseudoephedrine, was noted earlier.

It is still not possible to tell what the aggregate figures of diversions represent in terms of volumes of precursors actually diverted from legitimate trade. Similarly, it is not possible to estimate the volume and distribution of clandestine manufacturing on the basis of precursor data only. If, however, the aggregate figures are considered in conjunction with data on the number and size of clandestine laboratories as well as those on end-product seizures, they can help to establish significant trends, such as the increased importance of diverted ephedrine for clandestine methamphetamine manufacture.

The **trafficking routes of precursors of ATS** are highly flexible: abundant sources of licit supply of most precursor chemicals enable clandestine manufacturers to adapt quickly to the introduction of stricter controls in major supplier and transit countries. As a result, new source countries are explored by illicit operators, and trafficking / diversion routes change accordingly. Simultaneous worldwide orders for a given precursor chemical add to the unpredictability of diversion routes. Monitoring is further complicated by the complex routing of shipments through a number of intermediaries in different countries, including free trade zones and ports without adequate control of movements of precursors.

These techniques and the multi-stage character of precursor trafficking show some similarities to the trafficking of natural drugs and may indicate that the two markets are increasingly linked. It may well be that the same groups are involved in the trafficking of natural drugs and the precursor chemicals, thus indicating an increasing diversification in the illicit drug industry in several regions, for instance, the Golden Triangle [UNDCP/EGM, 1996].

The most comprehensive data on trafficking and diversion of precursors of ATS is available for ephedrine. Presently, two patterns seem to emerge [INCB, 1995b; INCB, 1995c]:

- (a) Ephedrine originating in the Far East (China, India) and being transshipped via western European countries (Germany, Switzerland, Belgium and the Netherlands) or via other Asian transit points (Hong Kong, United Arab Emirates) to its final destination, North America;
- (b) Ephedrine originating in Europe (Germany or the Czech Republic) and being shipped directly to North America (Mexico, the United States or Guatemala).

While Guatemala and, more recently, Uruguay [UNDCP/EGM, 1996] seem to be transit points for the precursor ephedrine, Mexico has been used as a transit country for ephedrine and as a manufacturing site for methamphetamine. The final destination and country of consumption of most of the methamphetamine is the United States. It has recently been estimated that more

than 75% of the ephedrine diverted into the United States originates in Germany and China, as synthetic or natural ephedrine, respectively [DEA, 1994d]. China, Romania and some CIS countries seem to be the major ephedrine suppliers for illicit Russian ephedrone (methcathinone) manufacture [BND, 1995]. Precursors for the clandestine manufacture of ATS in Australia and New Zealand are obtained from Europe or the United States [INCB, 1996b; INCB, 1996c].

Though large-scale clandestine manufacture of ATS is well known in the Far East, there are very few reports on precursor trafficking within this region. With regard to Africa, it should be noted that ephedrine and ephedrine-containing pharmaceutical preparations that are diverted from India or Europe to some African countries, including Liberia, Nigeria and Sierra Leone [INCB, 1996b; INCB, 1996c], are often meant for direct consumption as stimulants rather than for use as precursors.

The lack of a comparably ideal precursor for the 'ecstasy' group (as ephedrine is for methamphetamine and methcathinone) requiring only minor structural modification to yield the desired end-product is also reflected in different trafficking patterns. While ephedrine is usually shipped to the country of final consumption of the end-product as such, there is at least one report of a precursor of the 'ecstasy' group (3,4-methylenedioxy-P2P) being manufactured illicitly from another pre-precursor (isosafrole) in Slovakia and then exported to the Netherlands, where it was used in the illicit manufacture of the end-products MDA and MDMA [INCB, 1995c], thus implying a two-step manufacturing and trafficking pattern. The same phenomenon has been observed with P2P.

The **eight precursors for ATS under international control** are a heterogeneous group of chemicals in terms of their origin, legitimate uses, global manufacturing volumes and the form of the products marketed. Since there are probably no more patent protections for these substances and/or their manufacturing methods, there is a virtually open market for any new entrant who sees the potential and has the simple manufacturing know-how. The chemical industry provides a range of qualities and purities of these substances, the use of which is determined by the kind of application: research, industrial, analytical, medical, etc. The nature of the clandestine industry, and particularly the lack of any control of quality of the final products, mean that any of the above qualities of these precursor chemicals suit the purpose.

Figures 44 - 46 illustrate the wide range of **licit uses** of precursors of ATS. This complicates control and facilitates the access of clandestine operators to these substances. **Phenylacetic acid** and **P2P** are simple synthetic chemicals, marketed as such, and are used by a few branches of industry in addition to the chemical industry (see Figure 44). This prevents effective regulation of their manufacture and commerce in many countries.

Uses of P2P and phenylacetic acid

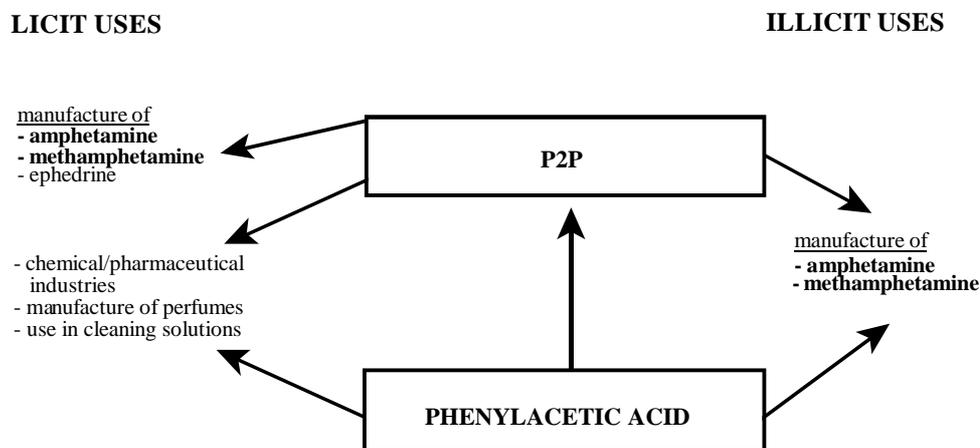


Figure 44

Ephedrine and pseudoephedrine are also significant drugs with a range of important pharmaceutical applications (see [Figure 45](#)). Their origin may be either natural, through extraction from various *Ephedra* plant species or through a stereospecific fermentation process, or synthetic. A number of synthetic methods are used in industry today. The growing significance of ephedrine and pseudoephedrine lies in the following:

- (a) The widespread availability of the pure substances as indispensable medicines, distributed and marketed through a sophisticated, structured commerce, in practically every country of the globe. Many pharmaceutical preparations containing varying amounts of ephedrine or pseudoephedrine are cheap, available without prescription and have a long-established history of use in the legal as well as parallel pharmaceutical markets in a number of countries. Many of these preparations contain quantities and are compounded in ways that make clandestine use not only feasible but also gainful for clandestine operators. Yet, the many important licit uses of the ephedrine group make it indispensable and difficult to replace with substitutes that are as cheap and versatile. At present, it is therefore difficult to foresee a particularly strict limitation on the licit supply of these substances, which, in turn, contributes indirectly to their appeal as illicit precursors;
- (b) Their availability in a wide range of crude extracts (made from *Ephedra* herb), concentrates and mixtures with other similar products. Such extracts and mixtures are widely used as dietary additives, **Aenergizer**® products or as herbal medicine with a steadily growing market (see [Figure 45](#)). The ephedrine content in these products is, again, high enough to make them profitable starting materials for clandestine manufacture of ATS [Hutchinson and Andrews, 1995];

- (c) The virtually unlimited supplies of the *Ephedra* plant raw material in some regions, particularly in Asia: in the central Asian republics of the CIS and in China, India, Pakistan and Nepal;
- (d) Their versatility as precursors, suitable for the manufacture of more than one amphetamine-type end-product, the most significant ones being methamphetamine and methcathinone;
- (e) The simplicity of the synthetic methods for converting the ephedrine into either methamphetamine, through the reductive elimination of the α -hydroxyl group, or into methcathinone, through a very simple one-step oxidation using such commonly available reagents as potassium permanganate or various chromium(VI) salts. An astonishingly simple and ingenious processing method for methcathinone, starting from the dried *Ephedra* plant, was developed in the former Soviet Union and could well diffuse widely;
- (f) The usually high yields obtained through these simple conversions, as a rule 50%-100%;
- (g) The optical purity of therapeutically used natural or synthetic ephedrine, together with the stereospecificity of the clandestine synthetic pathways yielding the methamphetamine or methcathinone isomer with the stronger CNS stimulant activity (P2P and other precursors yield the less potent racemic end-products).

The four internationally controlled **precursors of α ecstasy-type stimulants** (safrole, isosafrole, piperonal and 3,4-MD-P2P) are a mixed group consisting of substances of natural, semi-synthetic and/or synthetic origin. Safrole is made from various plant materials by steam distillation via intermediary essential oils which are marketed worldwide. The other three substances are either conversion products made from safrole (or directly from the essential oils rich in safrole) or may be directly synthesized from other starting materials. The family of precursors is therefore much larger than the four substances themselves. As illustrated in [Figure 39](#), it extends to a range of intermediary crude products such as essential oils (and ultimately to the plant materials themselves) and to various mixtures containing safrole in quantities attractive and suitable for direct conversion into ATS. A recent review of such products manufactured for the perfume, fragrance, flavour and soap industries, as well as for various synthetic purposes, showed that the number of these products is fairly large and their prices sufficiently low to make them attractive for clandestine operators [Remberg et al., 1994]. Several recent incidents involving the attempted diversion of sassafras oil indicate that this might yet become common practice. [Figure 46](#) summarizes both the licit uses and the clandestine application options for the α ecstasy-type precursors, pointing, once again, to the multitude of possible end-products already emphasized in this study. Much of what was noted about P2P and the ephedrine group also applies for the safrole group.

Uses of ephedrines (ephedrine/pseudoephedrine and norephedrine/norpseudoephedrine) and of the ephedra plant

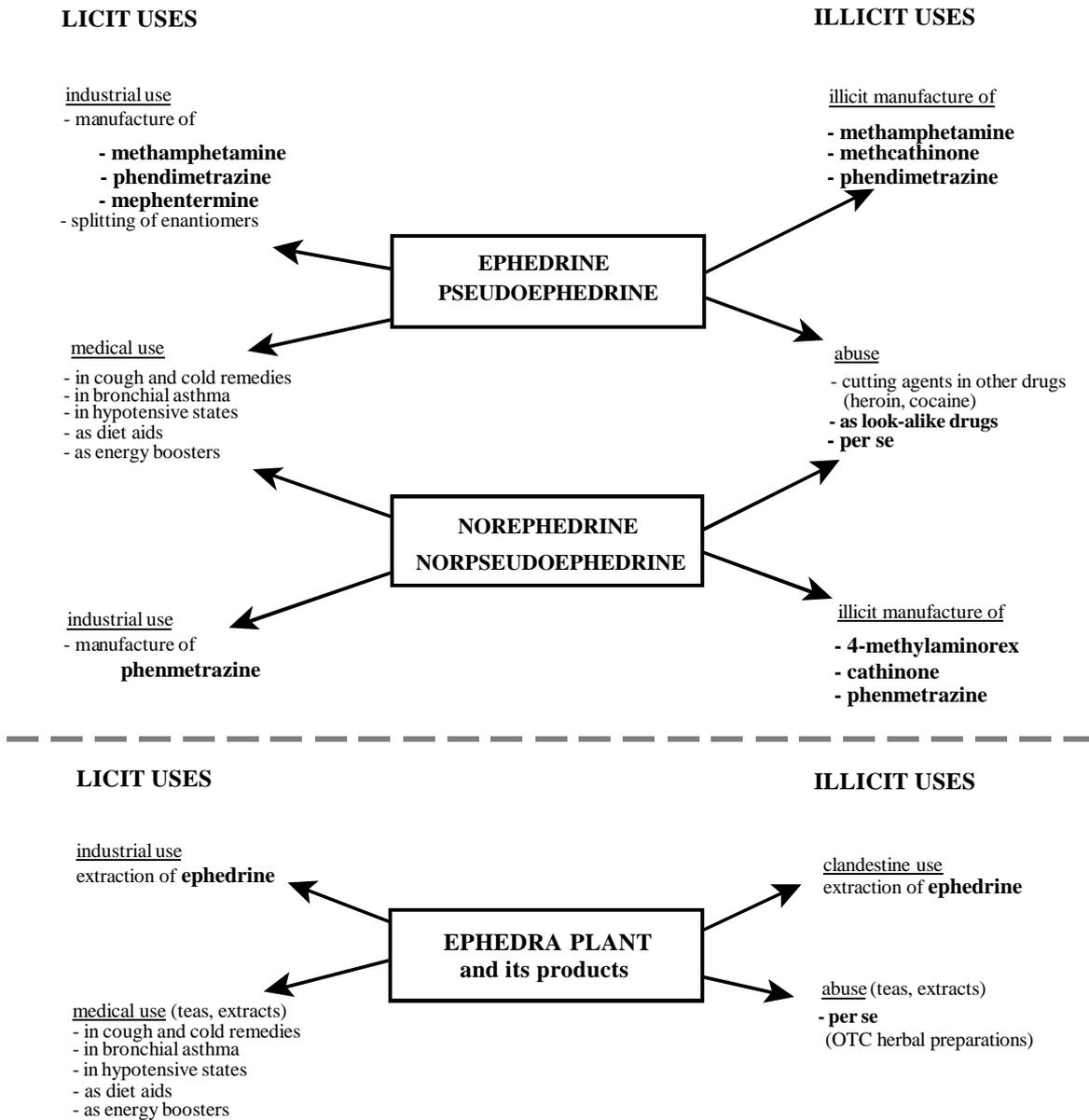


Figure 45

Uses of precursors of the 'ecstasy' group

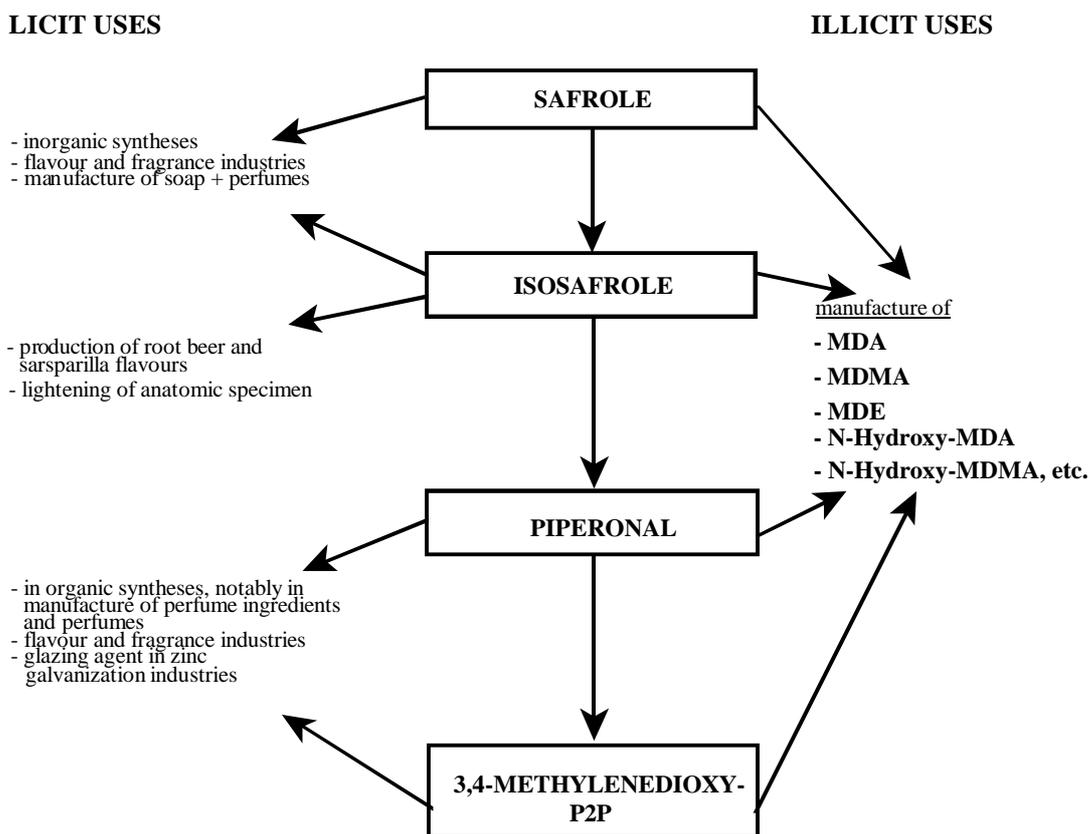


Figure 46

It was noted above that the pool of potential precursors of ATS is by no means restricted to the eight presently controlled ones. Reports to INCB as well as other technical reports point to the intense **clandestine experimentation** that takes place in a number of countries, manifested in perpetual **shifts between substitute precursors and starting materials**. Since the experimentation reacts to regulatory decisions, enforcement, availability, price and demand, it may well show regional differences. There are, nonetheless, some **general trends**, observed over the last decade:

- (a) A shift among commercially available, controlled precursors:
- For amphetamine and methamphetamine: P2P $\dot{\text{y}}$ phenylacetic acid $\dot{\text{y}}$ ephedrine (bulk ephedrine $\dot{\text{y}}$ ephedrine tablets $\dot{\text{y}}$ crude extracts $\dot{\text{y}}$ herb) $\dot{\text{y}}$ pseudoephedrine;
 - For the 'ecstasy' group: safrole, isosafrole, piperonal and 3,4-methylenedioxy-P2P have been used interchangeably;

- (b) The use of alternates not yet under international control, such as norephedrine, methylephedrine or ethylephedrine, in the manufacture of structurally related new drugs;
- (c) Clandestine synthesis of the controlled primary precursors (P2P, phenylacetic acid and 3,4-methylenedioxy-P2P) not only from simpler but also from more complex pre-precursor chemicals, controlled or not. A review of available synthetic routes and pre-precursors for P2P indicates that at least a dozen simpler chemical substances (e.g. benzaldehyde, benzyl chloride, allyl benzene) can be used efficiently for the purpose. Similarly, there is a substantial pool of more complex chemicals, such as esters of phenylacetic acid, which are not controlled but which yield the primary precursor upon simple hydrolysis - the so-called *hidden* precursors [UNDCP/EGM, 1996];
- (d) Simple alterations in the synthetic pathway using either a different synthesis method or replacing one, or some, chemicals in the process;
- (e) The use of natural raw materials such as various essential oils, perfume/aroma concentrates or plant materials rich in safrole for clandestine purposes. A similar development seems to emerge in the case of ephedrine, where the *Ephedra* plant itself or various extracts are increasingly used for the manufacture of methamphetamine or methcathinone. The simple method for making *home-made* methcathinone from dried *Ephedra* plant material noted above may well diffuse widely in countries where the plant is native and abundant. The *Ephedra* plant, plant parts and various concentrates therefrom are not under the purview of article 12 of the 1988 Convention, nor are they covered by most national regulations for the control of precursor chemicals.

Finally, the technical considerations noted in this chapter appear to have several **drug control implications**:

- (a) While efficient control of the raw material (or one key chemical) together with that of the end-product may provide for effective control of a plant-based narcotic drug, the strategic decision with amphetamine-type synthetic drugs is between an all-encompassing approach or an eclectic substance-by-substance approach on both the end-products and the precursors. In addition, the approach has to cover raw materials and various widely used industrial products containing or yielding those precursors. Both approaches have been applied; both have advantages as well as drawbacks. One major drawback is the differing scope of national control regimes;
- (b) At present, countries have widely differing scopes of national control, leading to an ever-increasing number of precursor chemicals under control by some countries but not by others. As noted earlier, nearly a hundred substances not included in Tables I or II of the 1988 Convention are under control in a total of 22 countries and territories. The number of substances controlled in individual countries range from only one to as many as 29 [INCB, 1996c]. All of this complicates standardization for effective international control. One pragmatic solution is to control clandestine manufacture by proscribing a few key chemicals, the selection of which has to be based both on chemical and practical considerations. This approach has been used in a number of countries and is essentially the basis of Tables I and II and article 12 of the 1988 Convention;

- (c) Another implication for enforcing the law on precursors arises from the fact that an ever-broadening range of industrial products as well as non-controlled vegetable materials, which are not necessarily produced and marketed by the same sectors of industry and commerce, will have to be targeted. For instance, the shift from bulk ephedrine to a myriad of pharmaceutical preparations and food supplementary products containing ephedrine and pseudoephedrine was not foreseen, and these products are, in fact, specifically exempted by the 1988 Convention. Considering the precursors of the «ecstasy»-group, the range of licit industry branches expands to new industries such as perfumes, fragrances, flavourings and soap/hygienic products, and the spectrum starts with many essential oil distilleries in several developing countries, mainly in Asia and Latin America. This implies understanding and compliance in these sectors of industry, a step which goes beyond the traditional interaction with the pharmaceutical and chemical industries;
- (d) The lack of a generic provision for stereoisomers of precursors in the 1988 Convention is reflected, among other things, in the fact that ephedrine and pseudoephedrine are scheduled as two separate items and that the cis/trans stereoisomers of starting materials like isosafrole are not addressed at all. This may not be sufficient to prevent future diversifications in clandestine manufacture using optically active forms of precursors;
- (e) Another aspect that deserves attention arises from the quantitative relationship between starting material and end-product (see Figure 40). Since clandestine manufacture of ATS can also take place in small-scale «kitchen» laboratories, the small amount of precursor substances needed may fall below the minimum threshold quantities requiring monitoring and record-keeping.

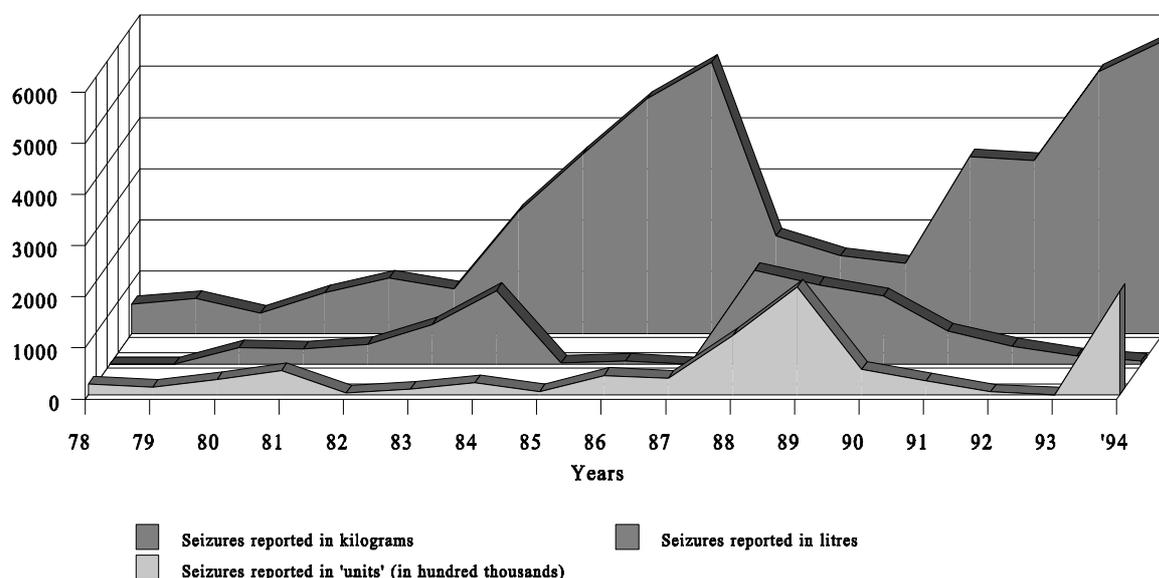
IX. Trafficking of ATS

ATS are usually manufactured in, or close to, the country of final consumption. This pattern is, however, beginning to change. There is now some evidence of interregional trafficking, particularly of ecstasy. For precursors, by contrast, interregional trafficking has been more common and continues to grow.

The main quantitative indicator for estimating the extent and pattern of trafficking is **seizure statistics**. Several caveats, however, should be borne in mind. Apart from the general problem of extrapolating the extent of total trafficking from the extent of seizures [see UNDCP, 1994], the situation is further complicated by the fact that most countries do not report on the purity of the substances seized. Furthermore, some countries report pure substance seizures while others report only the total weight of substances containing ATS that were seized. Aggregation is made even more difficult by the fact that seizures are variously reported in kilograms, in litres and in units, with no globally accepted standard measure of conversion. Seizure data are thus presented below primarily in the unit of measurement they were reported. Even if a reasonable conversion factor was assumed, and the data aggregated, one vital element of the seizure data would be lost. This concerns the origin of the substance: whether it comes from licit sources or illicit ones. Such information is particularly important in the context of the ATS since they may originate from either a licit or an illicit pool. When seizures are reported in kilograms, it is reasonable to assume that they originate in the clandestine sector; when they are reported in units, they could also have been diverted from licit sources. Exceptions do, however, occur.

Figure 47 shows the development of **seizures of ATS** between 1978 and 1994, keeping the three units of measurement separate. For all the limitations, the best single indicator for estimating global trends is seizures made in kilograms. It is the most frequently reported unit of measure and by far the most important one in terms of total quantities represented. This also supports the thesis that the bulk of supply originates in the clandestine sector. The figure shows that seizures gained strongly in importance in the mid-1980s, declined in the late 1980s but are fast regaining importance in the 1990s. The amount (in kilograms) seized in 1994 was 10 times larger than the amount in 1978, showing that on average they increased by 15% per year over the 1978-1994 period. Part of the decline in the late 1980s was due to the United States changing its reporting from kilograms to units, similarly, part of the increase in the 1990s can be attributed to United States reporting changing again to kilograms before switching back to units in 1994.

Global seizures of ATS* in kilograms, litres and units



* Data do not include the 'ecstasy' group.

Source: UNDCP ARQ Data.

