UNITED NATIONS
INTERNATIONAL DRUG CONTROL
PROGRAMME

DRUG CHARACTERIZATION/ IMPURITY PROFILING

Background and Concepts

MANUAL FOR USE BY NATIONAL
LAW ENFORCEMENT AUTHORITIES AND
DRUG TESTING LABORATORIES

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United Nations Office
for Drug Control
and Crime Prevention

UNITED NATIONS INTERNATIONAL DRUG CONTROL PROGRAMME
Vienna

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MANUAL FOR USE BY NATIONAL LAW ENFORCEMENT AUTHORITIES AND DRUG TESTING LABORATORIES

Scientific Section

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PURPOSE AND USE OF THE MANUAL

Worldwide, characterization/impurity profiling of seized drugs is increasingly viewed as a valuable complement to routine law enforcement investigative work, adding valuable, scientific information in support of law enforcement intelligence gathering and operational work. In principle, and provided the existence of an adequate institutional framework and close cooperation between the different authorities, drug characterization/impurity profiling studies can help to answer a wide variety of questions ranging from dealer-user relationships, drug source, distribution networks, and trafficking routes to manufacturing methods and precursors used. Some of that information may also be used by regulatory authorities, for example, to identify precursors and other chemicals for control.

In practice, however, there is frequently a discrepancy between the enthusiasm for setting up characterization/profiling programmes and the expectations associated with such programmes on the one hand, and the acknowledgment of individual roles and responsibilities and the operational use of their results on the other.

The present manual is intended to fill this gap by providing an introduction not only to the concept and operational value of characterization/profiling, but also to its limitations. The manual is mainly aimed at law enforcement and laboratory personnel intending to set up operational programmes for drug characterization/impurity profiling.

Subsequent manuals will deal with individual drugs and the chemical analytical approach to their characterization/impurity profiling. The present manual, and other manuals, dealing with the identification and analysis of various groups of drugs under international control can be requested from UNDCP's Scientific Section (see address below).

UNDCP's Scientific Section would welcome observations on the contents and usefulness of the present manual. Comments and suggestions may be addressed to:

Scientific Section
Policy Development and Analysis Branch
Division for Operations and Analysis
United Nations International Drug Control Programme
Vienna International Centre, VIC
P.O. Box 500
A-1400 Vienna
Austria
Fax: +43-1-26060-5967
e-mail: Lab@undcp.org

01-83778_pre.p65 3 23/01/2004, 11:11

CONTENTS

01-83778_pre.p65 5 23/01/2004, 11:11

Summary

1. Drug characterization studies can provide information useful for drug law enforcement authorities. Chemical links between samples can be established, and material from different seizures can be classified into groups of related samples. Consequently, and most useful for law enforcement authorities, specific links for instance between suppliers and users can be established, drug distribution patterns/networks can be built up, and the source, including the geographic origin of drug samples may be identified. The exact purpose of any comparative study determines the analytical approach. The forensic chemist has to take care in interpreting the results, taking into account peculiarities of different drug types and the implications of the presence or absence of different types of impurities, namely manufacturing impurities and cutting agents. Close cooperation between laboratory and law enforcement personnel is essential to maximize the operational value of drug characterization studies for law enforcement investigative work.

Introduction

2. Whether ''plant-based', such as heroin, cocaine or cannabis, or synthetic, such as the various amphetamines, illicit drugs are normally complex mixtures which rarely contain the drug alone. As a consequence of the crude clandestine laboratory conditions under which they are produced, their chemical composition shows large variability. As well as containing the drug itself, samples may contain one or more of the three different types of key components:

- ❒ **natural components** present in raw materials (e.g., coca leaf, opium) used for the production of certain ''plant-based' drugs such as cocaine or heroin, which are co-extracted during drug production, and which are not completely removed from the final product,
- ❒ **by-products** generated during drug manufacture and related to the method of manufacture, and
- ❒ **cutting agents** which may be added at any point in the distribution chain, subsequent to drug manufacture.

3. Although all samples of the same drug prepared in the same way could be expected to contain the same impurities (excluding cutting agents which may be added at any stage in the distribution chain), their relative concentrations may show large variations. These variations may be attributed to the exact nature of the starting materials or to the specific method by which the drug has been processed, manufactured, distributed, or stored.