Figure 47

Changes in reporting practices, as noted for a number of countries, may, however, distort the picture of overall trends. Some attempt at standardization to create a composite picture may thus be desirable. In the absence of precise conversion rates of >units= or >litres= into >kilograms=, **rule-of-thumb conversion measures** are the only feasible option. Table 5 illustrates the variance, in the literature, of what a standard >dosage= or >unit= may mean. It also includes heroin and cocaine for the purposes of comparisons to be made later. Since most >unit= estimates for amphetamine and methamphetamine fall within the 5 mg to 15 mg range, a rule-of-thumb conversion rate of 10 mg per unit, or 100,000 units per kg, has been chosen. The establishment of a similar rule-of-thumb conversion rate for litres into kilograms is more difficult and does not appear to have been investigated in the literature⁵. It is known that both individual >litre= and >kilogram= seizures show an enormous variation in purities and concentrations, ranging from less than 5% to almost 100%, with differences both within and between countries. There is, however, some evidence to suggest that, on average, the amphetamine content of >litre= seizures should not

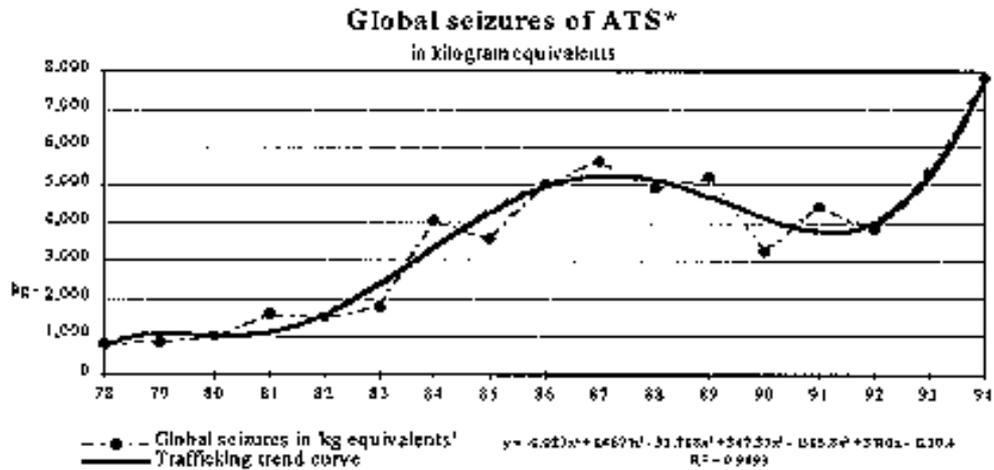
⁵ The two countries which frequently report significant quantities of seizures in litres are the Netherlands and Egypt. Seizures of liquid amphetamine in the Netherlands are reported as >amphetamine oil=, which suggests the presence of almost 100% pure amphetamine base. In the case of Egypt, the litre seizures concern what is locally known as AMaxiton Forte®. When this pharmaceutical preparation was first marketed in the 1960s, it was a solution of 50% dexamphetamine tartrate. The exact composition of the clandestine AMaxiton Forte® seized today is not known, neither in terms of the amphetamine derivative (dexamphetamine or methamphetamine) nor in terms of purity. It can be assumed, however, that the >pure= dexamphetamine or methamphetamine content of AMaxiton Forte® seized in Egypt is much less than that of the >amphetamine oil= seized in the Netherlands.

deviate dramatically from that of kilogram seizures. A simple 1:1 rule-of-thumb conversion rate for litres into kilograms has thus been selected.

Table 5: Dosages in milligrams (proxy for units=)				
	Standard dosage unit= (DEA)	Effective Dose=*	Daily defined doses= (DDD) (INCB)	Street dose= (INCB)
Amphetamine	10	10	15	10-250
Methamphetamine	5	10	15	10-250
Dexamfetamine, levomethamphetamine, phentermine	-	10	15	-
Methylphenidate	-	-	30	-
Pemoline			40	
Fenetylline, phenmetrazine			50	
MDA	100	-	-	100
MDMA	-	125	-	100
Cocaine hydrochloride	10	100	-	100-200
Crack cocaine		15	-	
Heroin	5	4	30	100
* For an adult with a weight of 70 kg. Sources: [Gable, 1993; INCB, 1995a; INCB, 1995c; INCB, 1995d] DEA, <i>Standard Dosage Units</i> (ARQ data).				

Using these conversion rates, [Figure 48](#) provides a **composite picture of seizures of ATS** over the 1978-1994 period. Based on kilogram equivalents, a trend curve has been superimposed: it smooths annual fluctuations, reduces distortions from random factors and should therefore better reflect underlying trafficking trends.⁶ The resulting trend curve suggests that there was a strong increase in trafficking in the 1980s up to around 1987, some decline thereafter and again a dramatic increase in the 1990s, particularly since 1992. A record high was reached in 1994. The trafficking trend curve thus shows a pattern similar to the kilogram seizures illustrated in [Figure 47](#). There is only one major difference. The aggregated data of [Figure 48](#) suggest that the downward trend in trafficking in the late 1980s may have been less significant than indicated by kilogram seizures. For the present decade, both figures show a strong increase in trafficking.

⁶ Results for individual years can only be considered as estimates. Nevertheless, even significant variations in the conversion rates applied (1 litre = 0.2 kg to 1.5 kg and 1 unit = 5 mg to 30 mg) would not lead to significant changes in the trend pattern reflected in [Figure 48](#).

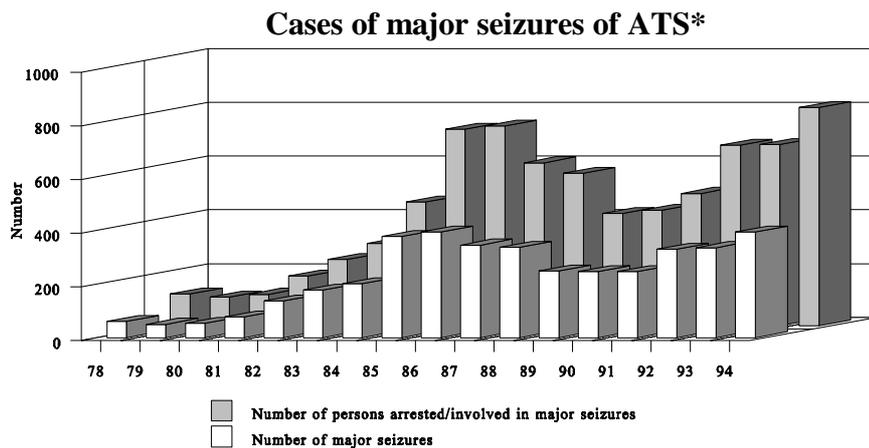


* Data do not include the 'ecstasy' group.

Source: UNDCP ARQ Data.

Figure 49

This trafficking pattern is also confirmed by Interpol. Figure 49 shows Interpol data on **major seizures** of international importance over the same period, as well as the number of people involved, or arrested, in these cases. The latter is an indirect indicator of the importance of the seizures since there is usually a positive correlation between the number of people involved in a case and the amount being trafficked. Both UNDCP and Interpol data, independently compiled, confirm that seizures of ATS have been characterized by an overall upward trend, with one peak in 1987/88, some decline thereafter, and a strongly rising trend in the 1990s.



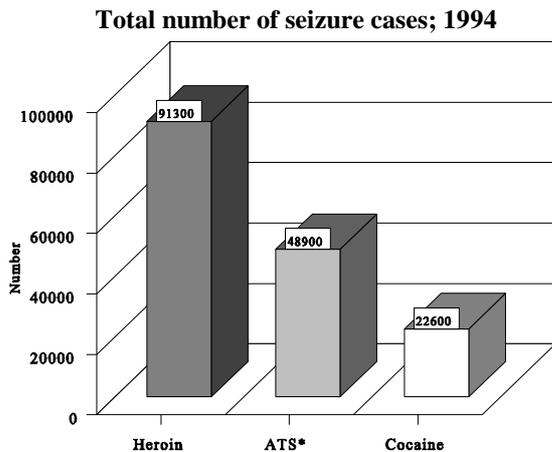
* Data do not include the 'ecstasy' group.

Source: Interpol.

Figure 49

Figures 50 and 51 compare global seizures of ATS (excluding the 'ecstasy' group) with those of cocaine and heroin. In terms of number of seizure cases, ATS already play an important role at the global level, although their relative importance *vis à vis* heroin and cocaine may be exaggerated⁷ in these statistics (Figure 50). By contrast, in terms of quantities seized (in kilograms) ATS appear to be underrepresented (see Figure 51) for a number of reasons. Their trafficking is local (within one country) or intraregional and in general involves smaller shipments. The trafficking of cocaine and heroin is interregional and is thus better represented in such data. Moreover, in many countries enforcement authorities focus on heroin and cocaine, creating a bias in favour of these seizures. Finally, comparisons based on weight units may be biased against ATS. The street dosages that can be obtained from a gram of pure methamphetamine may be about the same as for heroin, but they can be two to ten times more than for cocaine (see Table 5). Taking these factors into account, as well as adding 'litre' and 'unit' seizures, the relative importance of ATS would increase to a level greater than that shown in Figure 51 but still below cocaine and heroin. Figure 52, based on Interpol data, provides further evidence for this conclusion. The number of major seizures of cocaine and heroin has been consistently higher than that of ATS over the 1978-1994 period.

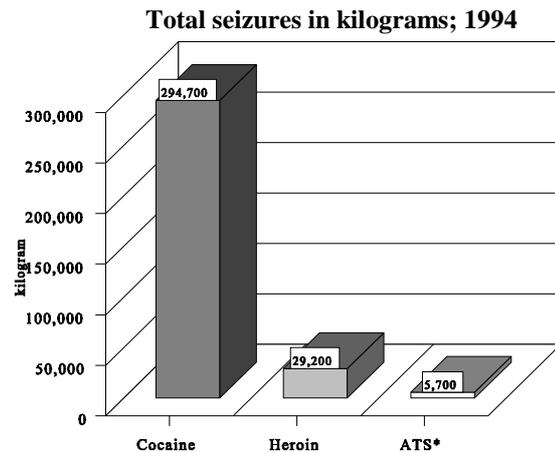
Drug seizures: ATS compared to heroin and cocaine



* Data do not include 'ecstasy' group.

Source: UNDCP ARQ Data.

Figure 50



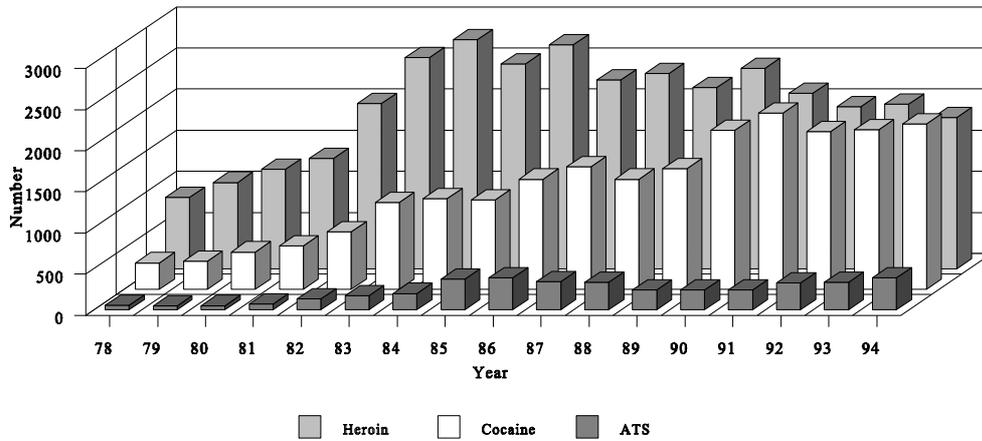
* Data do not include the 'ecstasy' group

Source: UNDCP ARQ Data.

Figure 51

⁷ In general, there are more countries reporting kilogram seizures than the number of seizure cases, i.e. not all countries providing UNDCP with data on the former report on the latter. The resulting under-reporting in the number of cases statistics seems to be, however, more important for heroin and even more so for cocaine than for the ATS. In total, 71 countries/territories provided UNDCP with data on the number of seizure cases in 1994; 146 countries supplied UNDCP with information on quantities seized (seizures in kg). For ATS the number of countries/territories providing data on number of seizure cases and seizures in kg were 34 and 36, respectively; for cocaine 38 and 103; and for heroin 50 and 112. This reporting pattern thus suggests that in statistics on the number of seizure cases both heroin and cocaine have been under-represented while the ATS may have been, in relative terms, over-represented.

Cases of major seizures of ATS* compared to cocaine and heroin



* Data do not include the 'ecstasy' group.

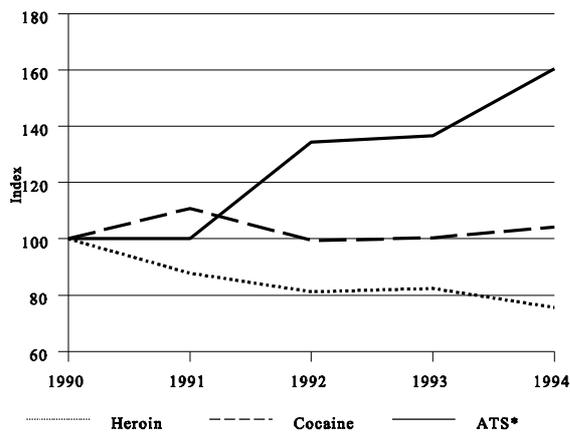
Source: Interpol.

Figure 52

While this analysis suggests that trafficking in cocaine and heroin is still more widespread, the **relative importance of ATS** in the present decade has definitely increased. Figure 53, based on Interpol data, shows that major seizures of cocaine and heroin have been stagnant in the present decade, while those of the ATS have been rising strongly. Their share in all seizure cases, as reported to UNDCP, grew from less than 5% in 1988/89 to more than 10% in 1993/94 (see Figure 54). The upward trend would have been even more pronounced if seizures and prevented diversions of precursors had been included as well. This would better correspond to a major difference between ATS and plant-based drugs, i.e. the relative importance

Cases of major drug seizures

Index: 1990 = 100

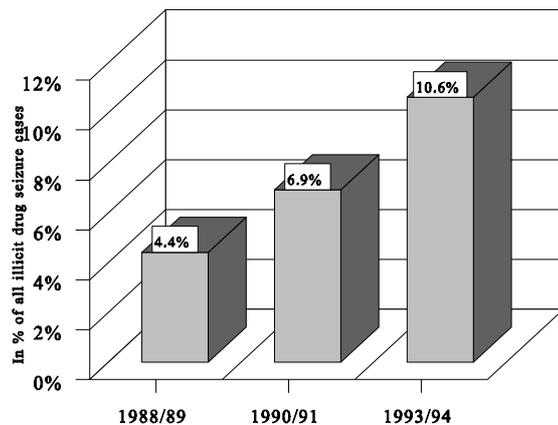


* Data do not include the 'ecstasy' group.

Source: Interpol.

Figure 53

Share of ATS* in total number of drug seizure cases



* Data do not include 'ecstasy' group

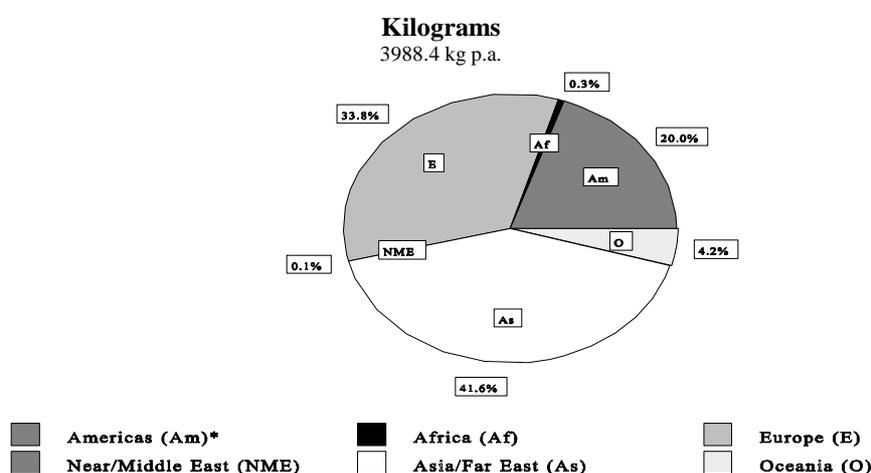
Source: UNDCP ARQ Data.

Figure 54

of starting materials and end-products in seizure statistics. While in the case of cocaine and heroin a higher proportion of end-products, compared to raw materials/precursors, is trafficked, the opposite is true for ATS. Chances for detection of ATS precursors are thus larger than those for amphetamine-type end-products. In recent years, diversion attempts of precursors, particularly ephedrine, have indeed been growing dramatically and exceed by far the amounts of end-products seized [INCB, 1996b; UNDCP/EGM, 1996].

Figures 55 - 57 illustrate **seizures by regional breakdown**, covering the period from 1991 to 1993, in kilograms, litres and units. Though the three units of measurement cannot easily be converted into a single measure for reasons noted above, the three figures should be seen in conjunction. Figure 55, also for reasons already noted, is probably the most representative. It shows the large concentrations in the Americas, Europe and Asia, although Oceania is not insignificant. The Near and Middle East shows up more prominently in the litre and unit measures, and Africa in the latter. While the litres are mostly due to seizures of **AMaxiton Forte** in Egypt (originally a pharmaceutical preparation containing dexamfetamine diverted from Europe, which in recent years seems to have been replaced by locally produced solutions of methamphetamine), the large number of seizures of units reflects the importance of both Africa and the Near and Middle East for diverted ATS.

Seizures of ATS: regional breakdown 1991-1993 average

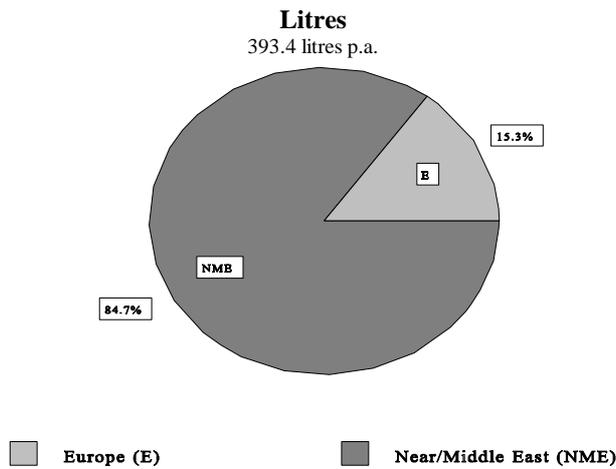


Note: Data do not include the 'ecstasy' group.

* Data for USA are based on 1992 and 1993, when seizures were reported in kg.

Source: UNDCP ARQ Data.

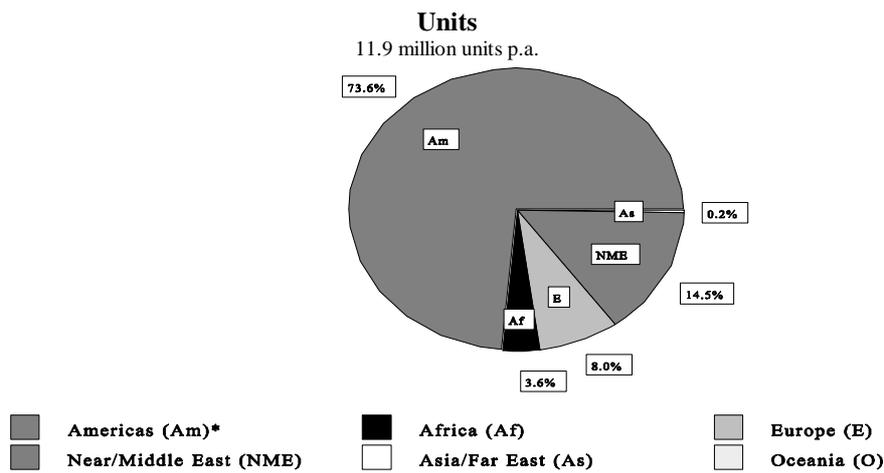
Figure 55



* Data do not include the 'ecstasy' group.

Source: UNDCP ARQ Data.

Figure 56



Note: Data do not include the 'ecstasy' group.

* Data for USA are based on 1991, when seizures were reported in units.

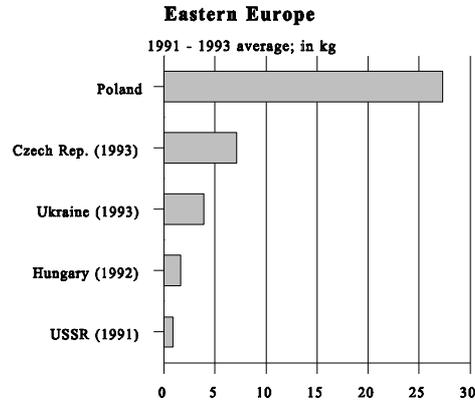
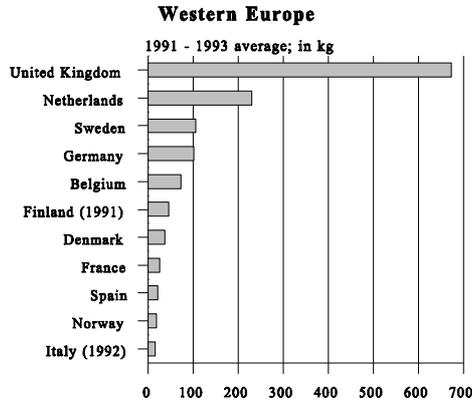
Source: UNDCP ARQ Data.

Figure 57

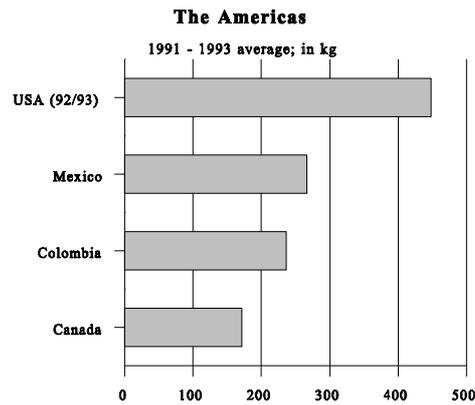
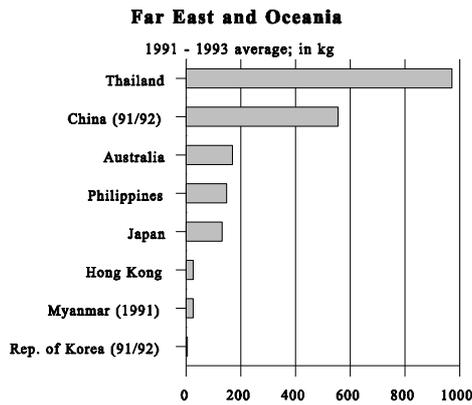
Figures 58 - 62 narrow the regional focus down to the most significant **seizures reported by individual countries** within each region. Figure 63 draws the countries with the highest reported seizures, from all regions, into one illustration to get some comparative sense in the data. These seizures represent amounts seized within the countries, as well as on their respective borders. They can thus be used to illustrate the salience of the ATS problem in countries within each region. Data show that the main countries affected by trafficking in the Far East/Oceania region are Thailand, China, Australia, the Philippines and Japan; in the Americas, the United States and Mexico; in Africa and the Near and Middle East, Egypt and Saudi Arabia; in western Europe, the United Kingdom, the Netherlands, Sweden and Germany; and in eastern Europe, Poland, the Czech Republic, and to some extent, Russia and Bulgaria.

Seizures of ATS*

Figures 58 to 62



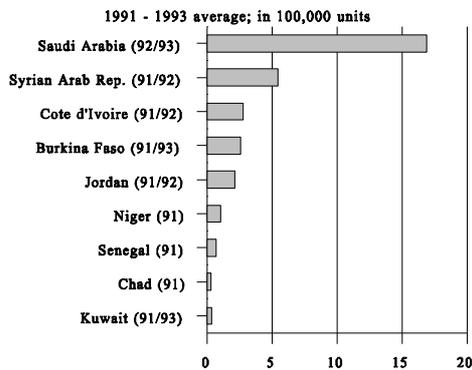
Other countries reporting trafficking of stimulants in the region include Austria, Cyprus, Greece, Iceland, Ireland, Portugal, Switzerland, Turkey.



Other countries reporting trafficking of stimulants in the region include Brunei, Indonesia, Singapore, Sri Lanka, New Zealand.

Other Countries reporting trafficking of stimulants in the region include Argentina, Chile, Uruguay.

Africa and the Near and Middle East



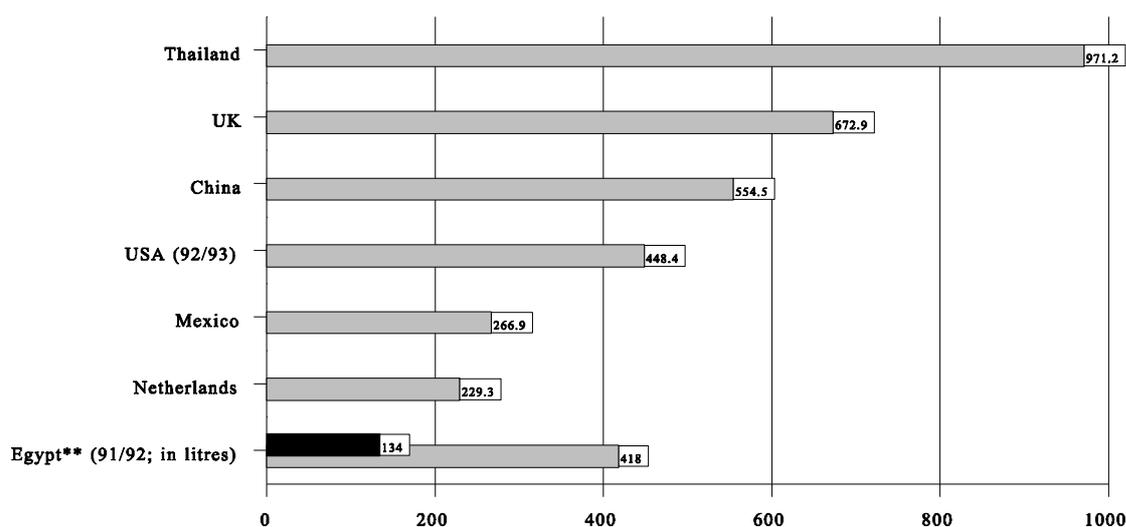
Major seizures of ATS have been reported from Egypt averaging 418 litres (91/92); trafficking of ATS has also been reported from Nigeria (reports in kg.), Qatar, Israel, United Arab Emirates, Bahrain, Gabon, Sudan, and the United Republic of Tanzania.

* Data do not include the ecstasy-group.

Trafficking in eastern Europe shows a particularly strong upward trend, partly reflecting the progressive relocation of clandestine manufacture from 'traditional' consumer areas in western Europe. In 1994, Interpol reported an increase of European amphetamine seizures originating in Poland by 47% on a year earlier [ICPO/INTERPOL, 1995]. Trafficking in the CIS region is slightly different in character. In 1994 the Russian Federation reported seizures of 1.5 million tablets of ephedrine, which was a 16-fold increase in terms of quantity and a 3.5-fold increase in terms of frequency compared with 1993. The ephedrine seizures represented 99% of all seizures of psychotropic drugs, as defined in the Russian Federation, and 6% of all cases of illicit drug seizures in 1994. In three quarters of all cases the seizures were made on the border with China [State Customs Committee of the Russian Federation, 1995]. The fact that the ephedrine tablets were seized implies that they were intended for illicit use; it is unclear, however, whether they were for direct consumption as stimulants or as precursors for synthesizing methamphetamine or methcathinone.

Countries with highest reported seizures of ATS*

1991-1993 average; in kilograms



* Data do not include the 'ecstasy' group.

** The lower figure is a kg estimate, based on the original chemical composition of 'Maxiton Forte'.

Source: UNDCP, *Seizures of Narcotic Drugs and Psychotropic Substances in 1993*, 7 March 1995.

Figure 63

The largest **relative importance of trafficking in ATS compared to trafficking in other drugs** is reported from a number of countries in the Far East and from Sweden. Table 6 shows that in Japan 88% of all violations against drug laws concerned the stimulant drug control law in 1994. Comparable figures were 60% in the Philippines, 50% in the Republic of Korea, and around 33% in Sweden in recent years, increasing to 45% by 1994. In Europe's largest amphetamine market, the United Kingdom, the comparable share for ATS was 13%, in the United States, 11%. Figure 54 showed that ATS account for about 10% of all seizure cases at the global level.

Table 6: Arrests for ATS offences						
Country	People arrested for trafficking and/or possession					
	Total number		Share of ATS	Population (in million)	per million inhabitants	
	ATS	all illicit drugs			all illicit drugs	ATS
Taiwan Province of China (1993)	44,000	-	-	20.9	-	2,105
Belgium (1994) ^{a/}	4,324	19,467	22.2%	10.0	1,947	432
Sweden (1994)	2,825	6,351	44.5%	8.7	730	325
Australia (1994)	4,307	51,267	8.4%	17.6	2,913	245
Norway (1994)	945	9,308	10.2%	4.3	2,165	220
Iceland (1994)	53	349	15.2%	0.3	1,317	200
Thailand (1993)	9,742	117,836	8.3%	58.1	2,028	168
UK (1993)	9,104	68,044	13.4%	57.9	1,175	157
Japan (1994)	17,564	19,896	88.3%	124.5	160	141
Germany (1994)	5,411	118,193	4.6%	81.3	1,454	67
Spain (1994) ^{b/}	1,455	31,703	4.6%	39.5	803	37
Switzerland (1994) ^{d/}	246	61,715	0.4%	7.0	8,816	35
Philippines (1994)	2,077	3,464	60.0%	64.8	53	32
Austria (1994) ^{d/}	219	12,623	1.7%	8.0	1,578	27
Republic of Korea (1993) ^{e/}	1,121	2,256	49.7%	44.1	51	25
Chile (1994)	267	9,990	2.7%	13.8	724	19
Hong Kong (1994)	74	15,601	0.5%	5.9	2,644	13
Czech Rep. (1994)	124	173	71.7%	10.3	17	12
USA (1994); (federal level) ^{d/}	2,045	19,297	10.6%	257.8	75	8
Lithuania (1994)	25	245	10.2%	3.7	66	7
France (1993) ^{e/}	157	51,567	0.3%	57.5	897	3
Greece (1994)	7	4,730	0.1%	10.4	455	1
Indonesia (1994)	8	1,048	0.8%	187.2	5.6	0.04

a/ Number of people reported to police for having violated the narcotics/psychotropics laws; more than half of the offences of ATS in Belgium and Austria were related to MDMA.

b/ Trafficking only.

c/ The Republic of Korea reported a strong decline of people arrested for methamphetamine offenses in recent years.

d/ The total number of people arrested for drug abuse violations in the USA was 1,066,400 in 1992.

e/ Includes arrests for LSD trafficking/possession; for 1994, France reported a 126% increase on a year earlier of the number of people arrested for ecstasy=trafficking/possession .

Sources: UNDCP, ARQ Data; UNDCP/EGM, 1996; Office of the Narcotics Control Board, *Thailand Narcotics Annual Report 1993*, Bangkok ; Centralförbundet för alkohol- och narkotikaupplysning (1995), *A lcohol- och narkotikautvecklingen i Sverige*, Rapport 95, Stockholm; Home Office Research and Statistics Department (1994), *Statistical Bulletin*, Issue 28/94, 20 December; Federal Bureau of Investigation, *Uniform Crime Reports*, quoted in Office of National Drug Control Policy (1994), *National Drug Control Strategy*, Washington; Bundesministerium für Inneres (1995) *Jahresbericht 1994 über die Suchgiftkriminalität in Österreich*, Vienna; UN/HONLAP, Nineteenth Meeting of Heads of National Drug Law Enforcement Agencies (HONLEA), Asia and the Pacific, Wellington, 14-18 November 1994 - Country Report by France; World Bank (1995), *World Development Report 1995*, Washington.

Table 6 provides a further measure of salience. It ranks countries according to the number of people arrested for trafficking and/or possessing ATS per million inhabitants. This is another (indirect) measure of the importance of trafficking in ATS in different countries. Taiwan Province of China leads this ranking, followed by Belgium, Sweden, Australia, Norway, Iceland, Thailand, the United Kingdom, Japan and Germany. In absolute figures, the largest numbers of ATS-related violations are reported from Taiwan Province of China, Japan, Thailand and the United Kingdom.

Within this broad picture of the extent of illicit trafficking of the ATS, there are a good many areas which, if analyzed in detail and combined with data on clandestine manufacturing, reveal interesting results. One example is offered here for illustrative purposes. Figures 64 and 65 show, by region, the average number of illicit laboratories detected and the amounts of ATS seized over the 1991-1993 period. The Far East shows the highest amount of seizures, yet the lowest number of illicit laboratories detected, and a low amount of precursors seized (see Chapter VIII). However, intraregional trafficking is high, and the stimulants do not appear to be coming into the Far East from other regions. This then leaves a puzzle which can only be solved by answering the question of where, and at what technical level, the ATS in the region are manufactured.

ATS: clandestine manufacture versus trafficking

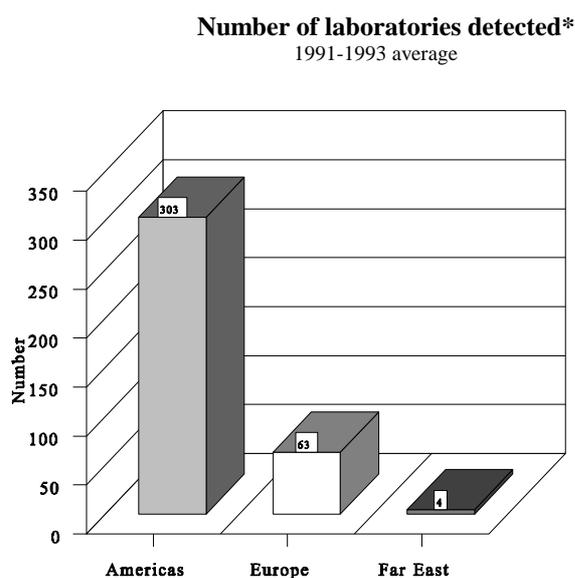


Figure 64

* Data do not include the ecstasy-group.

Source: UNDCP, *Seizures of Narcotic Drugs and Psychotropic Substances in 1993*, 7 March 1995.

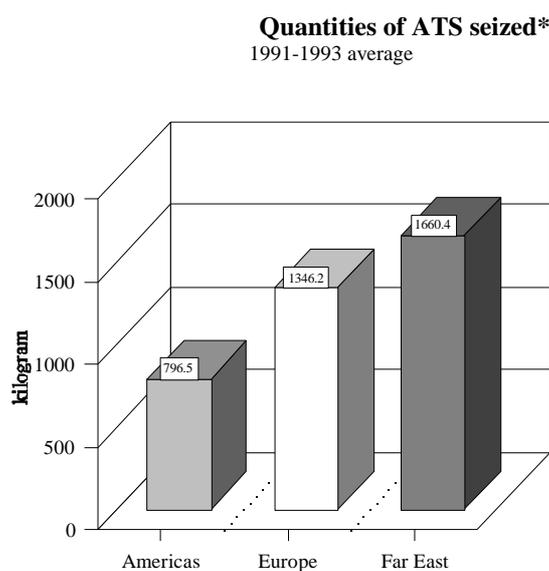
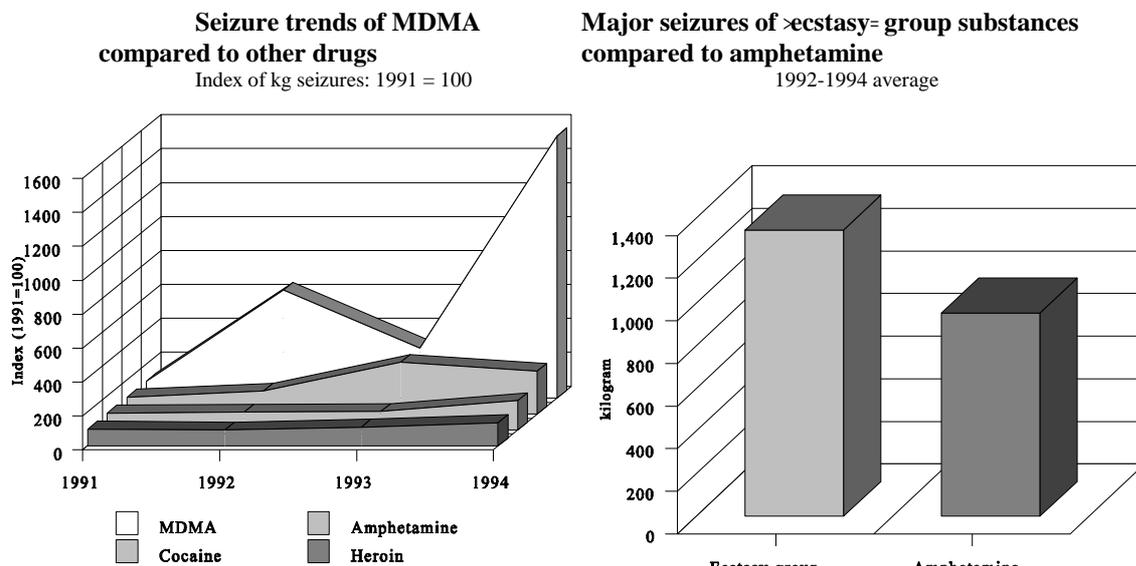


Figure 65

Seizure data on the 'ecstasy' group of substances substantiate the trend already noted in the chapter on illicit manufacture above: the enormous increase of illicit manufacture in Europe. The largest growth rates within the 'ecstasy' group are reported for MDMA. According to Interpol data, MDMA already accounted for 95% of all 'ecstasy' seizures in units over the 1992-1994 period. For seizures reported in kilograms, the relative importance is less, though rapidly growing.

Figure 66 shows the increase in major seizures of MDMA in Europe from 1991 to 1994. Growth rates clearly exceed those of amphetamine, cocaine or heroin. Figure 67, based on Interpol data, shows that major seizures of the 'ecstasy' group (MDMA, MDA, MDEA) in Europe are already larger than those of amphetamine averaged over 1992-1994.

Seizures of 'ecstasy' in Europe



Sources: Interpol, UNDCP ARQ Data.

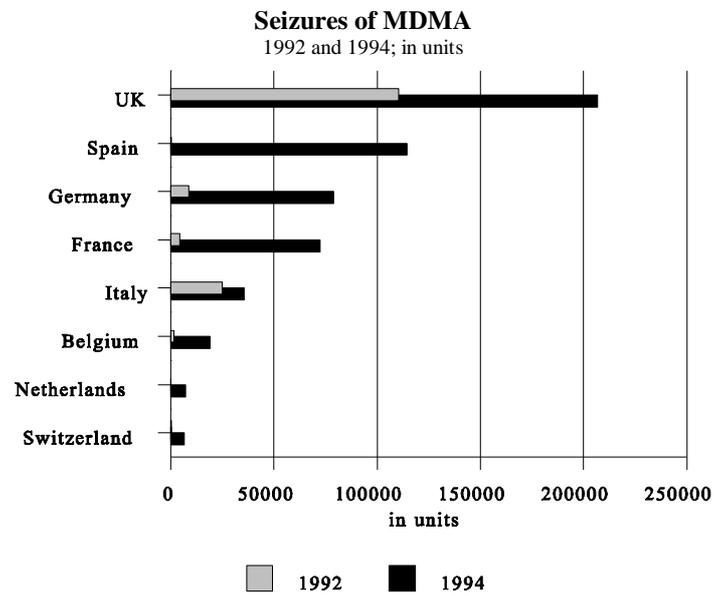
Source: Interpol.

Figure 66

Figure 67

Figure 68 tries to establish the relative magnitudes for individual European countries, in terms of seizures of MDMA units in 1992 and in 1994. Figure 69, based on the same data set, shows the average annual growth rates in selected European countries. The three countries with the largest seizures, the United Kingdom, Spain and Germany, are then detailed in Figures 70 - 73. In Europe's largest 'ecstasy' market, the United Kingdom, the number of MDMA seizures already starts to approach those of heroin and cocaine (see Figure 71). Trafficking of MDMA and amphetamine combined is already significantly more widespread than trafficking in heroin or cocaine. In almost all European countries, trafficking in MDMA has become the fastest growth area in the illicit drug markets in the 1990s. The European situation with 'ecstasy' thus looks like the beginning of a new wave, similar to what happened with cocaine in the late 1980s.

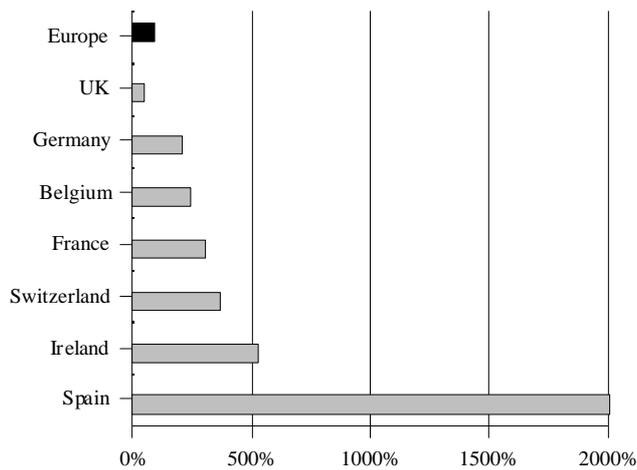
Seizures of ecstasy in Europe: country breakdown



Source: Interpol.

Figure 68

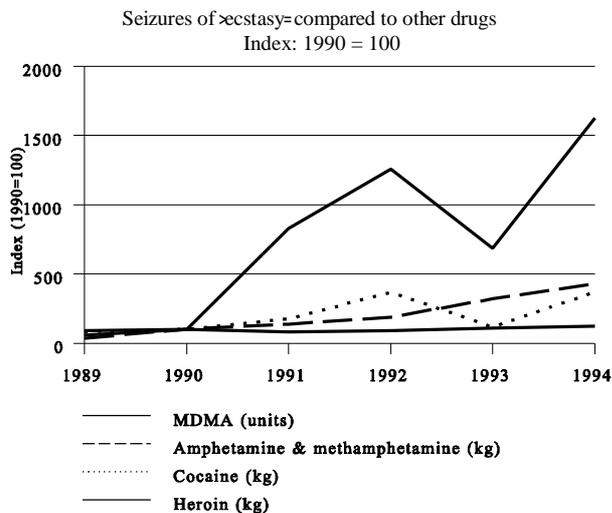
Average annual growth of MDMA unit seizures
1992 to 1994



Source: Interpol.

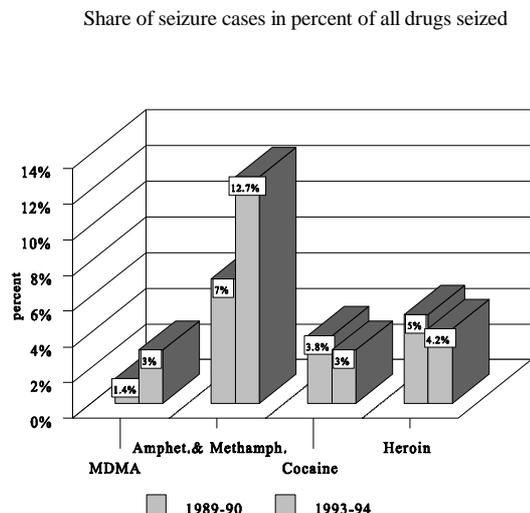
Figure 69

United Kingdom



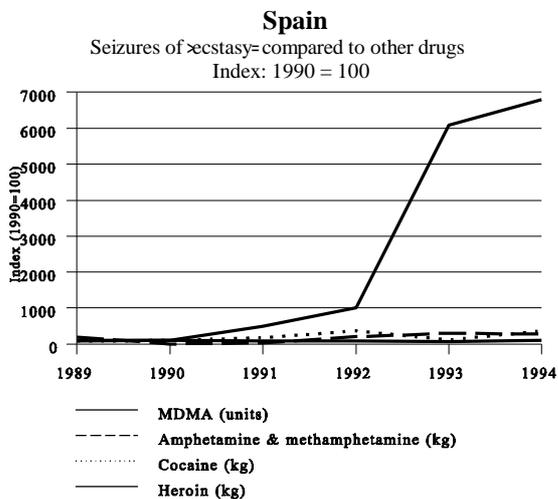
Source: Home Office, *Statistical Bulletin*, December 1995.

Figure 70



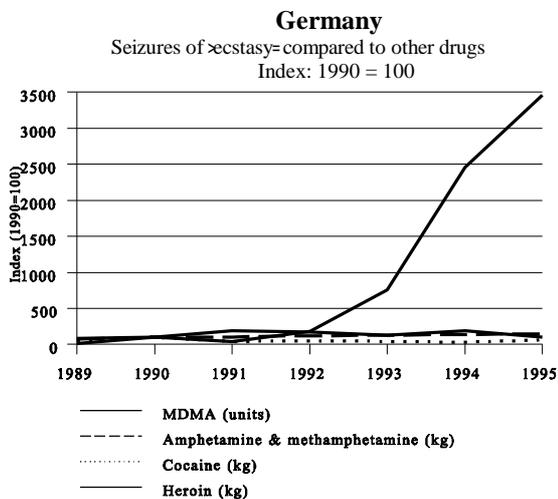
Source: Home Office, *Statistical Bulletin*, December 1995.

Figure 71



Source: UNDCP ARQ Data.

Figure 72



Source: BKA, *Special Aspects on Ecstasy Tablets (XTC)*, Wiesbaden, February 1996.

Figure 73

X. Economic incentives for manufacture, trafficking and consumption of ATS

This chapter examines the **economic incentives** driving the manufacture, trafficking and, ultimately, abuse of ATS. The main economic incentives for expansion are high **profits**, indirectly fueling demand (supply push), low levels of expected **risk**, as well as low **prices** (demand pull). The analysis is based on the assumption of rational behavior [Niskanen, 1992; Becker and Murphy, 1988] of manufacturers, traffickers and drug consumers reacting to incentives (price signals) and disincentives (risks). Table 7 provides an overview of the factors driving or restricting manufacturing, trafficking and consumption. Though economic incentives are certainly not sufficient to fully explain developments in clandestine drug markets, particularly as far as the more complex question of consumer preferences is concerned (see Chapter XI), they are, nevertheless, among the key factors influencing the behaviour of the main actors.

Table 7: Economic incentives and disincentives in illicit drug markets
<p>A) Manufacturing level</p> <p><u>Incentives:</u> - Manufacturing profits, comprising:</p> <ul style="list-style-type: none"> * Gross profit margins * Volume of manufacture * Fixed costs <p>- Manufacturing know-how</p> <p><u>Disincentives:</u> Risks:</p> <ul style="list-style-type: none"> * Detection * Dangers related to the manufacturing process (e.g. explosion, accidents) * Non-availability of supply of precursors/chemicals
<p>B) Trafficking level</p> <p><u>Incentives:</u> Trafficking profits, comprising:</p> <ul style="list-style-type: none"> * Gross profit margins * Volume of transactions * Number of trafficking steps between wholesale and retail level <p><u>Disincentives:</u> Risks:</p> <ul style="list-style-type: none"> * Detection * Relation with distribution networks for other drugs (e.g. level of violence) * Reliability of supply
<p>C) Consumption level</p> <p><u>Incentives:</u> Low opportunity costs:</p> <ul style="list-style-type: none"> * Low prices compared to other drugs * Pharmacological effects of substance * Easy availability * Other incentives (image, peer group attitudes, etc.) <p><u>Disincentives:</u> Risks:</p> <ul style="list-style-type: none"> * Detection * Health risks

The following analysis, based on UNDCP annual reports questionnaires (ARQ) data (unless stated otherwise), compares profits and prices of ATS with those of cocaine and heroin. The third factor after profits and prices, the **risk factor**, will not be explicitly addressed in the analysis. It can be assumed, however, that the risks associated with the manufacture, trafficking and consumption of ATS are no greater than those associated with cocaine or heroin.

Table 8 summarizes the **concepts used to investigate the economics of ATS manufacture and trafficking**. Profits are the main incentive on the supply side. The main

problem in economic analysis of clandestine markets is the lack of data to establish profits and profitability according to generally accepted accounting principles. As a proxy, the difference between output prices and input prices is used. The mean values of maximum and minimum prices are used for the input and output price levels. The resulting difference between input and output prices, which in economic theory constitutes the >value added= of economic activities, is termed >gross profits= for the purposes of this paper. Gross profits as a percentage of input costs are used as indicator for >profitability=. In order to arrive at >net-profits=, manufacturers/traffickers would have still to deduct labour costs, rent, depreciation for equipment, bribery costs, legal costs etc. These additional costs, however, are not likely to differ substantially for different illegal substances. Thus the profitability ranking should not change even if these additional costs were taken into account. Retail prices are used as main indicators for economic incentives on the demand side. Low and falling retail prices and, even more important, a relatively low price as compared to other drugs with similar pharmacological properties are a major economic incentive for consumers to choose a specific drug.

Table 8: Working concepts to establish profitability and opportunity costs	
i) <u>Supply side:</u>	
Economic incentives for manufacturers and traffickers:	<i>high profits</i>
Concept to make profits comparable: In finance/accounting defined as:	$\frac{\textit{profitability}}{(\textit{profits}) \textit{ equity}} * 100$
<u>Proxies</u> used for clandestine drug markets:	$(\textit{gross profits}) \textit{ input costs} * 100$
- at the <u>manufacturing</u> level:	$\frac{\textit{gross manufacturing profit margins (average wholesale prices less average costs of precursors)}}{\textit{average costs of precursors}} * 100$
- at the <u>trafficking</u> level:	$\frac{\textit{gross domestic trafficking profit margins (average retail prices less average wholesale prices)}}{\textit{average wholesale prices}} * 100$
ii) <u>Demand side:</u>	
Economic incentives for consumers:	<i>low opportunity costs</i>
<u>Parameter</u> used for clandestine drug markets:	<i>retail prices</i>
-	<i>development of retail prices of ATS over a period of time (time series data)</i>
-	<i>comparison of retail prices of ATS with those of other drugs</i>

Based on the concept of >value added= or >gross profits=, some general observations can be made at the very outset. ATS are typically manufactured in the country of final consumption; this point is crucial, for it suggests that in the country where the drug is consumed, the overall >value-added= for ATS will be higher than for illicit plant-based drugs. Since the total >value added= in consumer countries includes internal trafficking and manufacturing profits, the overall

profitability of ATS is higher than that of imported plant-based drugs. For cocaine, for example, only minor manufacturing processes such as converting cocaine hydrochloride into crack cocaine take place in the country of final consumption. Heroin is normally manufactured in a country close to the cultivation of opium poppy. Thus, virtually no manufacturing profits are made in the industrialized countries.

Previous economic studies of plant-based drugs have shown that half to about two thirds of the final retail price represents the >value-added< (most of which is a risk premium) generated in the country of final consumption [UNDCP, 1995c]. In the case of ATS, almost all of the total retail price remains as >value added< in the country of final consumption. The point is crucial since **profitability** of ATS is particularly high **at the manufacturing level**. This is true for methcathinone, methamphetamine and even more so for the more knowledge-intensive ring-substituted amphetamines such as MDMA. Table 9 compares gross profit margins for the most popular stimulants on the illicit market in the United States and illustrates the enormous profit potential of clandestine drug synthesis. It shows that gross profit margins for all ATS are significantly higher than for crack cocaine⁸.