4. Detailed chemical analysis of drug samples enables measurement of the relative concentrations of major, minor and trace components (with appropriate analytical methods, complex chemical profiles can thus be obtained with different drug

01-83778_1.p65 1 23/01/2004, 11:11

samples). By such an approach, a characteristic chemical signature can be assigned to every drug sample. These **impurity profiles** may contain natural components, by-products and cutting agents. Examination of all the components of a sample, in theory, provides a complete "history" of the sample, and may therefore play a key role in characterizing samples.

I. Drug characterization studies: possible information

5. Law enforcement authorities often require evidence to link drug dealers and users; or they may want information on local distribution networks. Forensic laboratories are then asked to determine whether samples of seized drugs are related. By identifying similarities and differences between drug samples, the information generated by drug characterization studies can be used to help answer the following questions:

- ❒ are two or more drug samples connected?
- ❒ does this relationship provide a link between, for example, a drug dealer and a user?
- ❒ does the relationship between samples provide any useful information relating to local, national, regional or international drug supply and distribution networks or any information as to the extent of such networks?
- ❒ where does the sample come from (e.g., geographic origin, laboratory source)?
- ❒ what is the method of clandestine drug production? Which specific chemicals are employed in the manufacturing process ?

6. From an investigative point of view, sample characterization studies can therefore be carried out either for **evidential** or for **intelligence purposes**. They may thus be used either to help to confirm a connection between two (or more) samples in, for example, drug supply cases for prosecution purposes. Or they may be used to provide more general intelligence information such as the identification of local, regional or international distribution networks and sources of drug supply, in support of law enforcement investigations.

7. Depending on the nature of the drug sample investigated, the information generated through drug characterization studies may be used to identify from where, how, and to what extent the drug has been distributed. It may be used to provide background intelligence on the number of sources of drugs, on whether those sources are within a country or are "internationally" based, and on points of drug distribution and drug distribution networks. Information from drug characterization studies may also be used to estimate how long a particular laboratory has been operating, and to assess the scale and output of a drug operation.

8. At the national and international levels, examination of samples may provide valuable information to identify new or established trafficking routes and distribution patterns. Further, in some cases, the identification of geographic origin (region or country), and sources of international supply, may be used to estimate what percentage of the drug reaching a country has come from which of the different drug producing areas of the world. Drug characterization/impurity profiling may also assist in the identification of output from new illicit laboratories, and in the moni-

01-83778_1.p65 2 23/01/2004, 11:11

toring of common methods used for clandestine drug manufacture. This, in turn, may provide information helpful to the maintenance of other intelligence gathering tools, for example, precursor monitoring programmes. Finally, drug characterization studies may provide supportive evidence in cases where a differentiation of illicitly manufactured drugs from those diverted from legitimate sources is required.

9. The *Annex* provides some more scientific/technical details and background information necessary to appreciate both the potential and the limitations of drug characterization/impurity profiling studies, and the conclusions which can be drawn from them.

II. Operational value of drug characterization studies for law enforcement investigations

10. From an investigative point of view, drug characterization/impurity profiling studies can serve different purposes; in particular, they may help to: *(a)* establish specific links between two or more samples; *(b)* classify material from different seizures into groups of related samples, thus building up distribution networks; and *(c)* identify the source, including the geographic origin, of a drug sample. This information may be used for evidential purposes, or it may be used as a source of intelligence to identify samples which have a common history. A fourth purpose of drug characterization is to monitor clandestine drug production methods, and the chemicals employed.

11. Drug characterization is a multi-disciplinary collaborative exercise. Maximum usefulness of drug characterization studies can only be expected if close collaboration between laboratory personnel, police and customs authorities, and mutual understanding of the purpose, needs, possibilities and limitations of drug characterization/impurity profiling studies, are ensured. Since the specific aim of any comparative study determines the analytical approach, there is thus the implicit need for law enforcement personnel to be clear in specifying the information they expect from the forensic scientist.

12. It is also important to recognize that drug impurity profiling is not a routine analytical technique. In order to allow more insight into a seized drug sample than by normal chemical analysis, and to identify any links between two or more seized drug samples, experienced chemists and dedicated equipment are required. Moreover, any drug characterization/impurity profiling programme must be ongoing to build appropriate databases of results for interpretative purposes.