Table 9: Manufacturing level: gross profit comparisons in USA, based on 1991-1994 averages					
		MDMA	METH-AMPHETAMINE	METH-CATHINONE	CRACK COCAINE
Raw material costs (in USA) for 1 g		\$0.3 ^{a/} - \$0.6 ^{a/}	\$0.3 ^{a/} - \$2.0 ^{b/}	\$0.3 ^{a/} - \$2.0 ^{b/}	\$15 ^{c/}
Wholesale price for 1 g (street purity) ^{d/}		\$60 - \$100	\$10.2 - \$50.6	\$25 - \$40	\$10.8 - \$40.5
GROSS PROFITS AT MANU- FACTURING LEVEL	Per kg	\$59,000 - \$99,000	\$8,000 - \$50,000	\$23,000 - \$39,700	up to \$26,000
	Average per kg	\$79,000	\$30,000	\$31,000	\$13,000
	In % of expenditure for raw material	9,900% - 33,200%	400% - 17,000%	1,100% - 13,000%	up to 180%
	Average profitability	17,800%	2,600%	2,700%	90%
<p>a/ Prices, assuming access to precursors from licit sources. DEA reports for 1995 show that prices for illicit ephedrine have gone up sharply, to \$2.3-\$5 per gram. Licit ephedrine was available at around \$0.15 per gram in the 1991-1994 period. Overall input prices for methamphetamine/ methcathinone may have thus increased to \$2.6-\$5.6 per gram in 1995. Even at this price level, manufacturing costs for methamphetamine/methcathinone are significantly lower than those for crack cocaine.</p> <p>b/ Price based on (licit) ephedrine tablets.</p> <p>c/ Initial purchases of some US\$ 15,000 worth of cocaine HCl are needed for conversion into 1 kg of crack cocaine.</p> <p>d/ Prices for MDMA are for 1994 only.</p> <p>Sources: UNDCP, ARQ Data; Merck and various other chemical catalogues; Andrews, K.M. (1995), 'Ephedra's role as a precursor in the clandestine manufacture of methamphetamine', <i>Journal of Forensic Sciences</i>, 40 (4), pp.551-560; DEA (1994), <i>Illegal Drug Price/Purity Report</i>, January 1991-June 1994; Shulgin A. and Shulgin A. (1992), <i>Pihkal - A Chemical Love Story</i>, Transform Press, Berkeley.</p>					

⁸ The table does not include manufacturing profits to be made from processing of coca leaf into coca base and cocaine hydrochloride. These profits, however, amount to less than US\$ 1,000 per kg of cocaine hydrochloride [Antezana, 1996].

Table 9 assumes a 50% conversion rate in transforming ephedrine, the principal and most expensive component, into methamphetamine. There is evidence, however, that actual yields in illicit synthesis may be considerably greater (up to 80%), which would make input prices per unit produced even lower. But there is also evidence that prices for ephedrine, if purchased in clandestine markets, have increased significantly, by factors ranging from 10 to 15, as a result of enforcement efforts in the present decade. The net effect for methamphetamine manufacturers who have no access to cheap ephedrine from legitimate sources could be manufacturing costs three times higher than stated in Table 9. Even at these higher costs, however, the manufacture of methamphetamine remains more profitable than the manufacture of crack cocaine.

In contrast to unequivocally higher profits at the manufacturing level, the situation is, at first sight, less clear-cut at the **distribution level**. A comparison of retail and wholesale prices in the United States suggests that gross domestic trafficking profits per kilogram methamphetamine (at street purity) are about the same as for cocaine, although less than for heroin. Gross domestic trafficking profitability= (gross profit margins expressed as a percentage of wholesale prices) of methamphetamine is less than for cocaine, but higher than for heroin (see Table 10).

Table 10: Trafficking level: gross profit comparisons in USA, based on 1991-1994 averages						
		MDMA	METH- AMPHETAMINE	METH- CATHINONE	COCAINE	HEROIN
Whole-sale price for 1 g (street purity) ^{a/}		\$60 - \$100	\$10.2 - \$50.6	\$25 - \$40	\$10.8 - \$40.5	\$50 - \$250
Retail price for 1 g (street purity) ^{a/}		\$80 - \$250	\$42.5 - \$162.5	\$75 - \$120	\$21.3 - \$181.3	\$65 - \$540
Average purity at wholesale level		n.a.	92%	n.a.	84%	82%
Average purity at retail level		n.a.	53%	n.a.	63%	45%
GROSS PROFITS AT (DOMESTIC) TRAFFICKING LEVEL unadjusted for changes in purities	Average per kg (street purity)	\$85,000	\$72,100	\$65,000	\$75,600	\$148,800
	Average in % of wholesale prices	100%	240%	200%	300%	100%
adjusted for change in purities	Average per kg pure substance	n.a.	\$160,400	n.a.	\$130,100	\$483,000
	Average in % of wholesale prices (pure)	n.a.	485%	n.a.	430%	260%
^{a/} Prices for MDMA are for 1994 only. Sources: UNDCP, ARQ Data; DEA (1994), <i>Illegal Drug Price/Purity Report</i> , January 1991-June 1994; DEA, Official Communication, 7 November 1995.						

However, if variations in purity between the wholesale and retail level are included in the calculations (purities for methamphetamine decline from more than 90% to about 50% between the wholesale and retail levels), the analysis suggests that trafficking in methamphetamine is more profitable than trafficking in either cocaine or heroin (see Table 10 and Figure 75, which draws

out trafficking profit margins for pure substances in percentages of wholesale prices). Trafficking profitability actually doubles once changes in purities are taken into account. Average gross profits⁹ of pure methamphetamine amounted to \$160,000 per kilogram, or 485% of wholesale prices, and are thus higher than the comparable ratios for cocaine (430%) or heroin (260%) (see [Figures 74 and 75](#)).

Trafficking profit margins for α -ice (smokable methamphetamine hydrochloride) are still higher. Even though there are hardly any additional trafficking profits made through adulteration - the purity of α -ice samples ranges from 90% to almost 100% - the average gross profit of trafficking α -ice amounted to \$340,000 per kilogram in 1994, twice the profits for normal methamphetamine, or 550% of the wholesale price [NNICC, 1995]. These high profits are mainly a consequence of high retail prices, \$300-\$500 per gram, i.e. some three to five times greater than the price of ordinary methamphetamine.

United States of America

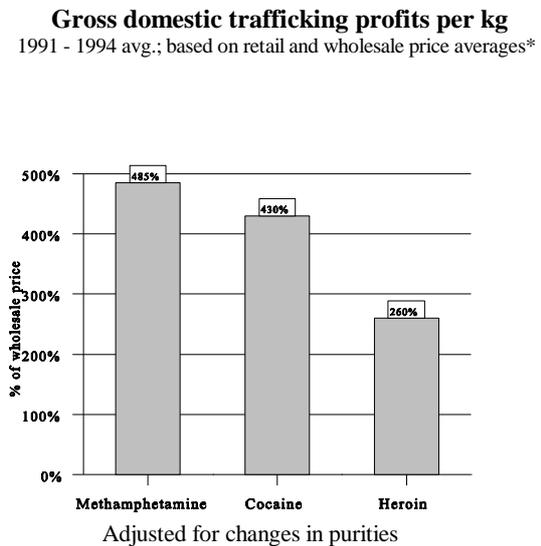
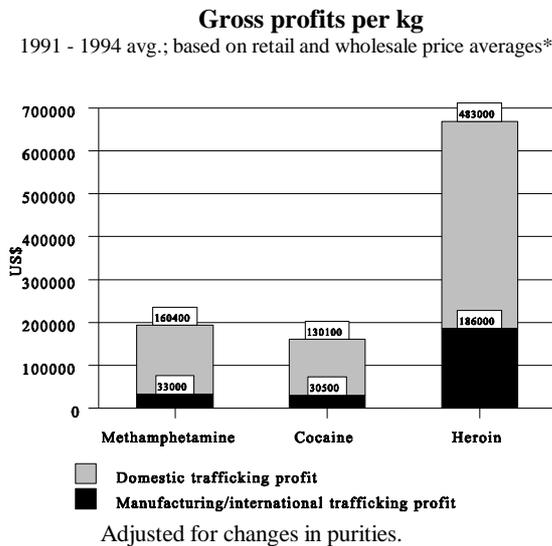


Figure 74

Sources: UNDCP ARQ Data; DEA, *Illegal Drug Price/Purity Report*; Communication by DEA, 7 November 1995.

Figure 75

[Table 11](#) combines the **manufacture and trafficking levels**. Given higher gross profit margins at both levels, it shows that profitability for ATS is higher than for heroin or cocaine in

⁹ It should be noted that in all figures on gross profits per kilogram, the category α manufacturing/international trafficking profit= does not include international trafficking profits for ATS since they are usually manufactured domestically.

the United States. Highest within the ATS category is profitability for MDMA, and the highest profit per kilogram is for methamphetamine. These high profits, in combination with widely diffused manufacturing know-how, suggest that the methamphetamine problem is likely to grow further.

		MDMA	METH-AMPHETAMINE	METH-CATHINONE	CRACK COCAINE	HEROIN
Manufacturing profits	per kg	\$79,000	\$30,000	\$31,000	\$13,000	- ^{a/}
Average trafficking profits	per kg (street purity)	\$85,000	\$72,000	\$65,000	\$76,000 ^{b/}	\$149,000
TOTAL GROSS PROFITS (unadjusted for change in purity)	per kg (street purity)	\$164,000	\$102,000	\$96,000	\$89,000	\$149,000
Average additional trafficking profits due to changes in purities	per kg (pure substance)	n.a.	\$88,000	n.a.	\$54,000	\$334,000
TOTAL GROSS PROFITS (adjusted for change in purity)	Average per kg (pure substance)	(\$164,000)	\$190,000	(\$96,000)	\$143,000	\$483,000
OVERALL GROSS PROFITABILITY	Average total gross profits in % of prices of raw materials acquired in USA	36,000%	16,500%	8,300%	950%	(260%)^{c/}

a/ Heroin is generally not manufactured in the USA.
b/ Figure for cocaine.
c/ Gross profits per kilogram in percent of wholesale prices (pure substance)

Sources: UNDCP, ARQ Data; Merck and various other chemical catalogues; Andrews, K.M. (1995), *Amphetamine's role as a precursor in the clandestine manufacture of methamphetamine*, *Journal of Forensic Sciences*, 40 (4), pp.551-560; DEA (1994), *Illegal Drug Price/Purity Report*, January 1991-June 1994; DEA (1995), Official Communication, 7 November 1995; Shulgin A. and Shulgin A. (1992), *Pihkal - A Chemical Love Story*, Transform Press, Berkeley.

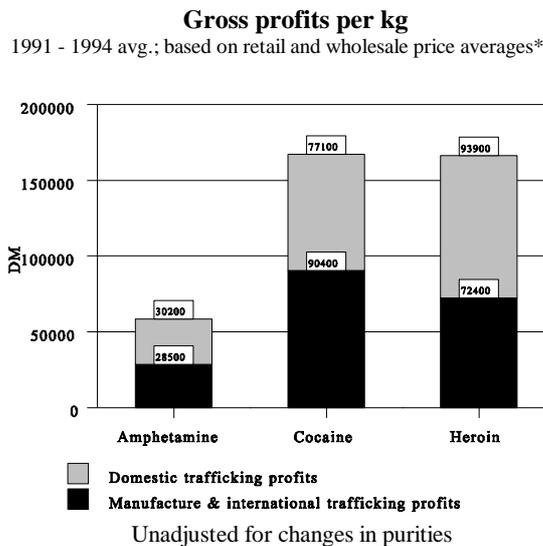
An additional factor contributes to financial attractiveness. The organization of manufacturing and trafficking of ATS tends to be less hierarchical than, for instance, in the cocaine trade. There are fewer stages within the overall chain of distribution. For a given turnover, average gross profits for a methamphetamine trafficker are thus higher than for a cocaine trafficker. The incentives and the potential for expansion of this trade are therefore significant, even more so as the risks involved are not higher than those associated with cocaine trafficking.

When similar analyses are done for other countries, they confirm the high profitability of manufacturing and trafficking ATS. At the same time, they show that the markets for illicit drugs, including ATS, differ considerably from region to region and even from country to country. The following discussion of individual country results starts with a few main trafficking and consumer countries in Europe and will be followed by an analysis of selected countries in the Far East.

A striking feature of the illicit **European drug markets** is the comparatively high street prices for cocaine per unit, which make ATS, at least in relative terms, more attractive for

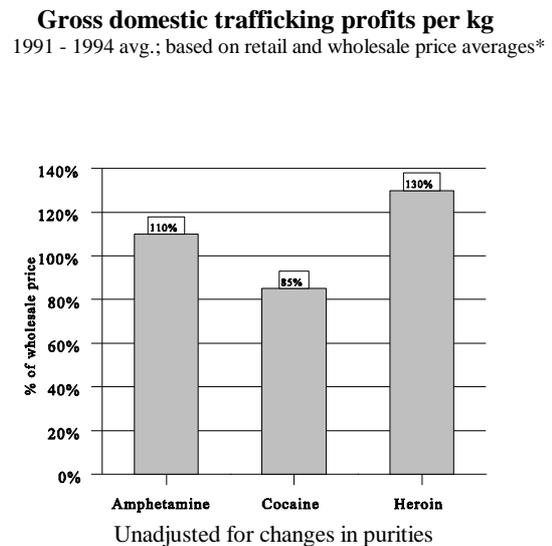
consumers than in North America. **Germany** is a good example. Both heroin and cocaine are on average some three times more expensive per gram for amphetamine (measured at prevailing street purities). The other side of the coin is that gross trafficking profits per given unit weight are greater for both heroin and cocaine (see [Figure 76](#)). Gross profitability for amphetamine trafficking over the 1991-1994 period has been about the same as for heroin and cocaine (see [Figure 77](#)).

Germany



Source: UNDCP ARQ Data

Figure 76



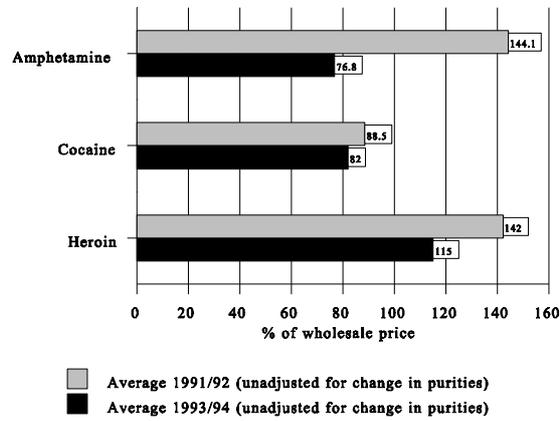
Source: UNDCP ARQ Data

Figure 77

A comparison of 1993/1994 with 1991/1992 averages suggests that gross profitability of amphetamine trafficking is growing. With retail prices for amphetamine relatively stable in Germany and wholesale prices falling (probably a reflection of less expensive but fast-growing imports from eastern Europe), gross trafficking profit margins for amphetamine are clearly rising, and so are the economic incentives for further expansion. By 1993/1994 gross profitability of trafficking in amphetamine was already higher than that of cocaine or heroin (see [Figure 78](#)).

Germany

Gross domestic trafficking profit margins 1991/92 avg. compared to 1993/94 avg.



Source: UNDCP ARQ Data.

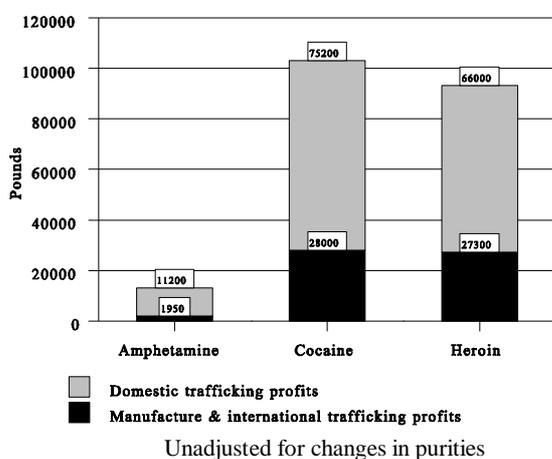
Figure 78

Changes in purities between the wholesale and the retail level have not been considered so far. In the case of the United States it was shown (see [Table 10](#)) that such changes increase profitability for ATS more than for other drugs. The German market is unlikely to be an exception in this respect. With average purities of amphetamine having fallen, from 40%-60% in 1990 (ARQ data) to 5%-30% by 1994 [UNDCP/EGM, 1996], probably a reflection of expanding recreational use, and average cocaine purities having remained relatively high (60% in 1994), one can expect that the profitability for trafficking amphetamine is higher than that for cocaine.

The market structure in the **United Kingdom** differs substantially from that in the United States and only somewhat from that in Germany (compare [Figure 79](#) with [Figures 74 and 76](#)). While in the United States retail prices of methamphetamine are at par with retail prices of cocaine, retail prices of one gram of cocaine in the United Kingdom have been about eight times higher than prices of amphetamine. Even though some of this considerable price difference may be attributable to low amphetamine purities in the retail market, fluctuating at around 5% [FSS, 1990-1995], the price of amphetamine compared to cocaine remains low. Indeed the price structure may be one important factor explaining the greater popularity of amphetamine in the United Kingdom (see also Chapter XI).

United Kingdom

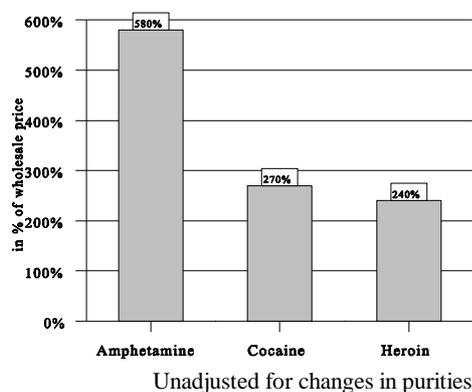
Gross profits per kg
1991 - 1993 avg.; based on retail and wholesale price averages*



Source: UNDCP ARQ

Figure 79

Gross domestic trafficking profits per kg
1991 - 1993 avg.; based on retail and wholesale price averages*



Source: UNDCP ARQ Data.

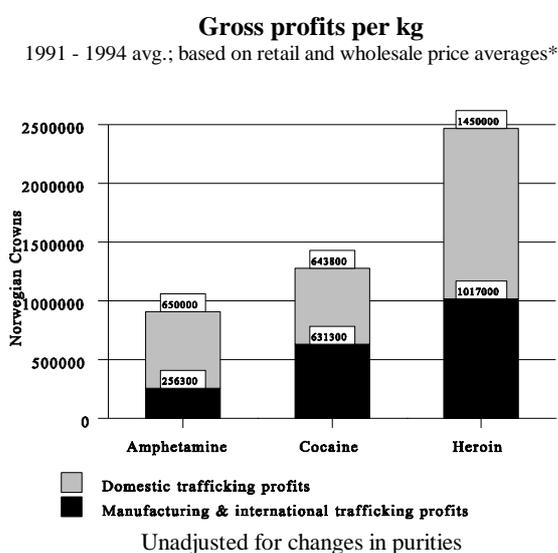
Figure 80

In terms of trafficking profitability, [Figure 80](#) shows that amphetamine fares significantly better than heroin or cocaine. The reason for the high gross profit margins for amphetamine are not high retail prices but rather low wholesale prices, indicating significant domestic manufacture and/or large-scale imports. While wholesale amphetamine prices in Germany, for instance, amounted to some \$17,000 per kilogram over the 1991-1994 period, prices in the United Kingdom fluctuated around \$3,000 per kilogram. Price differences were less pronounced at the retail level, particularly when taking the lower purities in the United Kingdom into account. In recent years, amphetamine was traded in the United Kingdom at \$15-\$20 per gram, in Germany at around \$35 per gram, and methamphetamine was traded in the United States at around \$100 per gram.

One characteristic of the amphetamine market observed in the United Kingdom and in other countries is the stable nature of unit-weight prices at street purity over time. De-facto price changes, reflecting changes in the market structure (such as enforcement success, new manufacturers, shifting consumer preferences), are effected through changes in purity levels rather than changes in unit-weight prices. This means that stable unit-weight prices of amphetamine can go hand in hand with strongly fluctuating pure amphetamine=prices. Between 1985 and 1990, reported purities fell from a range of 18%-29% to 3%-8%. Thereafter, average purities started to increase again but have remained below the above-mentioned upper limit of 8% [FSS, 1990-1995]. Even though international comparisons are partially distorted due to different concepts used to define the retail level, United Kingdom purity levels nevertheless appear to be on the low side. This suggests the existence of a large market for recreational users.

Analysis of the situation in **Norway** shows that gross profit margins for amphetamine as a percentage of wholesale prices are greater than for heroin or cocaine (see [Figure 81](#) and [82](#)). As in Germany, the gross profitability of amphetamine has been rising in Norway since 1992.

Norway



Source: UNDCP ARQ

Figure 81

Source: UNDCP ARQ Data.

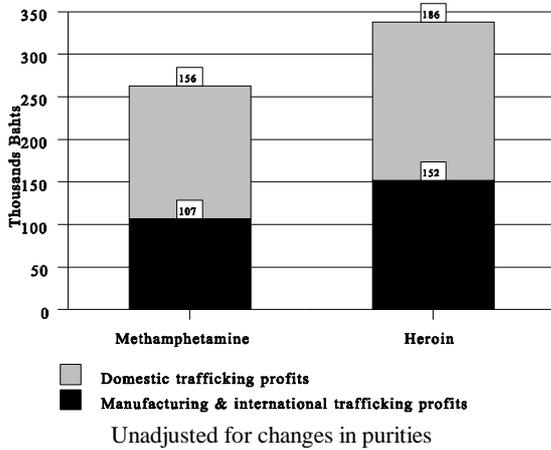
Figure 82

As with other countries in Europe, available purity data for Norway do not distinguish explicitly between the retail and the wholesale levels and thus do not allow for any further analysis of overall gross profitability. The overall range of purities was between 30% and 70%, which is, however, sufficient to conclude that average purity of amphetamine in Norway is much higher than in the United Kingdom and similar to the United States. High purity levels are also reported from other **Nordic countries** and Poland (95%). Purities in Finland are reported to be in the 20%-60% range. Purities of amphetamine in Denmark are at around 80% at the wholesale level and around 25% at the retail level (1993). Such high purity levels in the **Nordic countries** could represent a more serious public health concern [Rajs and Fugelstad, 1994; Olsson et al., 1994; Eriksson and Zetterström, 1994] than the typical recreational use of ATS [Measham et al., 1994; Pickering and Stimson, 1994; Saunders, 1994]. There is, however, some concern, for instance in the United Kingdom [Wright and Pearl, 1995], that recreational use may continue to grow and current recreational users might eventually become hard-core abusers.

The situation in the Far East is similar to Europe and North America with regard to the higher profitability of methamphetamine trafficking than of trafficking in other drugs. Figures 83 and 84 illustrate this for **Thailand**, which in recent years has reported the most methamphetamine seizures in the region.

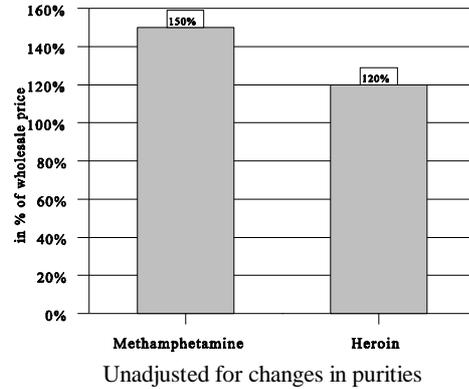
Thailand

Gross profits per kg
1991 - 1992 avg.; based on retail and wholesale price averages*



Source: UNDCP ARQ
Figure 83

Gross domestic trafficking profits per kg
1991 - 1992 avg.; based on retail and wholesale price averages*

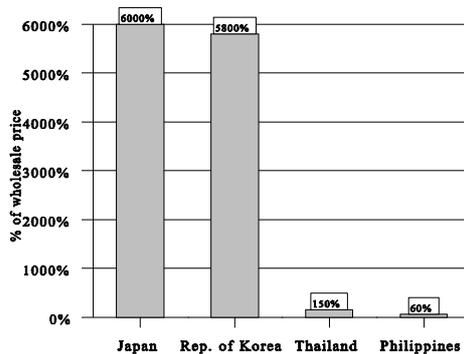


Source: UNDCP ARQ Data.
Figure 84

Gross trafficking profit margins among countries in the Far East, differ much more than among countries in Europe or North America. Gross profit margins for methamphetamine are currently extremely high in **Japan** and in the **Republic of Korea** while in **Thailand** and the **Philippines** they are at about the same level as in Europe or North America (see [Figure 85](#)). The high gross profit margins in Japan and the Republic of Korea may, in part, be explained by

Far East

Gross domestic trafficking profits per kg
1991 - 1994 avg.; based on retail and wholesale price averages*



* UN adjusted for changes in purities.
Source: UNDCP ARQ Data.

Figure 85

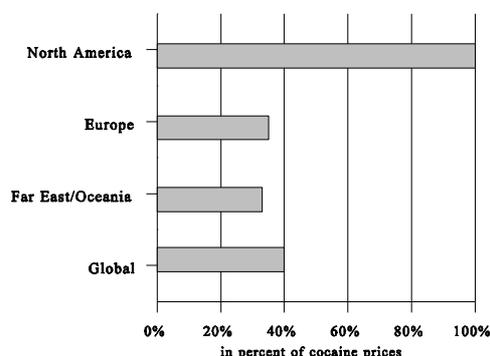
successful enforcement efforts, which have substantially increased the retail prices for these substances. Wholesale prices did not increase proportionately to retail prices, suggesting that enforcement efforts at the manufacturing level were apparently less successful than at the trafficking level. Another interesting feature of markets in Asia, which may have to do with the consumption of *ice*, is the very high purities (more than 95% in Japan; 90% and more in the Republic of Korea; some 75% in the Philippines).

The focus of the analysis, thus far, has been on the economic incentives on the supply side, which may fuel expansion of manufacture/trafficking and may eventually prompt consumption increases (supply push). There are, however, **economic incentives on the demand side** as well. Within limits, drug consumers, like consumers of any other commodity, can be expected to choose among a variety of substances which are able to satisfy their needs and wants. Among a number of parameters influencing the final decision, such as availability, image of a certain drug, pharmacological properties and side-effects (see Chapter XII), economic considerations play a role as well. Economic incentives on the demand side become particularly relevant when there is an alternative substance available which provides a consumer with similar pharmacological effects at lower prices (demand pull). Thus cross-price elasticities among substances with similar pharmacological properties, such as among the various ATS and between ATS and cocaine, can be expected to be high. Studies in the United Kingdom have confirmed the readiness of consumers to switch between ATS and cocaine once relative prices change [Klee, 1992].

A **review of prices** (1993/1994) confirms that ATS are cheaper than cocaine in most countries. This suggests that there are indeed strong economic incentives for consumers to switch to and/or stay with ATS. Amphetamine/methamphetamine prices per gram, on average, amount to just about 40% of cocaine prices. This ratio has not, however, been adjusted for differences in street level purities. The incorporation of purities in the calculations might shift the global amphetamine/methamphetamine average closer to cocaine prices, but it is unlikely that they would exceed the prices of cocaine.¹⁰ Figure 86 gives a breakdown of major ATS markets: in Europe, the Far East and Oceania, amphetamine/methamphetamine retail prices are even lower than the global average of 40% of cocaine prices; in the United States and Canada they are about the same as cocaine prices and thus less competitive, but changes are under way, as will be shown later.

¹⁰ Identical amounts of cocaine and ATS would provide more dosages of ATS than cocaine; the price of ATS per *hit* or *high* is thus lower than that of cocaine (see Table 5 in Chapter IX above).

Amphetamine/methamphetamine retail prices
as a percentage of cocaine retail prices; 1993/94



Note: All prices are unadjusted for differences in purities.

Sources: UNDCP ARQ Data; WCO; DEA; NCIS; Price Project Report (Internet).

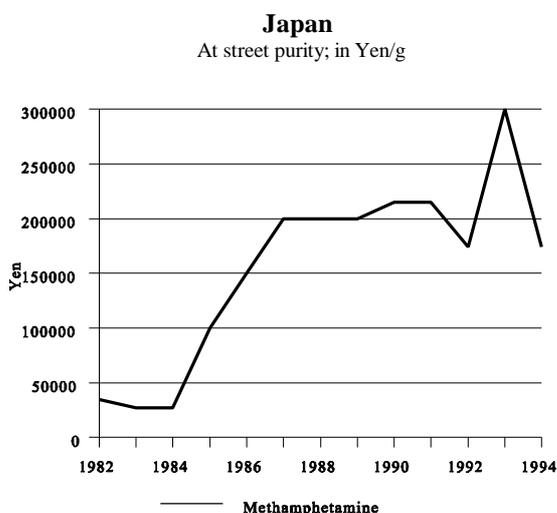
Figure 86

An analysis of relative prices would show that where amphetamine/methamphetamine are cheaper than cocaine, they are also trafficked and consumed to a greater extent than cocaine. Geographical proximity to areas of manufacture is a significant factor in explaining price differences. Methamphetamine/amphetamine prices that are less than 30% of prevailing cocaine prices have been reported from Hong Kong, Australia, the Netherlands, the United Kingdom, Ireland, Belgium and Hungary.

A related issue with implications for the economic attractiveness of ATS to consumers is the **development of retail prices over time**. UNDCP data suggest that on the whole amphetamine and methamphetamine retail prices, in nominal terms, remained relatively stable over the last decade. However, results still vary from region to region and, within regions, from country to country.

Price developments in the Far East region have been particularly interesting. After having increased strongly in the early 1980s, methamphetamine retail prices (in nominal terms) in Japan remained relatively stable in the late 1980s and in the 1990s, except for one year (see [Figure 87](#)). Rising prices in the 1980s and the subsequent maintenance of a very high price level helped to break the strong upward trend in abuse that was registered until the mid-1980s. Methamphetamine prices have risen particularly strongly in recent years in the Republic of Korea (see [Figure 88](#)), largely a consequence of successful enforcement efforts. Parallel with very high prices, methamphetamine abuse is reported to have declined significantly from the levels of the late 1980s. In the Philippines and Thailand, retail prices expressed in local currencies increased slightly (see [Figures 89 and 90](#)); these increases, however, do not yet appear to have had a major impact on consumer behaviour.

Far East: Average retail prices



Source: UNDCP ARQ Data; WCO; ESCAP Region Monthly Bulletin, Nov. 1994 and April 1996

Figure 87



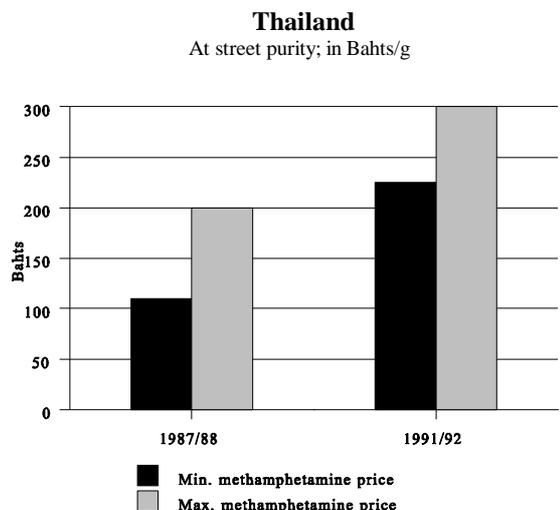
Sources: UNDCP ARQ Data; MHQ (1996), Overview of Narcotic and Stimulants Admn.

Figure 88



Source: UNDCP ARQ Data.

Figure 89



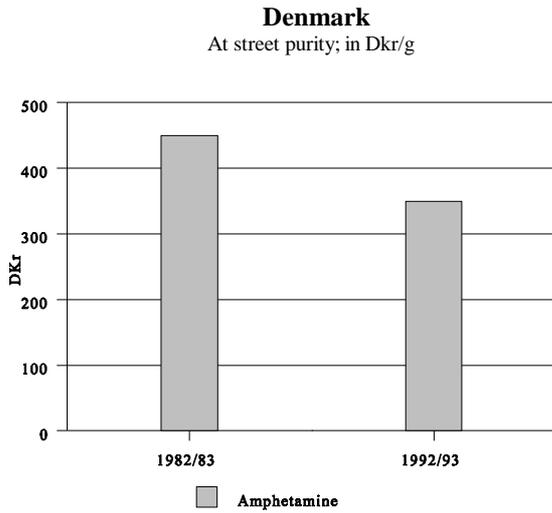
Source: UNDCP ARQ Data.

Figure 90

Most **European countries** reported either a stable development or moderate ATS price declines in recent years. Such trends have also been noted in a recent report [Pompidou Group of the Council of Europe, 1995a]. The Nordic countries were particularly affected by falling prices (see [Figures 91 and 92](#)), though they remained largely stable in Sweden. Stable to slightly falling prices were also reported from Europe's largest illicit amphetamine markets, the United

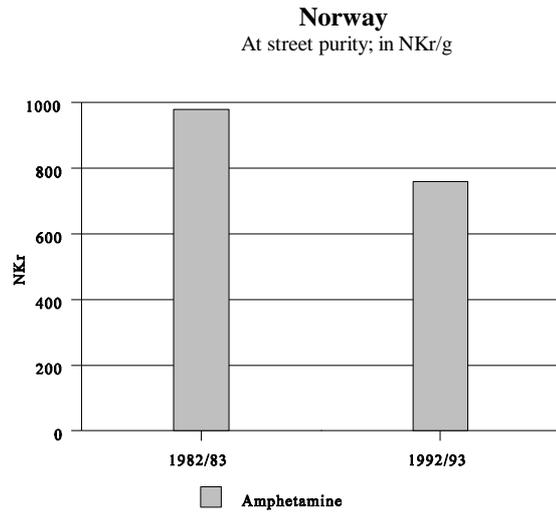
Kingdom and Germany (see Figures 93 and 94). Data for the Netherlands, one of Europe's main producers of ATS, suggest that prices remained stable at a comparatively low level. As in the Far East, European retail price data indicate that there are significant economic reasons for consumers to choose ATS rather than the more expensive cocaine.

Europe: Average retail prices



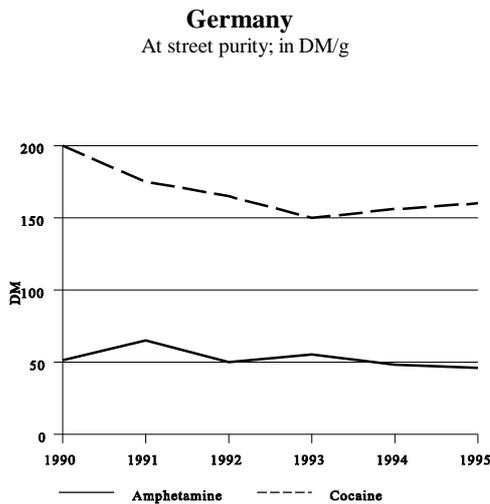
Source: UNDCP ARQ Data.

Figure 91



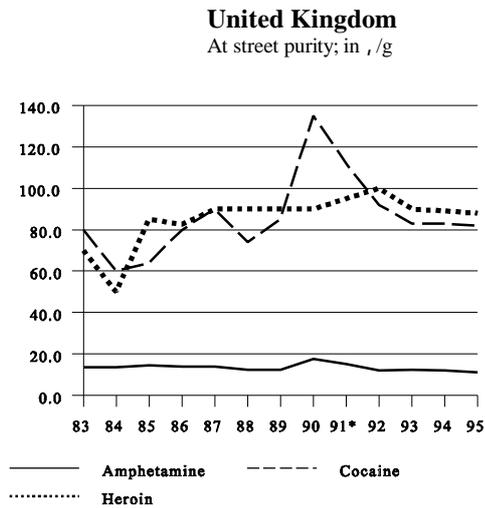
Source: UNDCP ARQ Data.

Figure 92



Source: UNDCP ARQ Data; BKA

Figure 93



Source: UNDCP ARQ Data; National Criminal Intelligence service, Nexus, Jan. 1996.

Figure 94

Data for the **United States**, at first sight give a less clear picture of incentives favouring ATS. In contrast to Europe or the Far East, prices per unit weight, at street purities, in the United States have been at about the same level as cocaine prices over the last decade. Methamphetamine prices have risen slightly in nominal terms (see [Figure 95](#)); in real terms, they have stagnated. The picture changes when pure substance prices are considered. Until the early 1990s, methamphetamine was significantly more expensive than cocaine; since then, however, rapidly increasing purity levels have led to strong de-facto price declines for methamphetamine. By 1994, methamphetamine appears to have become cheaper than cocaine (see [Figure 96](#)). Economic incentives for abusers have thus started to shift from cocaine to methamphetamine.

USA: Average retail prices

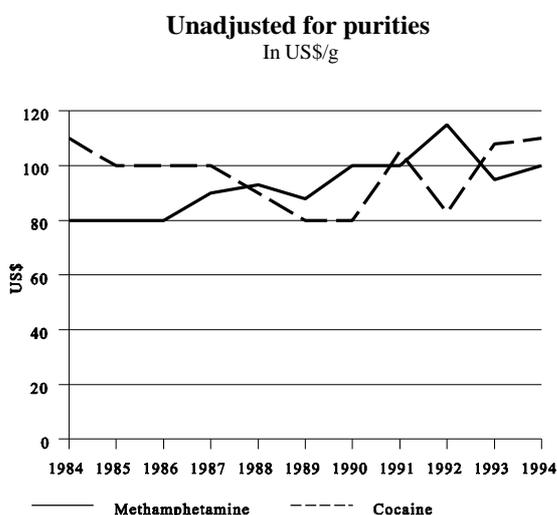


Figure 95

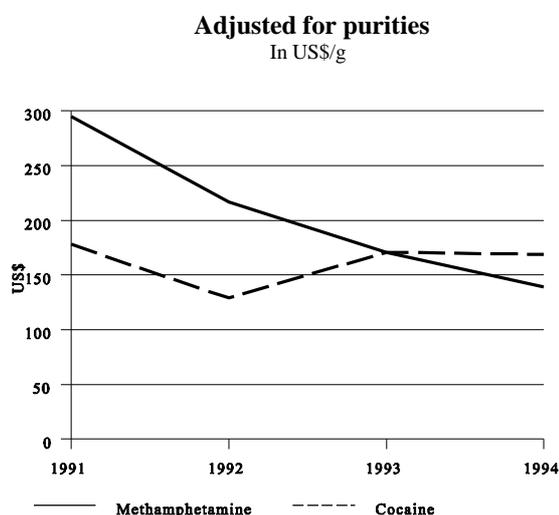


Figure 96

Sources: UNDCP ARQ Data; DEA (1994), *Illegal Drug Price/Purity Report*; DEA (1987), *The Illicit Drug Situation in the United States and Canada, 1984-1986 - Special Report*; DEA (1995), *Quarterly Intelligence Trends*, 12, (2).

Though all quantitative data describing illicit markets, as noted at the beginning of Part two are subject to wide margins of error, the foregoing analysis, from both a supply-side and a demand-side perspective, seems to provide sufficient evidence to conclude that economic incentives for a further expansion of manufacturing, trafficking and consumption of ATS are considerable. Clandestine manufacture and trafficking of ATS are financially highly lucrative activities, at least as profitable as for cocaine or heroin, and - depending on the profitability measures used - even more profitable in a number of cases. At the same time, the economic disincentives, or risks, associated with manufacturing and trafficking ATS tend to be lower than those associated with heroin or cocaine. Given the frequent manufacture of ATS in the country of final consumption, the chance of detection while crossing international borders is obviously less than for heroin or cocaine.

On the demand side, relatively low retail prices in most countries, as compared to other drugs, are an economic incentive for consumers to turn to ATS. The example of the United States has shown, moreover, that prices, although stable in terms of unit-weights, may be dropping if purities are taken into consideration, which may help explain the increasing attraction of these substances. Even as pure substance= retail prices are falling and input prices (for example, ephedrine) are rising, the economic incentives for expansion remain strong.

Given such strong economic incentives, it seems to be only a matter of time until more clandestine manufacturers and traffickers are tempted to enter and exploit this lucrative market. Although this might lead to a further decline in retail prices and thus in profit margins, the market as a whole can be expected to expand, driven both by new consumers attracted to lower prices and by the multitude of easily available precursors. This scenario could, however, be prevented if international efforts to strengthen the control system, particularly on precursors, would lead - as economic theory predicts - to further increases in retail prices without increasing profit margins, thereby limiting the economic incentives for future expansion.

XI. Extent of abuse of ATS

The abuse of ATS has emerged as a global problem in recent years, though given high levels of cocaine or heroin abuse, it may not always be perceived as such in many countries. The traditional consumption of natural-plant-based stimulants appears to have facilitated the spread of synthetic ATS. The use of substances such as coffee or tea as stimulants is not only accepted but is highly valued in most societies. A number of rituals and ceremonies have been built around their consumption, underlining a widespread demand for substances with stimulant properties. Similarly, in a number of countries, other plant-based stimulants have been consumed for centuries, thus becoming integral parts of the local culture: coca leaves in the Andean countries, khat in east Africa/southern Arabia and betel nuts in Asia. With the isolation of the cocaine alkaloid from coca leaves in the second half of the nineteenth century and the emergence of synthetic ATS at the beginning of this century, new groups of more potent stimulants appeared. The synthetic stimulants carried the image of being both modern and relatively safe. Some of their pharmacological properties, such as enhancing performance, endurance and self-confidence and inducing anorectic or entactogenic effects, contributed to their increasing popularity. Virtually in tandem with legitimate medical use, the abuse of these potent new stimulants began to appear in a few countries of North America, Europe and the Far East, gradually spreading to neighbouring countries in the respective regions as well as to other regions. By the mid-1990s, abuse of ATS has become a global phenomenon. There is a considerable body of both qualitative and quantitative evidence which clearly points in this direction. This chapter will draw together some of this evidence and analyze patterns and trends of abuse; Chapter XII will discuss the health and social impacts of consumption.

Though there is much evidence of ATS abuse from several countries, it is difficult to aggregate these data and establish the precise **extent of abuse at the global level**. This is due to a general lack of uniform, and thus cross-nationally comparable, data. Only a limited number of countries have conducted epidemiological studies that are representative of the nation as a whole. Most studies are confined to specific risk groups in specific locations. Some countries report lifetime prevalence, others annual and monthly prevalence data. Age groups of population segments investigated differ from country to country. Some countries only report the number of people found in official drug registers, while many other countries do not have such registers. Some of these shortcomings can be overcome by using non-traditional approaches for aggregating data and building qualitative information into estimating techniques. Where this is not possible, general trends are extrapolated from selected countries that have sound epidemiological data.

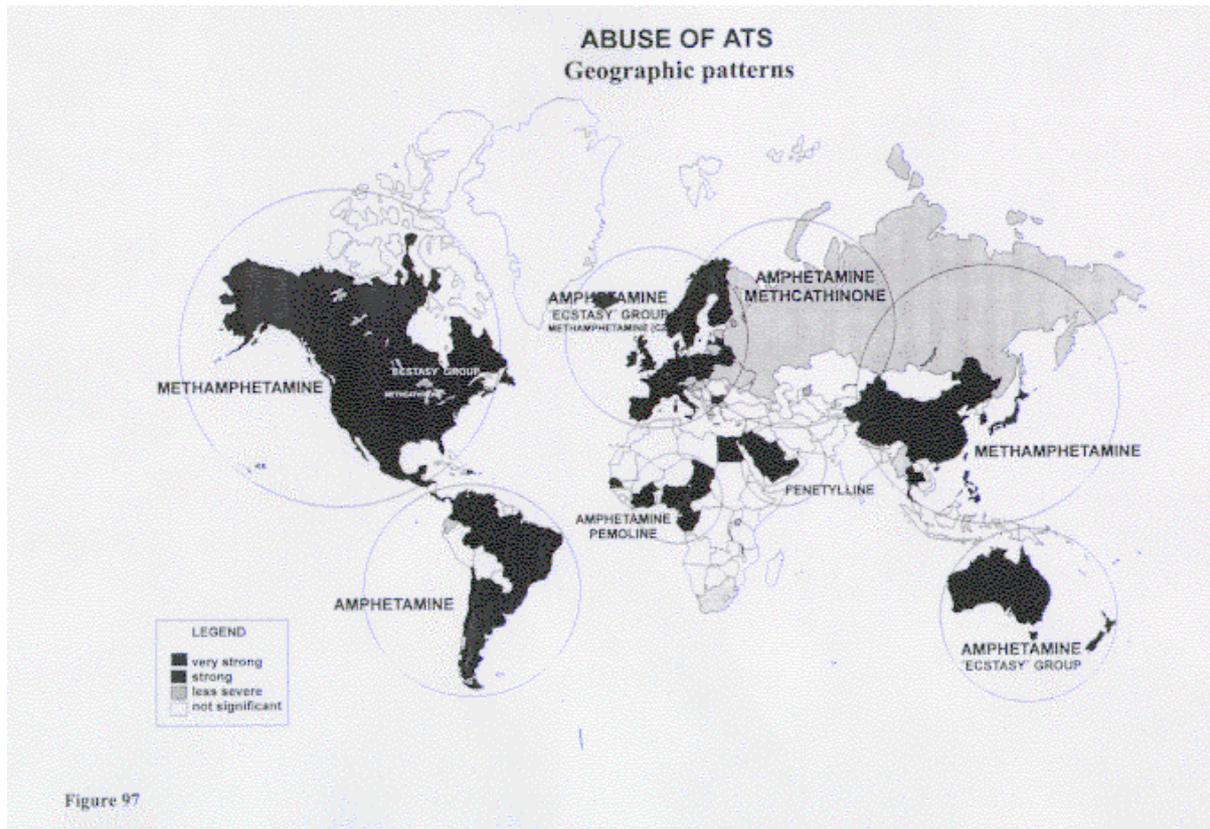
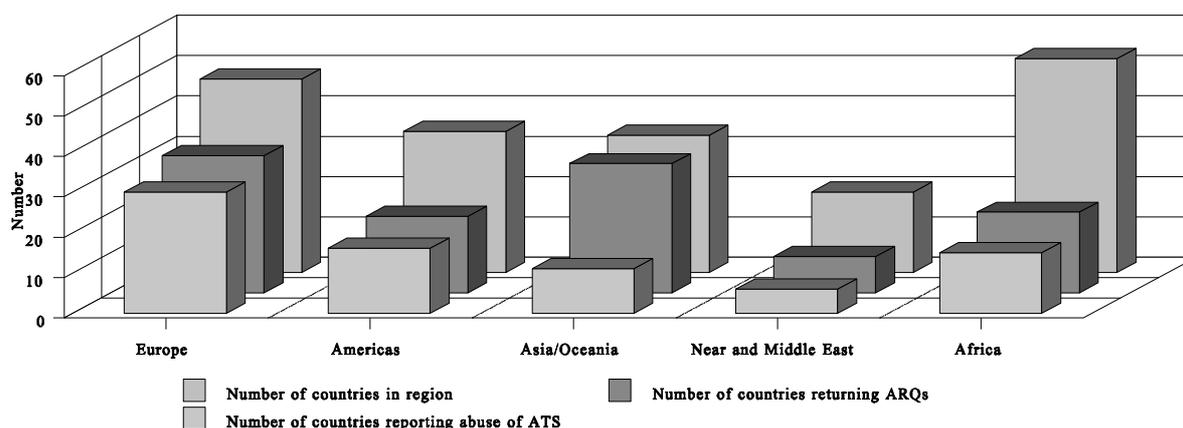


Figure 97 shows the **geographic spread** and differentiates between the specific substances. The figure substantiates the assertion that ATS abuse is now a global problem even though distinct regional abuse patterns continue to exist. UNDCP country profiles, based on annual report questionnaire (ARQ) data, provide further substantiation. Of the 111 countries for which detailed information is available, 71% reported abuse of ATS over the 1989-1994 period. Comparable proportions for cocaine and the opiates were 77% and 95%, respectively. Although these data are limited by the fact that they contain no measures of salience, it is still worthwhile to consider them in a regional context. The largest number of countries reporting ATS abuse are in Europe, followed by the Americans (see Figure 98). Another general measure of magnitude is that 29 out of 111 countries report the ATS to be among the three most frequently abused drugs.

Number of countries reporting ATS abuse



1989-1994

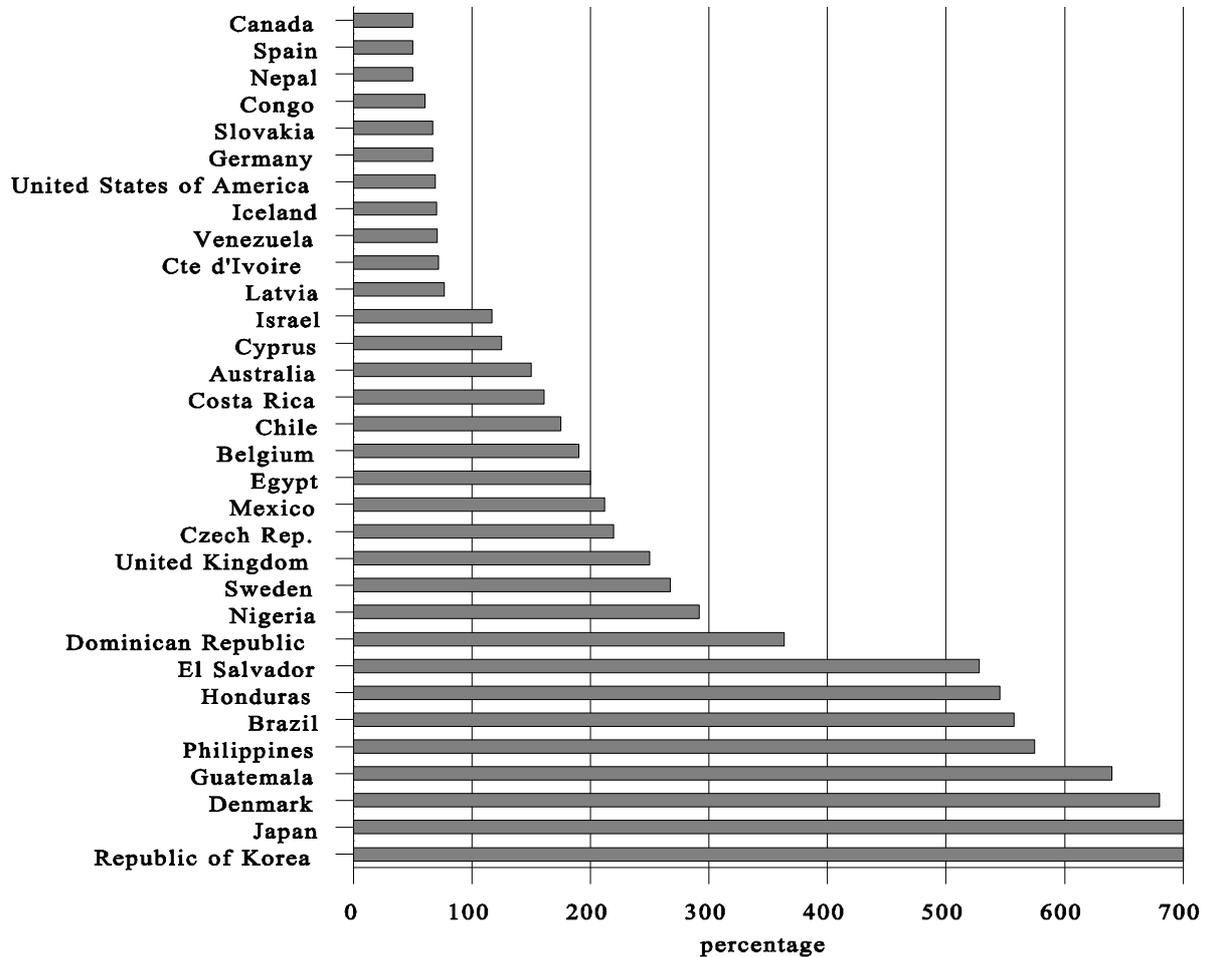
Source: UNDCP ARQ Data.

Figure 98

The **relative significance** of ATS abuse can be established by **comparing it to heroin and cocaine abuse**. Prevalence estimates, and in their absence other indirect indicators such as drug registers, people arrested for drug abuse, number of drug addicts treated in hospital emergency rooms etc., suggest that in some 20 countries the abuse of ATS may be more widespread than the abuse of cocaine and heroin combined (see Figure 99). This ranking puts a number of countries in the Far East (Republic of Korea, Japan, Philippines), northern Europe (Denmark, Sweden, United Kingdom) and Latin America on the top of the list, while for countries such as the United States and Canada, the relative importance is less. This ranking, however, does not always correlate with the actual extent of ATS abuse, which is detailed below.