13. The practical value of drug characterization/impurity profiling studies for routine law enforcement investigative work in the four different areas outlined above can be summarized as follows:

A. Establishing specific links between two or more samples

14. Attempts to link samples are aimed at establishing a connection between the samples. Ultimately, that information may be used by law enforcement to establish links between different individuals from whom those samples were seized. Links

01-83778_1.p65 3 23/01/2004, 11:11

between samples can be established at various levels, such as source (drug production) or the different stages of drug supply. The fact that impurity profiles can be shown to coincide is of high evidential value, particularly in local distribution cases such as dealer/user cases. Ultimately, the establishment of a relationship between two drug samples may have a major impact on charges/penalties for the individuals involved (e.g., trafficking charge versus possession, etc.).

15. While providing sound scientific facts, however, chemical characterization studies are only a part of drug comparisons work overall, particularly in cases for evidential purposes where evidence of links is to be presented in court. Results have to be complemented by other information about the samples in question, for example on purity, appearance, packaging, etc, and with information relating to the presence or absence of cutting agents.

B. Establishing drug distribution patterns

16. It is possible to classify material from different seizures into groups of related samples. The identification of such groups may provide useful information in relation to trafficking patterns and distribution networks. Established groups may represent different laboratories or different drug related organizations. The size of a group and the time span over which samples falling within the group have been seized can furnish information on the scale and period of drug operations. Chemical comparisons of clandestine drugs are particularly useful for the investigation of small-scale or local drug supply networks. Such information is, in turn, of value in relation to the confiscation of financial assets.

17. For *natural and semi-synthetic drugs*, such as cocaine, heroin or cannabis, the establishment of distribution patterns and networks is not easy. This is largely the consequence of the nature of clandestine production processes of such drugs, namely the absence of distinct production "batches" (see *Annex* for further details). Moreover, the nature of international trafficking in natural and semi-synthetic drugs is frequently such that the product of a laboratory operation at any given time ("batch") may be distributed in different supply chains, to a variety of destinations. As a consequence, the use of laboratory resources for chemical comparison of such samples would appear to be an ineffective approach to drug law enforcement; it would be unrealistic to expect a collation of regional or even international results from a single "batch" of drug in such a way that enforcement agencies could act positively on the information. Chemical comparison of such samples may thus not help to target major trafficking organizations, since a sufficiently large information base could probably never be developed to allow identification of related seizures in large networks.

18. In the case of *synthetic drugs* such as amphetamines, by contrast, large groups of related samples can be identified, both nationally and internationally (see *Annex* for further details). This is of value in that it lends drug enforcement agencies both the time and the opportunity to investigate and then follow up background information associated with a series of related drug seizures. Good intelligence about major dealers in an operation may thus be obtained, and major centres of drug supply may be identified. While this is certainly realistic on a national basis, with improved cooperation between forensic chemists and law enforcement personnel across borders, the approach may also be possible on a regional and even international basis.

01-83778_1.p65 4 23/01/2004, 11:11

C. Identifying the source of drug samples

19. The main aim of determining the source of a drug sample is to identify its geographic origin, the clandestine drug production unit/chemist, or the source of supply or distribution of the sample.

20. In practice, however, assigning regions/countries of origin to drug samples is probably only relevant to routine law enforcement investigations in cases of importation charges. In general, the origin of drugs such as cocaine, heroin and cannabis is well known (for synthetic drugs, it is in their very nature that the geographic origin cannot be derived immediately (see *Annex*)). Moreover, specific knowledge of the region of origin of a drug would not, necessarily, be of great value in limiting traffic of a drug into a country; whether heroin, for example, originates in South West or South East Asia is of little concern to the practical interdiction of the drug along the supply routes. By contrast, determining the geographic origin of a drug sample may be useful for international policy initiatives, or in cases where evidence is sought to identify the exact origin of a sample.

21. As a consequence, identifying the source of supply is mainly used to link drug samples to specific illicit laboratory operations, and to establish sources of distribution.

D. Monitoring methods used for clandestine drug manufacture

22. Detailed examination of impurity profiles and identification of impurities may provide information on the method and conditions of drug synthesis, and of the chemicals used. Qualitative information thus generated may be a valuable tool to regulatory authorities, for instance, to identify new targets in precursor monitoring programmes and to alert to new drug trends. While this is obviously more relevant for synthetic drugs, with their higher flexibility in the clandestine manufacturing process, such an approach, routinely used, may also help to identify trends in the use of solvents and other chemicals for heroin and cocaine processing.