ATS abuse compared to cocaine and heroin in the 1990s

heroin + cocaine = 100

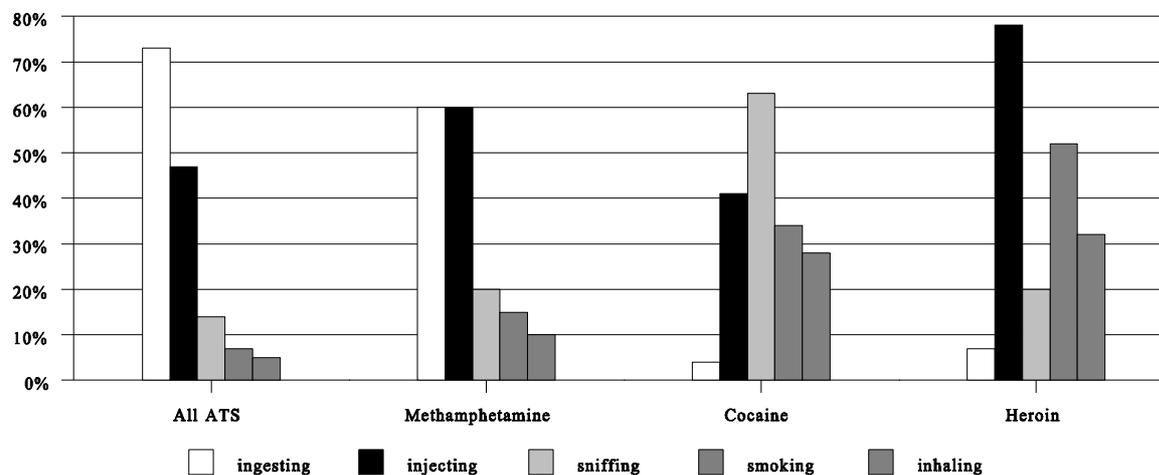


Source: UNDCP ARQ Data.

Figure 99

Comparing ATS with cocaine and heroin in terms of routes of administration also yields interesting results, illustrated in [Figure 100](#). A majority of countries report ingestion as the most frequent method of administration of ATS, followed by injection. In the case of methamphetamine, ingestion and injection are equally popular. Injecting ATS is more frequently reported than injecting cocaine, but less frequently than heroin. Injecting ATS is most widespread in the Far East/Pacific region and in North America, less so in Europe and almost non-existent in Latin America and in Africa. Sniffing, inhaling or smoking are also used as routes for administering ATS, though less frequently.

Main routes of administration*
in % of all countries reporting**; 1992-1994



* Modes of administration of a specific drug do not add up to 100% because countries often report more than one major mode of administration for a specific drug.

** Number of countries reporting =85.

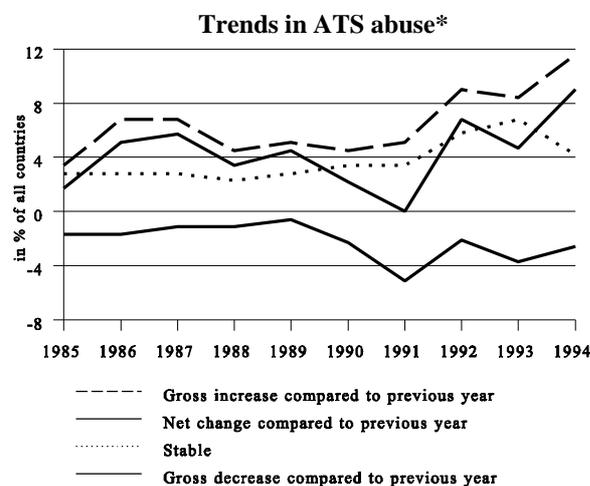
Source: UNDCP ARQ Data.

Figure 100

UNDCP receives qualitative information from several countries on **variations in the extent of drug abuse**. These data can help establish global trends by analyzing changes in the number of countries reporting increasing or decreasing ATS abuse.

Figure 101 shows that since 1985 the number of countries reporting increases in ATS abuse exceeded the number of countries reporting decreases. This suggests that illicit consumption increased at the global level. Reported increases and decreases are presented in Figure 101 as percentages of the total number (n) of ARQs sent out (n = 190 in 1994): 12% of all countries reported an increase of abuse in 1994, 3% reported a decline, leaving a net-increase of 9%. In terms of actual responses (r) to the ARQs received (r = 35 in 1994), 63% of the countries reported an increase, 23% a stable development and 14% a decline in 1994 as compared to the previous year. The number of countries reporting increases in abuse tripled between 1985 and 1994, with most of this increase taking place in the 1990s. It is interesting to note that this trend is very similar to the trends in laboratory detections and seizures of ATS, with one peak around 1987, some stagnation/decline until 1991, and a strong rebound since then.

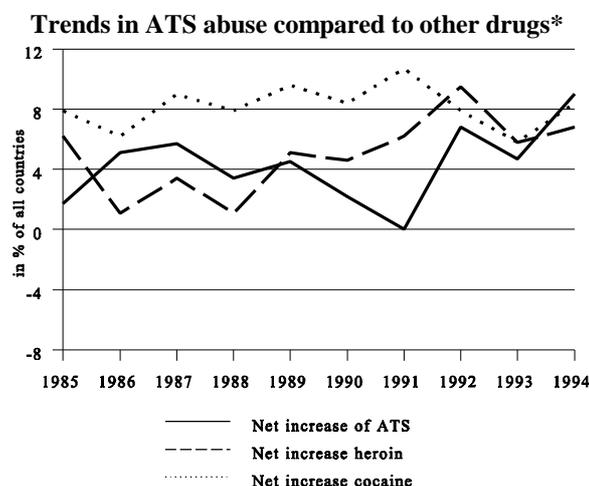
Global trends in drug abuse



* Number of countries reporting change on a year earlier as percentage of all countries receiving an ARQ.

Source: UNDCP ARQ Data.

Figure 101



* Number of countries reporting increase less
Number of countries reporting decrease as
percentage of all countries receiving an ARQ.

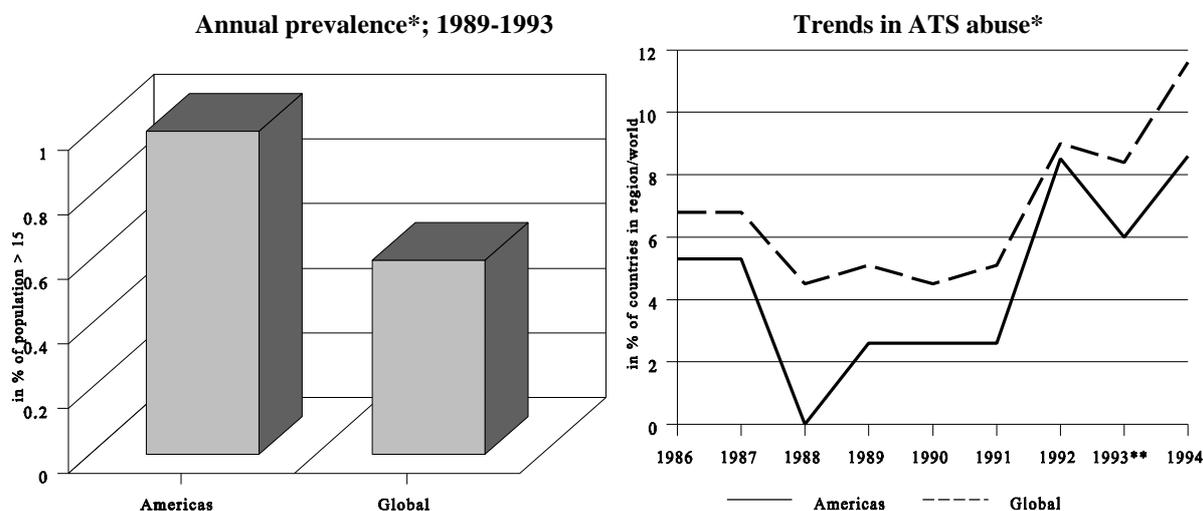
Source: UNDCP ARQ Data.

Figure 102

Figure 102 compares the number of countries reporting net-increases in ATS abuse with the number of countries reporting net-increases in heroin and cocaine abuse. Between 1985 and 1994, net-increases were greater for cocaine and more or less similar for heroin and ATS. The timing of the net-increases, however, shows a different pattern. Heroin consumption seems to have increased most between 1989 and 1992, ATS increased most between 1991 and 1994 and cocaine dropped in the 1990s. By 1994, the number of countries reporting net-increases was highest for ATS. If actual responses to the ARQs are considered, net-increases at the global level amounted to 49% (out of a total of 35 countries reporting) for the ATS, compared to 39% for cocaine and 30% for heroin.

The discussion on the extent of ATS abuse in different regions and countries that follows needs to be set in context. Estimates provided to UNDCP by countries in different regions suggest that the **global (unweighted) annual prevalence of ATS abuse** is, on average, 0.6% of the population above the age of 15. This figure is intended to serve as a benchmark for later comparison. The Americas are above this level; Europe and Asia below it. Differences among as well as within various countries can, however, be significant and are detailed below.

ATS abuse in the Americas



* Unweighted average of national estimate of countries reporting abuse problems of ATS.

* Countries reporting increase in amphetamine Abuse, as a percentage of total number of countries receiving ARQ

** Estimate

Source: UNDCP ARQ Data.

Source: UNDCP ARQ Data.

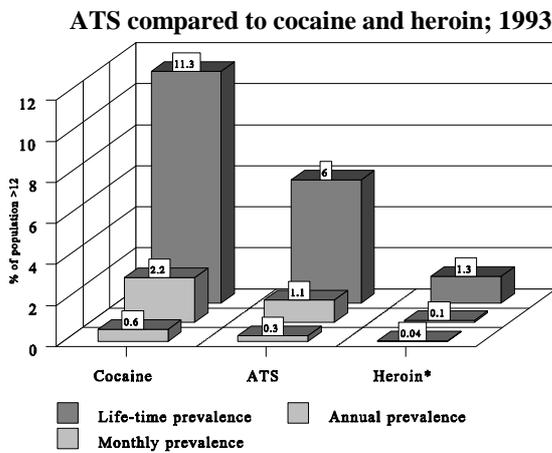
Figure 103

Figure 104

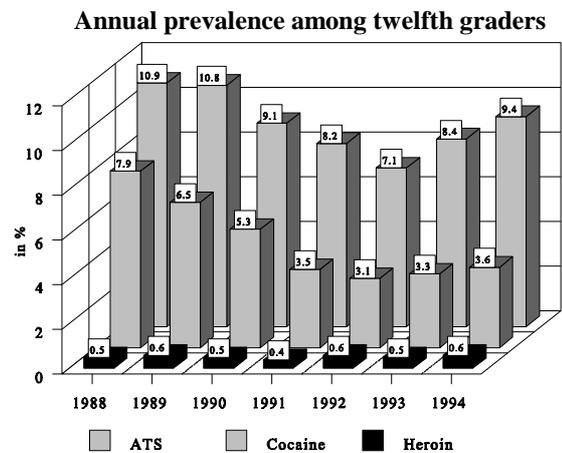
In the **Americas**, the number of countries reporting ATS abuse increased since the late 1980s (see [Figure 104](#)). This was mainly due to countries in South America, though in the 1990s countries in Northern America also reported increases. Significant increases in 1994 were reported from Mexico, Panama, Argentina and the Dominican Republic as well as from the United States. Currently the Americas seems to be the region with the highest prevalence rates for ATS (see [Figure 103](#)). High prevalence rates are reported from urban areas in Colombia, Chile, Venezuela, Brazil, several Central American countries, the northern border area of Mexico the United States and some areas in Canada.

The largest population abusing ATS in absolute terms (2.4 million in 1993) is in the **United States**. The annual prevalence of 1.1 % (of the population above 12 years) in 1993 is about five times larger than for heroin and half as common as for cocaine (see [Figure 105](#)). Most ATS abuse is related to methamphetamine. There is some methcathinone abuse concentrated around the area of the Great Lakes. Although ATS are on the whole more abused by men than by women, the relative importance of female abuse is larger than for other drugs. The proportion of women abusing ATS is about 60% of male abusers. For cocaine, the female share is 40%, and for heroin around 50%. Similar characteristics are observable in many other countries. Another interesting phenomenon is the concentration of ATS abuse among whites, Hispanics and the indigenous population of Hawaii. The share among the Afro-American population is comparatively low.

Drug abuse in the USA



Source: Substance Abuse and Mental Health Service Administration, National Household Survey on Drug Abuse Population Estimates 1993, US Dept. Of Health and Human Services 1994.



Source: NIDA (1995), Monitoring the Future.

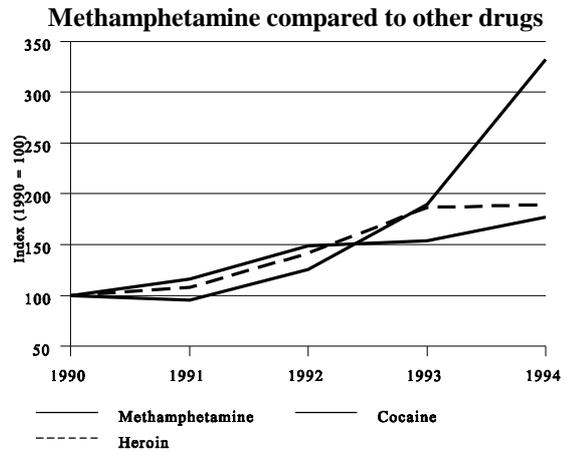
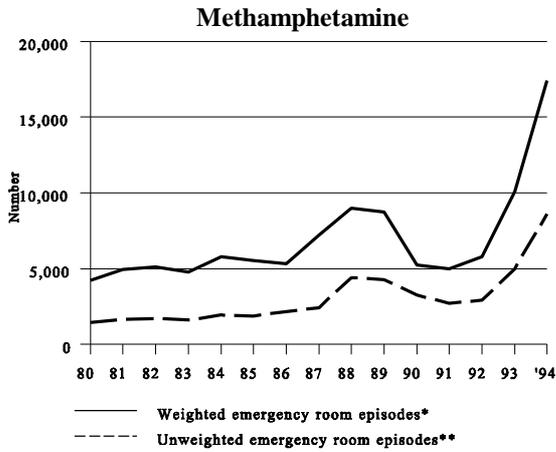
Figure 105

Figure 106

The youth population is particularly affected by ATS abuse. The highest prevalence rates in the United States are reported for the 18-25-year-olds. The relative importance of ATS *vis-à-vis* other drugs is most important among the 12-17-year-olds. Over the last decade, the number of drug abusers declined in the United States, and in line with this general trend, the abuse of ATS also fell. For young people, however, this downward trend came to a stop in the 1990s. [Figure 106](#) shows that since 1992, consumption of ATS among twelfth grade students has again shown an upward trend. In 1994, the proportion of students abusing ATS was seven times greater than the overall annual prevalence rate for ATS. The prevalence rate of students consuming ATS is twice as high as for cocaine.

Emergency room statistics are also a useful indicator for assessing drug trends. Emergency room episodes related to ATS, particularly methamphetamine, increased sharply in the United States between 1980 and 1994. Like laboratory detections and seizures, emergency room episodes reveal a peak during the 1986-1988 period as well as a steep upward trend since 1991 (see [Figure 107](#)). [Figure 108](#) shows the dramatic increase of methamphetamine-related emergency room episodes in the 1990s, apparently reflecting the growing number of 'unexperienced' users who began to experiment with methamphetamine. Emergency room episodes for methamphetamine grew even more rapidly than those for cocaine or heroin in the 1990s. The number of methamphetamine-related mortalities almost tripled between 1991 and 1994. Methamphetamine- and amphetamine-related mortality cases already accounted for about 10 per cent of all substance-abuse-related mortalities examined in 1994 [SAMHSA, 1996].

Emergency room episodes in USA



* 1980-1987 estimates, 1988-1994 reported figures
 1980-1984, 1986, 1989-1991 reported figures; others estimates.

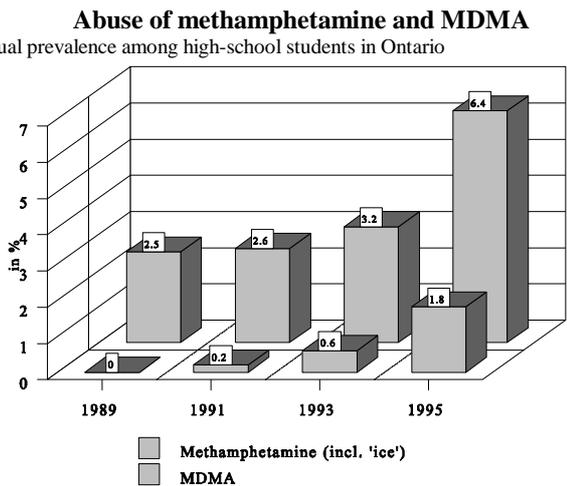
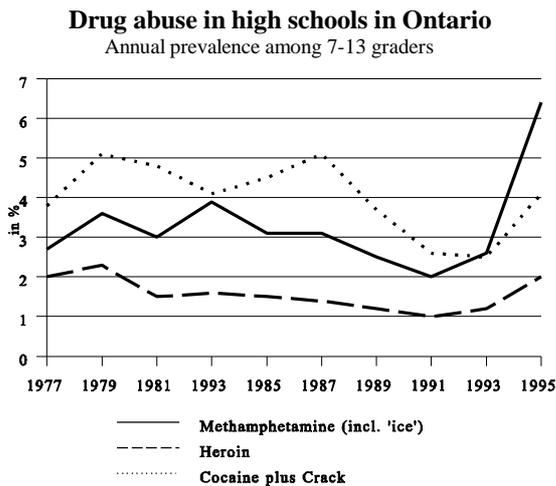
Figure 107

Figure 108

Sources: National Institute on Drug Abuse, *Annual Emergency Room Data, 1986, 1991, 1994*; DEA *Quarterly Intelligence Trends*, 12 (2), 1985; DEA, *Methamphetamine: 1992-1993 Threat Assessment*, June 1994.

This recent upward trend is also in evidence among high school students in **Canada**, where methamphetamine abuse has increased dramatically since 1989 and is now higher than cocaine abuse (see [Figure 109](#)). Ecstasy=abuse has increased even faster (see [Figure 110](#)).

Drug abuse in Canada



Source: The Addiction Research Foundation, Ontario Student Drug Survey, 1997-1995.

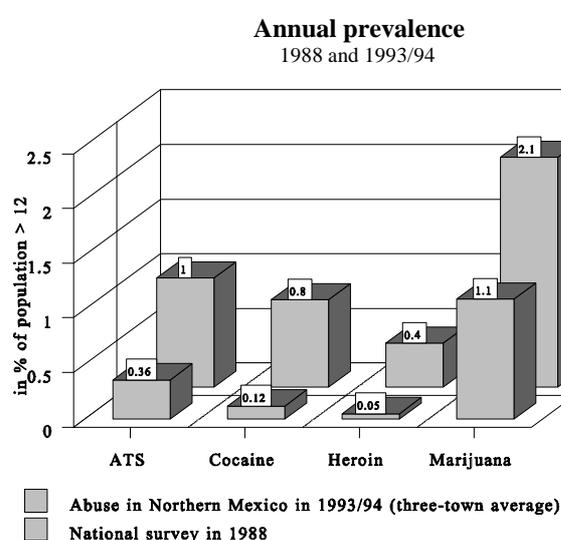
Source: The Addiction Research Foundation, Ontario Student Drug Survey, 1977-1995.

Figure 109

Figure 110

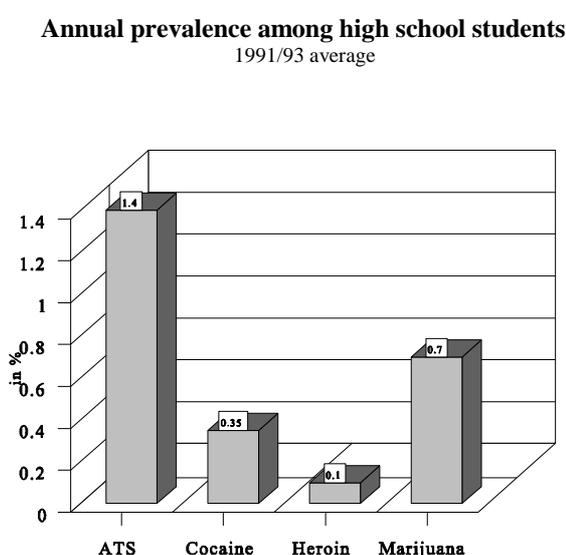
Epidemiological studies for **Mexico** suggest that consumption of ATS is more widespread than cocaine. Particularly in the northern border areas, which in recent years have become a major transit-trafficking point for methamphetamine and ephedrine, consumption of ATS has increased. With prevalence rates of around 1% of the population aged 12 and above, the northern border areas have a prevalence rate which is significantly higher than the national average and almost as high as in the United States (see [Figure 111](#)). Higher prevalence rates than for the population as a whole are reported for high school students, exceeding cocaine, heroin and even marijuana consumption. [Figure 112](#) also shows that ATS abuse among high-school students is four times more common than abuse of cocaine.

Drug abuse in Mexico



Source: Secretaria de Salud (1994), Encuesta Sobre El Consumo de Drogas en la Frontera Norte de Mexico; Secretaria de Salud (1988), Encuesta Nacional de Adicciones, in Poder Ejecutivo Federal (1992), El Control de Drogas en Mexico, Programa Nacional 1989-1994.

Figure 111



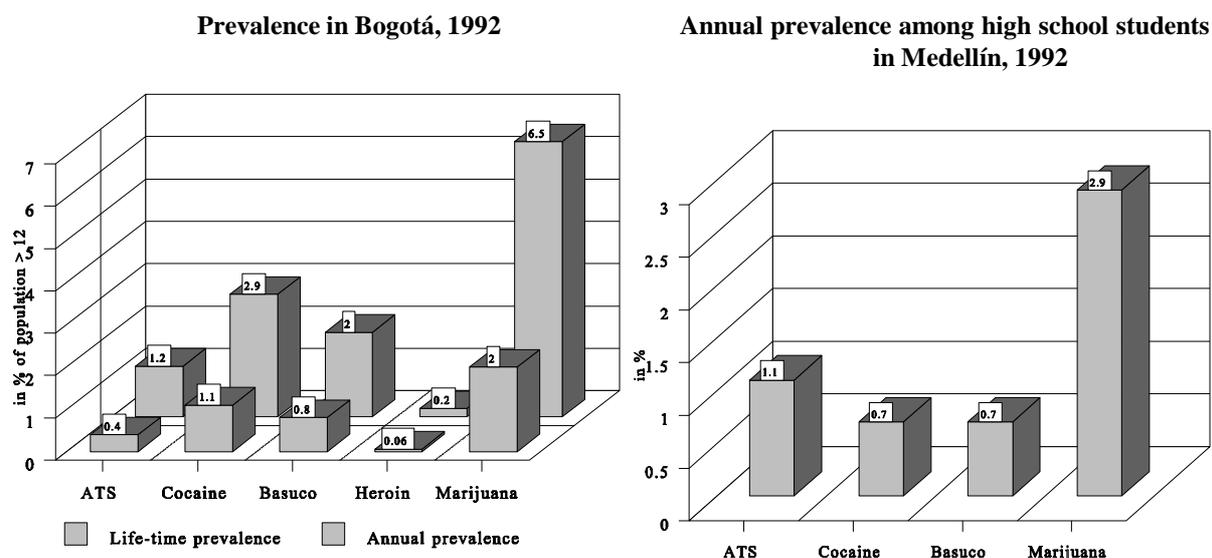
Source: Secretaria de Educación Publica, Encuesta Nacional sobre el Uso de Drogas entre la Comunidad Escolar, in National Program in Drug Control 1989-1994.

Figure 112

Even in Latin American countries, where natural-plant-based stimulants are available in abundance, ATS have a significant share in illicit drug markets. Drug surveys undertaken in Bogotá suggest that the annual prevalence of ATS abuse is 0.4% of the population above the age of 12 (see [Figure 113](#)), which is significantly higher than heroin abuse and equivalent to about one third of cocaine abuse. In **Colombia**, as well as in other developing countries, ATS abuse is concentrated in the upper classes. This is in contrast to abuse patterns in North America, Europe and Japan, where consumption is concentrated in the lower strata of society. As in Europe and North America, high-school students are particularly affected. A survey undertaken in Medellín (Colombia) showed that the annual prevalence of ATS among tenth- and eleventh- grade students in secondary education was 1.1% (1992) and thus higher than the corresponding prevalence rates of 0.7% for *basuco*, a mixture of coca paste and tobacco, or cocaine (0.7%) and

almost three times higher than the overall prevalence rate of ATS abuse in Colombia [UNDCP/Alcaldía de Medellín, 1993]. With increasing availability of cocaine in recent years, however, ATS abuse seems to have declined.

Drug abuse in Colombia



Source: UNDCP, Consumo de Substancias Psicoactivas En Santafé de Bogotá, June 1993.

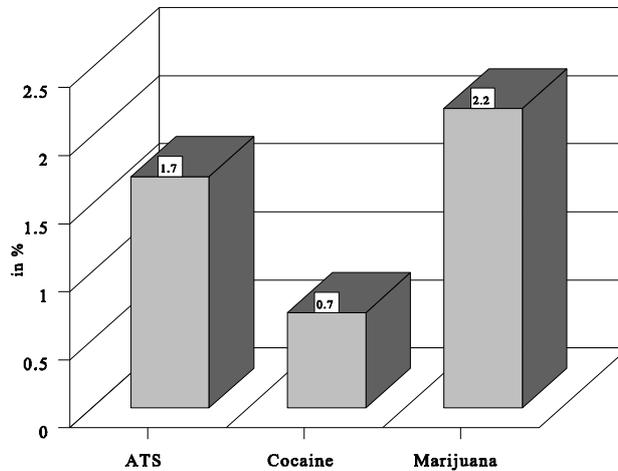
Source: UNDCP Alcaldia Medellín (1993), Resultados – Sistema de Vigilancia Epidemiológica.

Figure 113

Figure 114

Similarly, ATS abuse in **Brazil** appears to have declined slightly over the 1987-1993 period as the country was flooded with cocaine. The reduction in diversions from licit sources may also have played a role [UNDCP/EGM 1996]. The consumption of ATS is still widespread. The annual prevalence rate among high-school students amounted to 1.7% in 1993 (average of prevalence among high-school students in public schools in the 10 largest cities), i.e. a higher ratio than in Colombia or Mexico and more than twice the corresponding prevalence rate of cocaine among high-school students in Brazil (see Figures 112, 114 and 115).

Drug abuse in Brazil
Annual prevalence among high school students, 1993



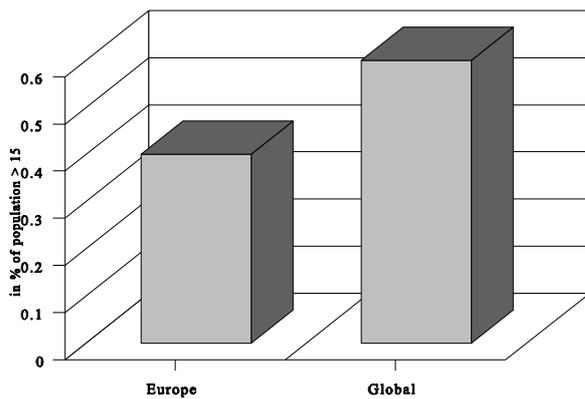
Source: Centro Brasileiro de Informaçoes sobre Drogas Psicotrópicas, June 1994.

Figure 115

Europe appears to have been most affected, in comparison to other parts of the world, by increases in ATS abuse. Most countries reported increases, particularly in the 1990s (see Figure 117). In western Europe, abuse is still concentrated on amphetamine, though the highest growth rates are reported for ‘ecstasy’. While overall abuse levels are lower than in the United States, the relative importance of ATS is greater in Europe.

ATS abuse in Europe

Annual prevalence*; 1989-1993

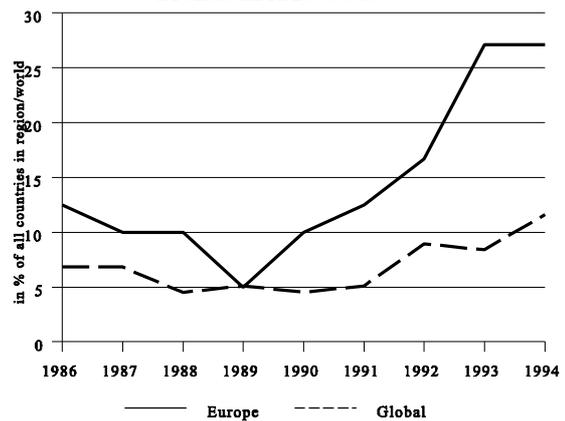


* Unweighted average of national estimates of countries reporting abuse problems of ATS.

Source: UNDCP ARQ Data.

Figure 116

Trends in ATS abuse*

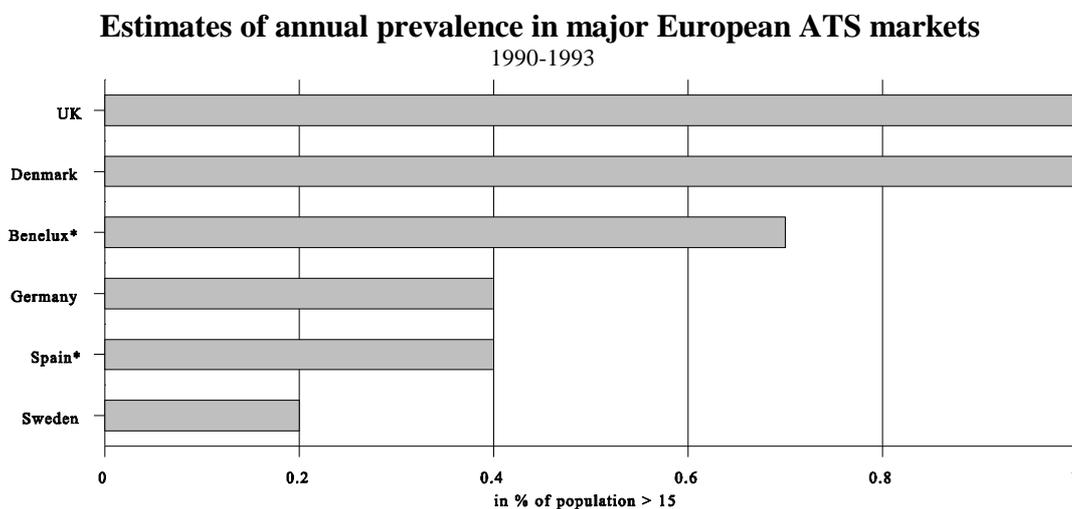


* Countries reporting increase in ATS Abuse, as a percentage of total number of countries receiving ARQ.

Source: UNDCP ARQ Data.

Figure 117

The countries reporting the largest ATS abuse problems in Europe are listed in [Figure 118](#) below. The country most affected is the **United Kingdom**, followed by **Denmark**. Though prevalence rates are lower in **Sweden**, more than one third of all convictions for drug-related offences are due to the abuse of ATS, which is by far the highest such proportion in Europe (see [Table 6](#) in Chapter IX).



* UNDCP estimates.

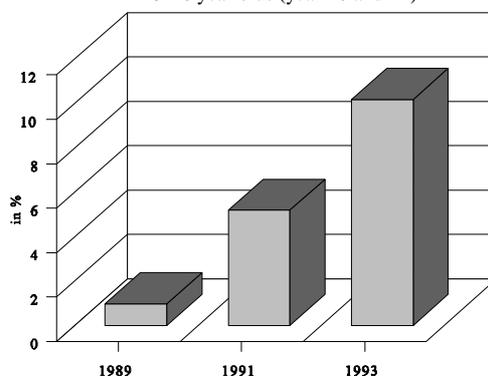
Source: UNDCP ARQ Data.

Figure 118

Different indicators confirm increases in ATS abuse in Europe. Examples from the **United Kingdom**, **Sweden** and **Germany** are shown below to illustrate this general trend (see [Figures 119, 120, and 121](#)).

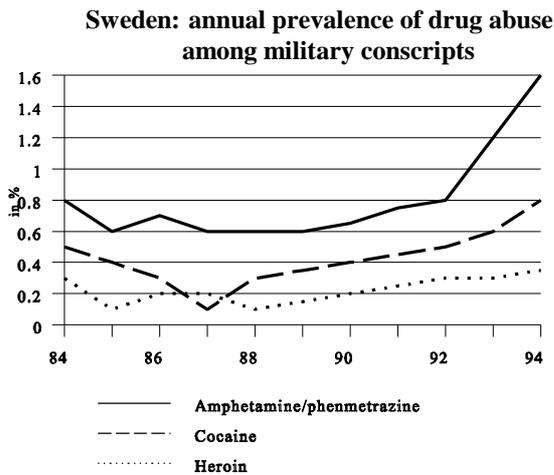
Trends of ATS abuse in selected European countries

UK: lifetime prevalence of amphetamine abuse in high schools 15-16 year olds (year 10 and 11)



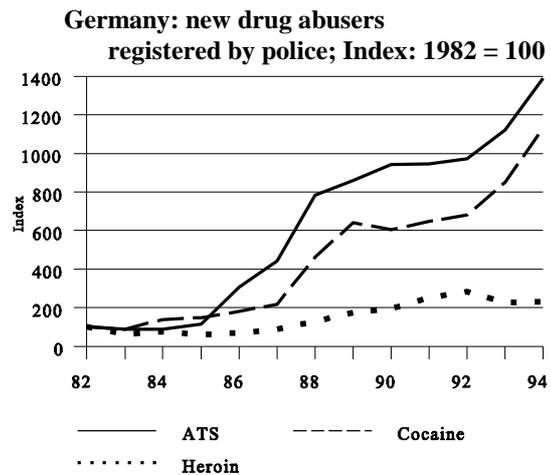
Source: Balding J. Schools Health Education Unit, Young People in 1993, University of Exeter, 1994, in ISDD, Drug Misuse in Britain.

Figure 119



Source: Folkhälsoinstitutet Centralförbundet för alkohol-och Narkotikautvecklingen i Sverige, Rapport 95, Stockholm 1995.

Figure 120



Source: BKA, Rauschgift Jahresbericht 1994, Wiesbaden 1995.

Figure 121

In addition to amphetamine abuse, **Europe** has witnessed a major **wave of ecstasy= abuse** in the 1990s, which appears to grow along with, rather than substitute for, amphetamine abuse [ISDD, 1994]. The European wave followed the spread of ecstasy= in the United States in the mid-1980s. It began in the holiday club-scene of Ibiza (Spain) in the second half of the 1980s and then spread to the **United Kingdom** and the rest of Europe, including to countries which had not had much of an amphetamine problem [Beck, 1993].

The 1992 **British** crime survey showed that annual abuse of ecstasy= was already as

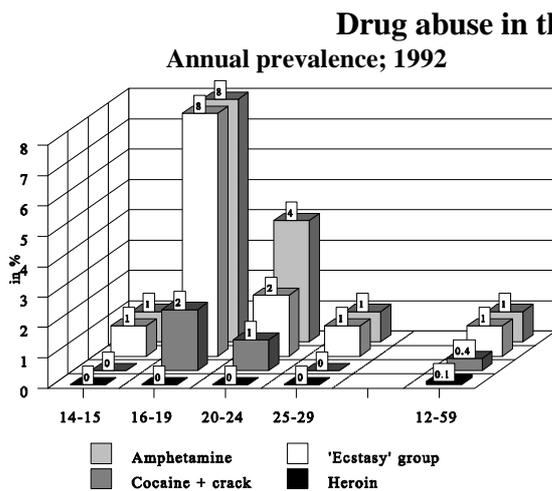


Figure 122

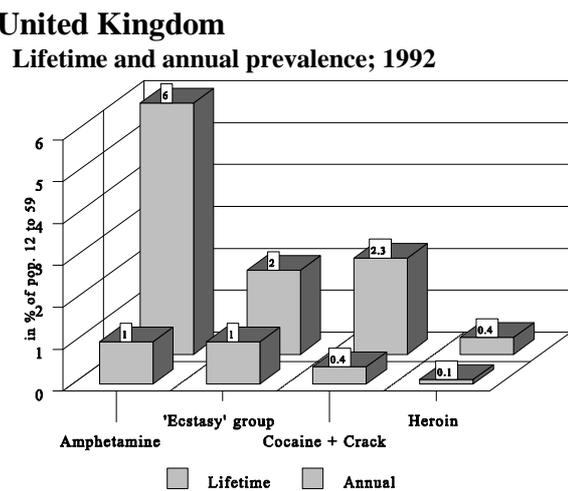


Figure 123

Source: J.Mott, C.Mirrless-Black, *Self-reported Drug Misuse in England and Wales, Findings from the 1992 British Crime Survey*, Research and Planning Unit Paper 89, Home Office, London, 1995.

widespread as amphetamine abuse and more prevalent than the abuse of heroin and cocaine (see [Figure 122](#)). Particularly among the 16-19-year-olds, both amphetamine and 'ecstasy' are widely consumed. The relatively small difference between lifetime and annual abuse of 'ecstasy' (see [Figure 123](#)) reflects the fact that it is a recent phenomenon. Similar patterns resulting from the rapid spread of 'ecstasy' are found in almost all European countries and are closely tied to the 'rave' scene.

The **Netherlands** serves as a good example for similar developments in other European countries. 'Ecstasy' was virtually unknown in 1987. By 1994, however, abuse of 'ecstasy' already exceeded that of cocaine, amphetamine or heroin (see [Figures 124 and 125](#)). Monthly prevalence figures suggest that by 1994 'ecstasy' abuse was almost three times higher than cocaine or amphetamine abuse (see [Figure 125](#)). Only cannabis still has higher prevalence rates. Among 16-19-year-olds, the annual prevalence of 'ecstasy' was 7.9% in 1994, up from 1.5% in 1990, and was thus significantly higher than the corresponding prevalence rate for amphetamine (1.6% in 1994). Compared to these figures, cocaine and heroin abuse in this age group appears almost negligible [Pompidou Group of the Council of Europe, 1995b].

Drug abuse in the Netherlands

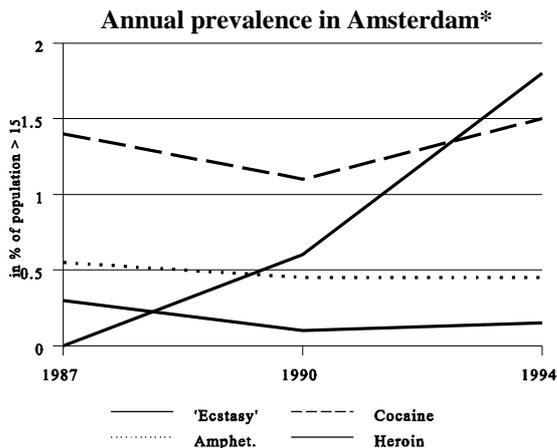


Figure 124

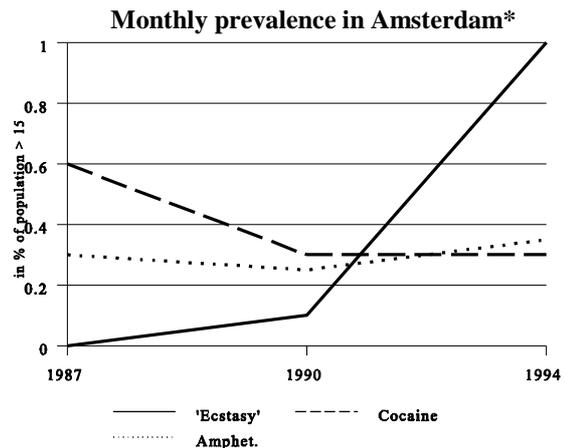


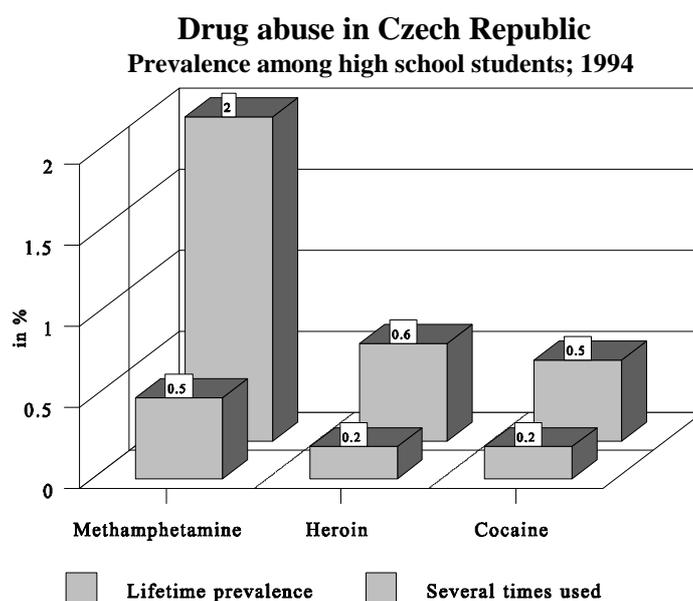
Figure 125

* Individual age group results have been weighted according to the distribution of the age groups in the population of the Netherlands.

Source: Pompidou Group of the Council of Europe (1995), *Multicity Study of Drug Misuse, 1985-1995 Update of Data, Amsterdam Report*.

The abuse of amphetamine and 'ecstasy' is also spreading in **eastern Europe**, and abuse of methcathinone (ephedrone) in **the countries of the former Soviet Union**, particularly in the Russian Federation and in the countries of central Asia. A further spread of methcathinone abuse to neighbouring Asian countries, where the *Ephedra* plant grows in abundance, seems to be only a question of time. In the **Czech Republic** and **Slovakia** methamphetamine is the most frequently abused ATS. Lifetime prevalence of methamphetamine (APervitin®) among high school students in the Czech Republic is four times higher than abuse of heroin or cocaine (see [Figure 126](#)). Only marijuana is still more widespread. **Poland** has a growing problem of amphetamine abuse, although there are no national estimates to determine the actual size of the problem. Some

reports suggest that in the main towns of the Russian Federation, some 20% of the illegal drug market may consist of synthetic drugs, with a significant share for amphetamine and ephedrone. Reports from **Belarus** note that in the large towns, MDMA is being increasingly consumed by school children. In **Latvia**, it is estimated that some 40% of drug consumers abuse ephedrone and various other ephedrine-based products. Significant levels of consumption of ephedrine-based products are also reported from **Lithuania** and **Estonia**. Similarly, **Kazakhstan** reports increasing levels of ephedrine and ephedrone abuse [DEA, 1994e; BND, 1995].



Source: Various epidemiological studies undertaken in Czech Republic, summarized in UNDCP (Mojmír Tyrlik et al), Rapid Assessment of the Drug Use Situation in the Czech Republic, Final Report, February 1996.

Figure 126

The world's highest prevalence levels of ATS abuse are reported from **Australia** (see [Figure 127](#)), with most of this apparently being related to amphetamine and methamphetamine. These two substances, as well as ephedrine, pseudoephedrine and other stimulant compounds, are frequently found in drugs sold as 'amphetamine' or 'speed' in clandestine markets. 'Amphetamine', defined thus, is the second most popular drug after cannabis in Australia. 'Ecstasy' emerged as the main new drug of abuse over the 1985-1993 period (see [Figure 128](#)) and already exceeds cocaine or heroin in prevalence. Abuse patterns are similar to those in Europe, particularly in the United Kingdom. Amphetamine abuse is most widespread in the 20- 24 age group.

Drug abuse in Australia

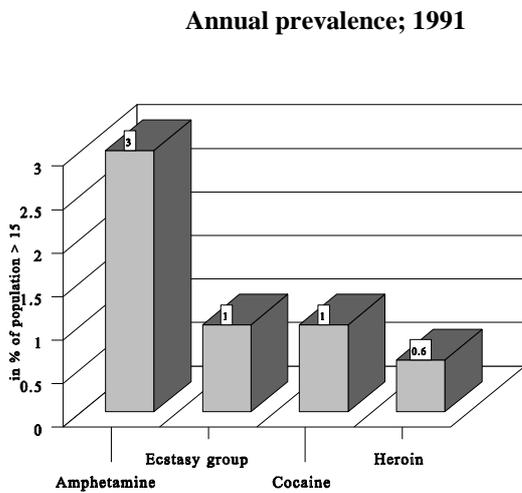


Figure 127

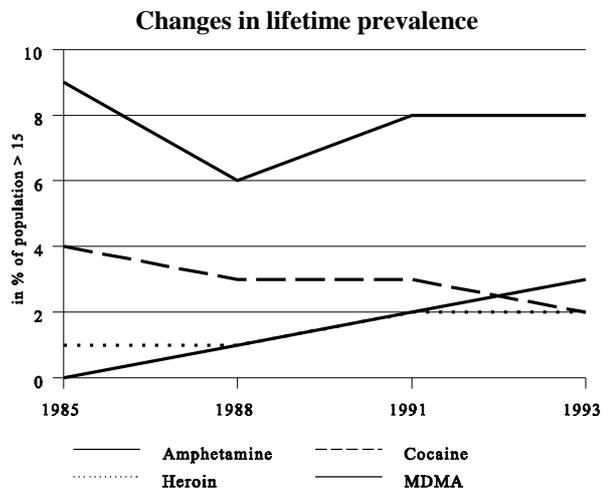
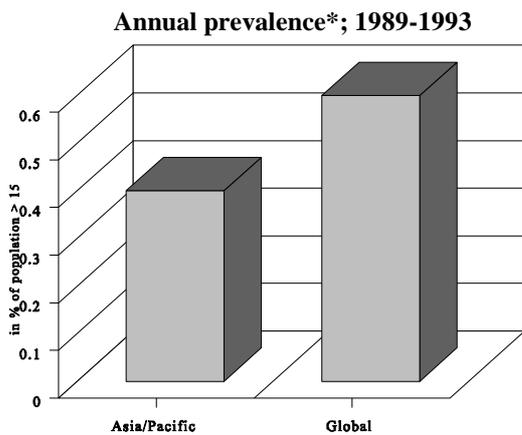


Figure 128

Source: NCADA National Household Survey (1985, 1988 and 1991) in *Statistics on Drug Abuse in Australia 1992*, Department of Health, Housing and Community Services, Canberra 1992.

In the **Far East**, the most frequently abused stimulant is methamphetamine. This is the case for Japan, the Republic of Korea, Taiwan Province of China, Philippines, Hong Kong and Thailand. Even though reported estimates for annual prevalence in the region do not seem to be very high (see [Figures 129 and 130](#)), the relative importance of ATS is considerable. In the Philippines, methamphetamine (*Ashabu*) is reported to have replaced cannabis as the most widely abused substance.

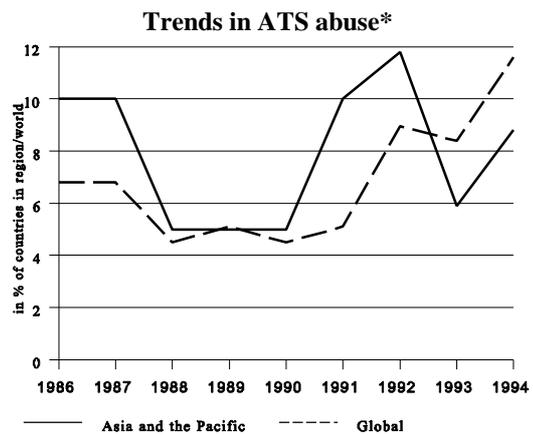
ATS abuse in Asia and the Pacific



* Unweighted average of national estimates of countries reporting abuse problems of ATS.

Source: UNDCP ARQ Data.

Figure 129



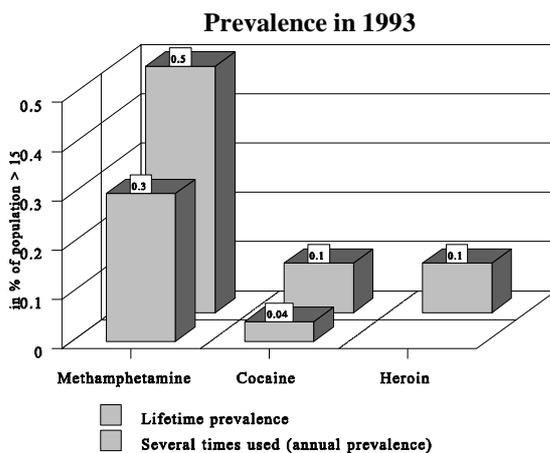
* Countries reporting increase in ATS abuse, as percentage of total number of countries receiving ARQ.

Source: UNDCP ARQ Data.

Figure 130

In **Japan**, almost 90% of drug related convictions in recent years concerned methamphetamine. Using the number of drug offences as an indirect indicator for trends in drug abuse, data suggest that following the first epidemic, in the mid-1950s, methamphetamine abuse ceased to be a problem until the early 1970s. Thereafter a strong rise was registered until the mid-1980s, followed by a downward trend and a stabilization in the 1990s, though at levels much higher than those in the 1960s (see [Figures 131 and 132](#)).

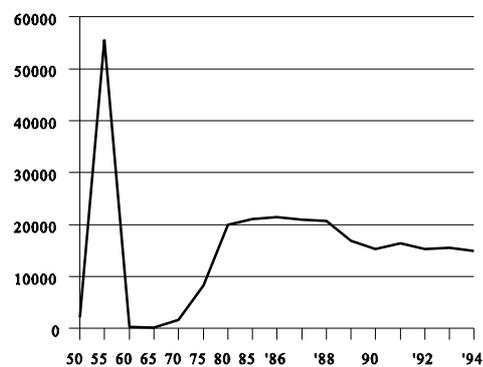
Drug abuse in Japan



Source: National Institute of Mental Health, Epidemiological Survey of Drug Abuse and Drug Dependence, Tokyo 1993.

Figure 131

Number of stimulant drug offenders



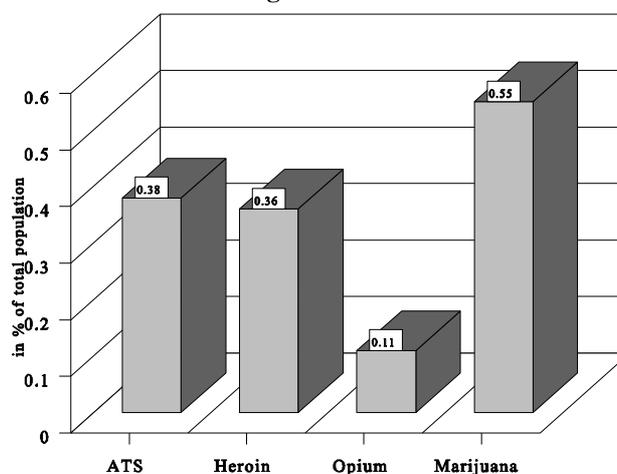
Source: Japan International Corporation of Welfare Services (JICWELS) (1996), Outline of Drug Abuse and Countermeasures in Japan.

Figure 132

Similarly, the **Republic of Korea** experienced a massive increase of methamphetamine abuse during the 1980s. Between 1981 and 1988 the number of offences related to methamphetamine increased more than 15-fold [Korean Customs Administration, 1993]. More than 80% of all drug offences were related to methamphetamine in 1988. This ratio fell back to some 30% by 1993. The number of offences related to methamphetamine is, however, 10 times larger than in 1981. UNDCP ARQ data (1993) indicate that almost 95% of all treatment and rehabilitation services for drug abusers are concerned with methamphetamine.

Thailand, which in recent years has reported the largest amounts of ATS seizures in the region, also reported strong increases in the level of abuse, particularly since 1993. Though ATS have been known in Thailand since the early 1960s, they only emerged in the 1990s as a major problem. In addition to «traditional users», such as long-distance truck drivers, new groups affected are industrial workers, farmers and fishermen as well as young people, who use it in discothèques. By 1993, ATS abuse was already more prevalent than heroin or opium abuse (see [Figure 133](#)).

Drug abuse in Thailand
Drug addicts in 1993



Source: Thailand Development Research Institute, December 1993.

Figure 133

In **Africa** and the **Middle East**, the number of countries reporting increases in ATS abuse were above the global average in the late 1980s and fell in the 1990s (see [Figures 134 and 135](#)). This can be interpreted as a success for international drug control efforts, which have apparently been effective in reducing diversions from licit channels. Some caveats are nonetheless relevant.