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23. Section 4.A in the *Annex* provides further practical details and scientific/technical aspects for consideration when carrying out drug characterization/impurity profiling studies, interpreting the results of such studies, or using them operationally.

01-83778_1.p65 5 23/01/2004, 11:11

Annex

SCIENTIFIC/TECHNICAL BACKGROUND TO DRUG CHARACTERIZATION/IMPURITY PROFILING STUDIES

1. Introduction

1. In order to explore the potential of comparative chemical analysis and to appreciate the difficulties in drawing conclusions from such studies, it is necessary to consider *(a)* the sources of information available to the forensic chemist for drug characterization/impurity profiling studies, as well as *(b)* the implications of the different stages of drug production and the different stages in the drug supply chain for the chemical profiles of drug samples.

2. Sources of information for drug profiling and characterization

2. Whether drug characterization work is for evidential or intelligence purposes, it is advantageous to obtain as much information on a drug sample as possible. The forensic chemist, in carrying out such characterization/profiling studies, largely relies on two different sources of information, **physical** and **chemical examinations**.

3. The most appropriate analytical approach for drug characterization studies depends on the type of sample, i.e., tablets, capsules, powders, liquids and "natural" materials (e.g., opium, cannabis products). The most simple type of investigation is a **visual inspection** of the physical characteristics of the sample. In many cases differences/similarities in, for example, the colour, texture or general appearance of samples can be observed. The forensic chemist, in combining this information with information from other sources, may be able to draw conclusions on whether or not two or more drug samples are connected.

4. Valuable information to show that samples may be more directly related can also be obtained by comparison of their **packaging** (including materials, the way of packaging, and the examination of any fingerprints on packaging), and by examination of any characteristic marks the samples may display. Different seizures of illicit tablets, for instance, may be linked to a distribution network, a single source of production, and in some cases to the actual equipment used for tableting, by examination of the defects or marks on the tablet surfaces.

5. In addition to the examination of physical characteristics, and especially where these have limited significance, samples can also be characterized by chemical analysis. The detailed chemical analysis of drug samples by modern analytical techniques assigns to every drug sample a characteristic chemical signature of major, minor and trace components. Careful examination of these **impurity profiles** offers a valuable means of comparing and grouping different seizures.

01-83778_1.p65 6 23/01/2004, 11:11

3. Chemical implications of clandestine drug production and supply

A. Clandestine drug production

6. In the case of *natural and semi-synthetic drugs* such as cocaine, heroin and cannabis products, the geographic origin of the raw materials (e.g. opium or morphine base, coca leaf, etc) and the general procedures used for the extraction, conversion and/or purification contribute impurities to the final illicit product.

7. Samples of *synthetic drugs* such as amphetamines may contain various synthetic impurities consisting of residual traces of chemicals essential to the drug manufacturing process and by-products resulting from side-reactions. The presence and relative concentrations of these impurities are dependent upon the quality of the starting materials used, the route of synthesis, the reaction conditions, the extent of purification of the final product(s), and overall, upon the skills of the clandestine chemist.

B. The concept of batch variation

8. When a drug is manufactured, separate and discrete "batches" of materials are usually processed at any one time. Because production conditions may never be reproduced exactly each time, variations will occur in the impurity content of final products from the same source, i.e., different batches from the same clandestine operator or "laboratory" will have different chemical characteristics (so-called **inter-batch variation**). In addition, because illicit products are usually non-homogenous, differences in impurity content may also be seen across a single batch of drug (so-called **intra-batch variation**). Under normal circumstances, it is reasonable to assume that inter-batch variations will be greater than intra-batch variations. However, it is difficult to say by how much samples should differ in their impurity content before they can be assumed to have come from different batches or sources.

9. Successful classification of samples is thus only possible if sufficient information is generated by the analytical method and if the variation in chemical composition observed between different batches is greater than that within the same batch. This means, in turn, that large intra-batch variations may result in a failure to match samples which are in fact related.