Traditionally, the supply of ATS in **western Africa** originated from licit channels. The stimulants consumed were mostly amphetamine and pemoline. However, in the 1990s, diversions seem to have declined. Most countries in the region ceased to report increases in abuse. For instance, Côte d'Ivoire, which up to 1992 regularly reported increases in abuse, started to report decreases as of 1993. Nevertheless, ATS are still among the three or four most abused substances in a number of countries in the region, including Côte d'Ivoire, Ghana, Gabon, Congo, Chad, Burkina Faso and Senegal. A rapid assessment study undertaken in Cameroon by WHO and UNDCP in 1993 suggested that prevalence of ATS was twice as large as that of cocaine and ranked second to cannabis [UNDCP/WHO, 1995]. Moreover, in the main consumer country of the region, Nigeria, ATS abuse is reported to still be increasing (ARQ 1993/94). One study of undergraduates in 1991 found that current abuse (two or three times per week) of ATS affected 3.5% of students [Adelekan et al., 1992], which is a marginally higher proportion than current ATS abuse in the United States among students of the same age group (3.2% in 1991). All of these data should be seen in the context of a number of other factors. Cocaine, easily available as a result of several west African countries having become important transshipment points, seems to have partly replaced ATS. In addition, ephedrine, mesocarb and a number of stimulants so far not under international control, often labelled as amphetamine, have appeared on illicit markets to fill the gaps created by curtailed diversions. Compared with western Africa, abuse of ATS in **southern and eastern Africa** seems to be relatively low. In most of eastern Africa, the predominant stimulant abused is still the locally grown *khat*.

In the **Arab countries**, abuse of ATS seems to be most severe in Egypt, Saudi Arabia and

the Syrian Arab Republic. The main ATS in Egypt is **Maxiton Forte**. Some estimates suggest that the annual prevalence of ATS abuse in Egypt may affect 1% of the total population (ARQ, 1990). Saudi Arabia and most other Arab countries in the region are affected by abuse of fenetylline (**Captagon**). In the 1990s, however, no major increases in the abuse of these substances were reported.

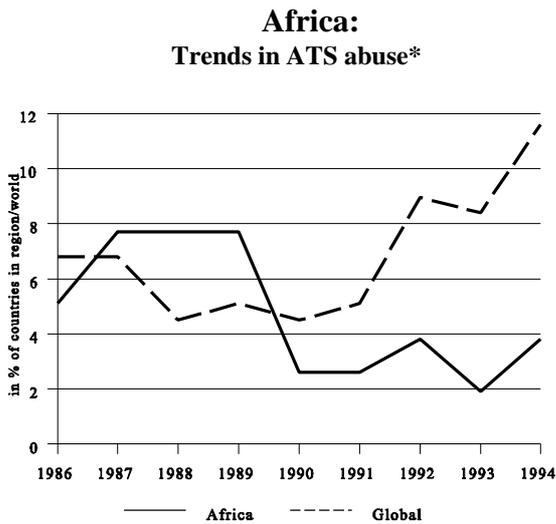


Figure 134

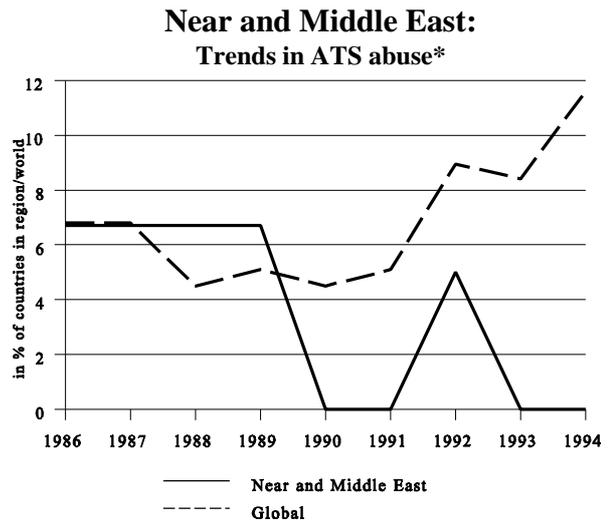


Figure 135

* Countries reporting increases in ATS abuse, as a percentage of total number of countries receiving ARQ.

Source: UNDCP ARQ Data.

XII. Impact of consumption of ATS

The previous chapter established, in quantitative terms, that abuse of ATS is growing in many parts of the world. Often facilitated by the traditional consumption of natural-product-based stimulants, this spread seems to have been exacerbated by a number of popular notions and perceptions about synthetic amphetamine-type substances:

- (a) The image of being modern and more potent substitutes for the traditional substances;
- (b) The image of being relatively benign as compared to cocaine or heroin;
- (c) The image of being socially acceptable;
- (d) The positive image, particularly of 'ecstasy', as a 'love drug', a 'peace drug' and a 'safe drug', which is widely perpetrated in popular literature;
- (e) The 'home-made' image, owing to the fact that they can be produced in a kitchen laboratory.

Apart from these, a number of intrinsic characteristics of ATS influence consumer preference:

- (a) Their special properties, providing self-confidence, alertness, endurance, better physical performance and an anorectic effect, which make them suitable for various sections of society not only for recreational use but also as a means of coping with professional pressure and enhancing endurance for military and athletic purposes;
- (b) Their high volatility in both base and salt (hydrochloride) forms, together with a relatively high lipophilicity and thermal stability so that they can be smoked, sniffed, inhaled, ingested or injected;
- (c) The duration of their CNS stimulant effect, which is longer than that of cocaine;
- (d) Their bioavailability, which is considerably higher than that of cocaine;
- (e) Their particular pharmacological profiles which can provide stimulant, hallucinogenic and entactogenic effects;
- (f) Their relatively low cost and easy domestic availability.

All of these factors seem to have favoured the new wave of ATS abuse that was identified in the previous chapter. The impact of ATS abuse, however, on the individual as well as on society as a whole tends to be underestimated, because the consequences are not as visible as those of other drugs, particularly heroin and cocaine. The range of types of users [UNDCP/EGM, 1996], of ways to administer the drugs and of reasons for their use further complicate the picture. Of all the illicit drugs, however, ATS appear to occupy a central position: on the one hand, by virtue of their injectability, they echo one of the worst manifestations of heroin use and on the other hand, an established stimulant market ready-made for the promotion of cocaine [Klee, 1992].

One of the main reasons for the perception that ATS abuse carries a lower health risk is the absence of severe physical side effects, or rather, of what is perceived to be a severe damage to the individual's health. In fact, ATS are associated with mental health consequences rather than physical ones. The time lag between drug use and the manifestation of some kind of psychological damage, together with difficulties in diagnosing this damage and establishing a link between drug use and the psychological manifestation, tend to blur the perception of health risks.

The **mortality** associated with ATS abuse is still lower than that of other drugs, even when considering the recent ecstasy-related deaths, which have been given much attention in the media. The fatality risk of CNS stimulants, including prescription drugs has, however, increased considerably over the past 20 years, though it has been stable for other types of drugs [Davies et al., 1991]. In the United States, for instance, the figure for annual methamphetamine-related deaths almost tripled between 1991 and 1994, to 433, and now accounts for 6% of all substance abuse mortality cases [SAMHSA, 1996]. The number of ecstasy-related deaths is even lower. In Europe, for instance, since its emergence in the 1980s, fewer than a hundred ecstasy-fatalities, i.e. less than 10 per year, have been reported [Buning, 1995].

The **direct health effects** of the various amphetamine-type substances are similar and strongly correlated with dose, frequency of use and administration route [Hall et al., 1996]. Potentially life-threatening complications are caused by an increase in blood pressure and heart rate and dangerously high body temperatures. They include the rupture of blood vessels (hemorrhage), stroke, cardiac arrhythmias and seizures, and also renal failure [Green et al., 1995] and liver damage [Milroy et al., 1996]. Other immediate health consequences are nasal ulcers from snorting and pulmonary dysfunction from smoking. Psychiatric consequences, which can give rise to aggression and apparently unmotivated violence, include anxiety, confusion, disorientation, hallucinations, paranoid delusions and amphetamine psychosis. The more severe side-effects are usually associated with amphetamine, methamphetamine and methcathinone rather than with ecstasy-type substances. This is, however, mainly the result of the different patterns of use: ecstasy, for example, is seldom associated with chronic intravenous abuse. The depression after withdrawal from ATS can be severe and may cause suicidal inclinations. Difficulty in bodily coordination, which may lead to accidents, is one of the side-effects most frequently, though indirectly, causing physical damage to the user and to others involved in these accidents.

The consequences of **fetal exposure** to ATS are still not fully established scientifically. Medically supervised use of pure amphetamine in low doses does not seem to cause birth defects. The situation is, however, quite different with regard to ATS abuse. For obvious reasons, studies investigating the consequences of maternal ATS abuse during pregnancy are rare. Animal studies are only of limited validity. It appears, however, that abuse of higher doses may lead to a delay in fetal growth, low birth weight and premature delivery. Furthermore, the babies born to amphetamine-abusing mothers may be anemic, and poor sleepers and feeders [Dixon, 1989]. The few existing long-term studies suggest an adverse influence on the growth and school performance of these children [Cernerud et al., 1996], including aggressive behaviour and a potential predisposition to substance abuse disorders.

The major risks of **intravenous use** which is considered a sign of progressive abuse (for a comparison of the frequency of ATS injection with that of cocaine and heroin, see [Figure 100](#) above) are HIV/AIDS, other infectious diseases such as hepatitis, and also vascular damage [Klee, 1994]. In addition, psychological disorders and dependence may develop more rapidly among ATS injectors, since intravenous use usually implies larger quantities at frequent intervals. The time lag between drug use progressing to addiction is commonly 2-4 years [Gawin and Ellinwood, 1988]. The emergence of injecting as a means of administering ecstasy adds a new dimension to the presently widespread use of these substances, which were previously considered to be less harmful precisely because they were not injected but taken orally [Frischer et al., 1995].

Typical amphetamine injectors, in contrast to those who inject opiates, were found to be younger and more sociable; they showed higher levels of sexual activity; they believed that they had control over their drug use and were reluctant to make contact with drug services; and they also tended to distribute their injecting equipment rather freely to others [Klee, 1992]. All of this adds additional dangers to society.

Another issue of considerable concern is the fact that the **long-term consequences** of ATS use are largely unknown. Scientific studies in non-human primates using almost the same dosage range per kilogram as used by many human drug users showed, however, that there is considerable potential for chronic neuropsychiatric difficulties and even for neurotoxicity [McCann and Ricaurte, 1993, cited in McDowell and Kleber, 1994]. Only few behavioural correlates of ATS neurotoxicity have been identified so far [Ricaurte et al., in Cho and Segal, 1994]. The similarity of ATS-induced neurochemical and structural alterations in the brain to the dementia occurring as part of the normal ageing process, suggests, however, a distinct type of mental disorder in the ageing population of casual ATS abusers [Schuster and Hartel, in Cho and Segal, 1994].

A particularly difficult issue in the context of ATS abuse is the **unpredictable nature of what is actually contained in the drug sold on the street** and, therefore, of its health consequences. More than heroin and cocaine, street samples of ATS vary not only quantitatively, in terms of their purities, but also qualitatively. This applies particularly to street samples of 'ecstasy', which may contain a wide variation of combinations of related substances, or even of other drugs of abuse. Although users, when buying 'ecstasy', buy a concept rather than a single pharmacology [Forsyth, 1995], the risk of harm arising from such unpredictability cannot be disregarded. Marketing in the form of various pills adds to the problem in that the user may be tempted to assume that the design of a tablet is indicative of its composition, even though experience has shown that this link may not always exist. Another factor making the health consequences of clandestinely manufactured ATS especially difficult to gauge is the presence of various by-products which are created in the synthesis process and which could have completely unknown side-effects. 'Designer amphetamines' add another dimension to the problems of the unpredictable nature of the health consequences: since many of them have never been tested clinically, there is nothing known about their pharmacological effects.

There is a close relationship between the social, health and economic consequences of drug abuse. In addition to the frequency and severity of the health effects of a particular drug, a number of factors, such as the prevalence of abuse, the age structure and the social background of the abusers, contribute to the **problem in societal and economic terms**. With regard to ATS, particularly 'ecstasy' group substances, it is precisely these additional factors which contribute to the growing threat to society and lay the ground for the insidious, and still largely unrecognized, changes in the illicit drug market that are presently under way.

With the 'rave' scene as the turning-point from which these drugs moved beyond a subculture to become integrated into mainstream youth culture, the exposure of the most vulnerable part of society to these drugs appears to have become the norm [Parker et al., 1995]. There are several characteristics of the ATS group that make them increasingly the **drugs of first**

choice in this situation. On the one hand, they offer possibilities for coping with today's performance-oriented society and social pressure on adolescents. On the other hand, they are used as representations of integration and socialization, of a fashionable lifestyle and collective identification. The basic idea of this type of drug use is to **consume pleasure** in a well-designed drug-taking event. In the long term, there is the risk that these substances may become as widely accepted as alcohol and tobacco. In view of the limited knowledge of the long-term psychological and behavioural consequences of ATS use, the economic and social consequences of widespread acceptance are unpredictable.

Considering the **recreational use** of ATS, there is a risk that patterns of dependence will develop and that other leisure-time activities may then seem pale and mundane in comparison with the experience of drug-taking. This type of dependence may develop insidiously and largely unnoticed by the consumer. Similarly, recreational drug users are often not aware of the extent to which the drug use affects their behaviour, their performance and bodily coordination. There is probably a correlation between the widespread recreational use of **ecstasy** in many European countries and the large proportion of young people involved in automobile accidents, particularly on weekends.

As a consequence of the **benign image** of ATS and because their stimulant effects are not socially stigmatized, users are difficult to approach and usually reluctant to seek professional help. This reluctance on the users' side is supplemented by the inability of most drug treatment and counseling centres to provide appropriate health care services for ATS abusers. More familiar with heroin and cocaine abuse, most institutions and professionals are not equipped to deal with problems associated with ATS abuse.

The harmless image of ATS implies the further risk that these substances may act as a **gateway** to drug abuse in general and also to more dangerous drug-using practices. A recent study found, for example, that 16-year-old non-drug-taking pupils, if they were to try drugs in the future, would be most likely to take **ecstasy** or LSD as the only alternative **starter** drugs to cannabis [Parker et al., 1995]. Methamphetamine, is considered a **gateway drug** to intravenous drug abuse [Hall, 1988]. There is also public concern about two trends closely linked to the belief that some street samples of ATS, particularly **ecstasy** group substances, contain more than one drug [Forsyth, 1995]. First, this belief may result in a greater readiness on the part of abusers to combine, on their own, the individual substances which they believe to have been part of a particular drug cocktail. But mixing drugs, of course, increases the risk of harm. Secondly, users may even switch to other drugs which they have never taken before, such as heroin, simply because they believe that these substances were present in their ATS and did them no apparent harm.

All of the above, mainly as a result of the widespread ATS abuse among youth, constitutes, or may soon emerge as, a considerable burden on society. Another economic aspect that applies to the use of any drug is the **impact on the productivity of the drug user**. The effect of a drug on the work performance of the user is a function of the type and the quantity of the drug consumed, as well as of the performance requirements of the job in question. In general, immediate memory and fine motor skills are more severely affected than mere physical labour. There is evidence that moderate use of ATS initially increases work performance. In the long term, however, productivity declines as increased levels of activity and performance change into

unproductive hyperactivity and as the likelihood of accidents sharply increases. The high proportion of recreational use, particularly of 'ecstasy'-group substances, by people of the middle and upper classes may contribute to an underestimation of the actual social and economic impact of these substances. But chronic effects of abuse may still cause considerable health care costs to society in the long term, especially in terms of health care expenditure for elderly, former ATS abusers.

Another aspect which has to be considered in the context of ATS abuse is **criminality**, of both the drug user and of the groups involved in illicit manufacture and trafficking. The tendency of the individual ATS abuser to engage in criminal behaviour is clearly the result of the paranoia/violence following the abuse of these substances, particularly of amphetamine and methamphetamine [Maden et al., 1992; UNDCP/EGM, 1996]. Though in most countries the criminal records of abusers of ATS are less serious than those of heroin or cocaine abusers, comparing intravenous amphetamine and heroin abusers who spend comparable amounts on drugs, amphetamine abusers tend to be more 'crime oriented' than heroin abusers [Klee and Morris, 1994]. The typical recreational 'ecstasy'-consumer, by contrast, does not show similarly criminal behaviour [Saunders, 1994].

Potentially more dangerous for society as a whole is the wide range of criminal activities associated with groups trafficking ATS. Driven by the extremely high profits, what is developing in this area can only be called an illicit 'industry' of growing international dimensions. While in some regions of the world, **organized crime** is only starting to deal with ATS, in others, criminal groups appear to already hold a position similar to that of the cocaine cartels in some Latin American countries in the late 1980s. Some of these groups, in fact, seem to be diversifying their activities from cocaine or heroin into ATS [e.g., UNDCP/EGM, 1996].

The severity of the dangers to society of organized drug crime is positively correlated with the organizational structure and the resulting violent behaviour of the groups involved. The highest risk in terms of violence and financial damage to civil society appears to be in the Far East, where well-organized, sophisticated criminal groups control intraregional and national trafficking of methamphetamine [UNDCP/EGM, 1996]. In North America, supply of the main precursors as well as manufacture of and trafficking in methamphetamine have been taken over by well-organized criminal groups in recent years. Manufacture and distribution of methcathinone in the United States, as well as of amphetamine and 'ecstasy'- in Europe, by contrast, are still largely decentralized activities [UNDCP/EGM, 1996]. Yet the discovery of several large-scale manufacturing sites for 'ecstasy'-type substances in Europe suggests that some concentration may already have started to occur. Moreover, since criminal drug trafficking groups appear to be increasingly involved in other kinds of crime [UNDCP/EGM, 1996], the dangers to civil society can be expected to increase.

All of these characteristics suggest that the current upward trend in abuse of ATS is set to continue. The widespread use among young age groups is of particular concern. ATS abuse is different from cocaine and heroin abuse. Its health consequences may be - on average - less severe than those of heroin or cocaine. It is, however, far from harmless. The rapidly growing number of young abusers as well as the largely unknown long-term health effects constitute major

risks for society. In view of the trend that ATS abuse may be increasingly viewed as »normal« behavior, the dangers of ever more widespread abuse and related side-effects (health, productivity, criminality) should not be underestimated. This calls for increased vigilance as well as for innovative approaches to counter the threat.

XIII. Conclusion

This review has shown that the ATS problem is a tractable one on the licit side of the equation, where the control system works reasonably well. On the illicit side, by contrast, the problem is more severe and the control system far more limited, since:

- (a) Illicit manufacture and trafficking of ATS have increased over the last two decades, with their growth rates even surpassing those of cocaine and heroin in the 1990s;
- (b) This general trend is an aggregation of particular trends for individual substances within the group and for different parts of the world. The traditional ATS, methamphetamine and amphetamine, are still the two most widely abused substances in the group. Methamphetamine is concentrated in North America and the Far East; amphetamine in Europe and Oceania. Of the other substances, the 'ecstasy' group constitutes the most dynamic growth area in many countries, especially in Europe. Though smaller in magnitude, methcathinone manufacture and abuse seem to be growing, primarily in the United States, and still prevail in some parts of the former Soviet Union;
- (c) What began originally as a displacement from the licit to the illicit sector in a small number of key countries in North America, Europe and the Far East now shows every sign of diffusion beyond these original focal areas into neighbouring ones. It is particularly alarming that many of these areas of diffusion now span different continents and involve countries with inadequate regulatory systems;
- (d) This intercontinental nexus opens a considerable potential for what were hitherto small subregional markets to evolve into an integrated global market.

ATS provide the best historical evidence of what is often called the 'balloon' effect. In the case of plant-based narcotic drugs, it is either the cultivation, extraction or purification/conversion that moves from one geographic location to another to escape enforcement. With synthetic drugs, the nature of the 'ballooning' is different. As this paper has demonstrated for ATS, tightening supply in a market with conditions of constant demand merely causes manufacture to shift from the licit to the illicit area, initially within the same country and then perhaps into a neighbouring one.

This process started with national controls in individual countries on amphetamine and/or methamphetamine. As licit supplies became tightly controlled, clandestine manufacture began to emerge. The chemical and pharmacological versatility of the group was transposed into innovation and flexibility in the clandestine industry: in the location and size of the manufacturing units, in the use of synthesis methods, in the variety of end-products and in the frequently changing precursors and additional chemicals.

Sporadic clandestine manufacturing attempts have been observed with licit ATS other than amphetamine and methamphetamine, but they have remained isolated cases rather than trends. This may not, as postulated above, be the case in the future. In addition, there are already real dangers with the 'ecstasy' group of substances and incipient ones with methcathinone.

All of this can be summarized in the proposition that the whole problem with ATS is equally driven by demand and supply. The particular nature of ATS supply can best be understood in economic terms, because the incentives for clandestine manufacture are greater than those for heroin and cocaine, and in terms of the chemical and pharmacological nature of the whole group:

- C The amphetamine-type end-products have a simple chemical structure, which makes them ideal for clandestine experimentation;
- C Many simple chemicals can serve in the various synthesis processes, either as building blocks or as facilitators, and are cheap and widely available in most countries;
- C A great number of simple synthesis methods and pathways have been developed, patented and/or published in the scientific literature, usually consisting of very few steps leading from a starting material (precursor) to the desired end-product;
- C This information, and its availability, have been growing since the first quarter of the century;
- C Ever-increasing technological awareness means that simple chemical conversion processes can today be performed by any amateur;
- C Since ATS are very similar in chemical structure, they are ideal targets for minor structural modifications to obtain a different end-product;
- C These modifications may be determined by the availability of the precursors or may be the result of a deliberate effort to circumvent legislation by manufacturing an ATS not covered by national law or international convention;
- C The latter approach is similar to the molecular designing strategy in chemical and pharmaceutical research. This strategy is transposed, via the grey area between the licit and the illicit, into the manufacture of what are called »designer drugs«, »designer amphetamines« or, more accurately, controlled drug analogues;
- C It is particularly revealing that over the last decade, at least 30 amphetamine-type substances of clandestine origin have appeared in different countries; most of them have never been tested clinically;
- C Finally, from the perspective of the drug user, or abuser, the *substitutive* nature of the whole group of substances should be noted: though with individual differences, they all provide pharmacological assistance in achieving very similar ends or effects.

This brings the discussion back to the question of illicit demand for the substances. While the larger questions about the nature of the demand for psychoactive substances are clearly beyond the purview of the present paper, what should be noted are the points that appear to be typical of, and specific to, ATS:

- C They are now consumed in practically every region of the world and can, by virtue of this, be called a global problem;
- C They carry a »modern« image in comparison to the traditional stimulants used in some developing countries, like cola nuts or betel nuts, and could easily, on the crest of a wave of modernization, replace the latter;
- C Their occupational use can quite easily shade over into recreational use because the distinction between the one and the other can never be absolute;
- C They sometimes carry a »home-made« image in quality terms, because they are usually made within the country of consumption and often in a »kitchen«-laboratory closely linked

- to the abuser;
- C They have a relatively benign image compared to cocaine, the other stimulant available on illicit markets;
- C They are often cheaper than cocaine, and usually have a longer-lasting effect;
- C They offer versatile application routes, because they can be ingested, sniffed, smoked, inhaled, or injected;
- C They are particularly attractive, especially in the 'ecstasy'-form, to young people, because they are perceived as enhancing performance and communication and have come to embody a fashionable lifestyle, as best evidenced by the recent explosion of information about them;
- C The public health risk they pose is frequently underestimated in public perception, as well as in the judicial and enforcement areas;
- C The recent trend towards decriminalizing the possession of small quantities of narcotic drugs and psychotropic substances for personal use, together with the 'kitchen technology' that is so typical of the clandestine manufacture of the ATS, and the concept of controls on chemicals only above threshold levels may well exacerbate the problem.

The last point raises the question of implications for drug control. According to the process laid down by Economic and Social Council resolution 1995/20, and reiterated in Economic and Social Council resolution 1996/29, these drug control implications are to be considered by a meeting of experts at Shanghai, China in November 1996, on the basis of the present study and the findings of a recent expert meeting on ATS convened by UNDCP at Vienna in February 1996 [UNDCP/EGM, 1996]. What seems to be required at the moment, therefore, is to emphasize the most salient points that have emerged from this study:

- C The problem is now a global one. Yet only a handful of countries, because of their historical experience, are equipped to deal with it. Such national responses become less effective as manufacture, trafficking and abuse spill over into other countries and start to form an integrated global market;
- C In the countries which are being drawn into this global market, the principal limitation is a continuing emphasis on traditional plant-based narcotic drugs. While this is perfectly valid, especially in view of the need to balance priorities with limited resources, it still creates a dilemma which leads to the synthetic drugs being given insufficient attention;
- C The lack of attention is both cause and consequence of limited knowledge and awareness of the synthetic drug problem among many drug control agencies, where there is limited technical capacity to perceive the problem, let alone resolve it. This is in marked contrast to the ever-more-sophisticated technical capacity of clandestine entrepreneurs;
- C Technical problems spill over into the legislative area. There is an enormous variability in national legislation, particularly as it pertains to ATS. More common ground has to be found, in regard to both national compliance with existing regulations and the cooperation of industry, if the international drug control conventions are to be more effective against the synthetic drug problem;
- C The 1988 Convention is a basis for controlling precursors; the 1971 Convention for controlling the end-products. Yet this study has identified a number of significant limitations, all pointing to the fact that the focus of control, for both precursors and end-products, has to be different for the synthetic drugs: unlike the narcotic drugs, there are no clearly identifiable botanical supplies but a huge variety of precursors; similarly, there

are not only a few easily identifiable end-products but an enormous variety of potentially substitutable substances;

- C Because the problem has shifted almost entirely into the illicit sector, the way forward would seem to require improvements in at least the following areas: precursor control; the international scheduling process; implementation of, and compliance with, the international control system; and monitoring of all dimensions of the ATS problem. Solutions to be worked out in each of these areas, however, will be limited by the technical dilemma already noted. They will require considerable technical expertise (chemical, forensic, pharmacological and legal), as well as financial resources. These cannot be guaranteed in the present circumstances.

Finally, it is quite apparent that traditional drug control approaches to this enormously flexible clandestine industry offer limited chances of success. Such approaches may even have inadvertently contributed to the shifts from the licit to the illicit areas of manufacture, as well as to the capacity of illicit markets to stay one step ahead of controls. In terms of the proposition set forth at the outset of this review, it looks as though the synthetic drugs, particularly ATS, will indeed be a problem of the next century. Particularly on considerations of availability, price, risk and consumer preference, the evidence adduced in this study seems to show that synthetic drugs have the potential to become a global problem of a magnitude comparable to that posed by the plant-based narcotic drugs.

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