1. Batch variation in natural and semi-synthetic drugs

10. The potential for batch variation is particularly high with *natural and semi-synthetic drugs* because of the crude laboratory conditions associated with their illicit production. In practice, however, little is known about the extent of variation in the impurity content of samples from within one country or one regional source. Also, little is known about the size of a single production batch in the processing of such drugs, or about the extent of inter- and intra-batch variations. Moreover, with raw materials frequently being added to continuously operating production lines, the concept of batch processing for natural and semi-synthetic drugs may not mirror the actual situation.

01-83778_1.p65 7 23/01/2004, 11:11

11. In practice, the different items of large multi-item seizures of natural drugs such as heroin and cocaine are often found to be made up of materials with quite different impurity profiles. This may mean that the intra-batch variation is large or that the seizure is made up of smaller batches of drug manufactured at different times (and possibly at different locations). As a consequence, it may be difficult to link the different items by their impurity profiles had they been seized separately. Examinations of physical characteristics and/or of the materials used for packaging the different items may in this case be required to provide sufficient information for linking the samples.

2. Batch variation in synthetic drugs

12. With *synthetic drugs*, batches themselves as well as intra-batch variations are relatively small, such that in most cases there is little difference in impurity content across a single batch of drug. Samples from a single batch synthesis may therefore be linked relatively easily. (This is not the case, however, if final products are packaged while "wet", since liquids may differentially separate impurities at the "top" or "bottom" of a package.)

13. Conditions of clandestine manufacture are usually more closely controlled with synthetic drugs than with natural and semi-synthetic drugs. Inter-batch variations may thus be sufficiently small so that different batches of a drug may still be linked by their impurity profiles. Practical experience has confirmed that samples produced by an established method, though in different batches, in the same illicit laboratory may be linked by their impurity profiles.

C. Drug supply

14. The drug supply chain is long and complex, consisting of (for the sake of argument) producer, trafficker, distributor, supplier and user (see figure 1). Once the drug is processed or manufactured, a drug producer may supply one or more traffickers, a trafficker may supply one or more distributors, a distributor may supply one or more suppliers, and a supplier may supply one or more drug users. At each stage of the chain, cutting agents may be added, with the result that the drug sample, and hence the impurity profiles, will become progressively more complex. The further away from the source of the sample (whether this is the country or region of origin, or the illicit laboratory where the drug was manufactured), the greater are the chances that diluents and adulterants will have been added.

15. Similarly, at the other end of the supply chain, a drug user may obtain his drug from one or more suppliers, who in turn may obtain drug from one or more distributors. Although in practice probably less likely, the distributor may also obtain supplies from one or more major traffickers, and the trafficker may obtain his/her drug from one or more producers. It is therefore clear that samples related by source (i.e., coming from the same producer) may be distributed in separate chains of supply.

01-83778_1.p65 8 23/01/2004, 11:11

4. Drug characterization in practice: interpretation of results

A. The significance of chemical similarities and differences between drug samples

16. In a drug supply chain consisting of production (source), trafficking, distribution and supply (see *figure 1*), the following connections between two or more samples may exist: *(a)* samples may be linked by a common history (i.e., they were produced by the same producer and distributed in the same chain of supply; case 1); *(b)* they may be linked by source, but not by their distribution (case 2); and *(c)* they may be related by distribution, but they originate from different sources (cases 3 and 4). The chemical implications of these scenarios are detailed below.

17. Where the chemical profiles[1] of samples are indistinguishable (figure 1, case 1), it is clear that samples are linked by a common history; they contain the same relative proportions of co-extracted and/or manufacturing impurities, and they contain the same cutting agents. For powdered drugs this means that the samples probably come from the same source (and the same batch) and are probably associated with the same distribution network; it would be unlikely that the same cutting agents would have been added to the samples in exactly the same quantities in different chains of supply.

18. It is important to recognize that a chemical link between the impurity profiles of two drug samples does not necessarily signify a direct link between the individuals associated with those samples; two or more unrelated drug traffickers, for instance, may each have separately imported small portions of a larger single batch. In the same way, results from drug comparisons work used without input from intelligence sources and/or additional information on physical properties, can not prove, for example, that a specific sample in the hands of a drug user came from a supply of drugs in the possession of a local dealer: two or more local dealers may each have obtained the same "type" of drug sample from a single wholesale consignment.

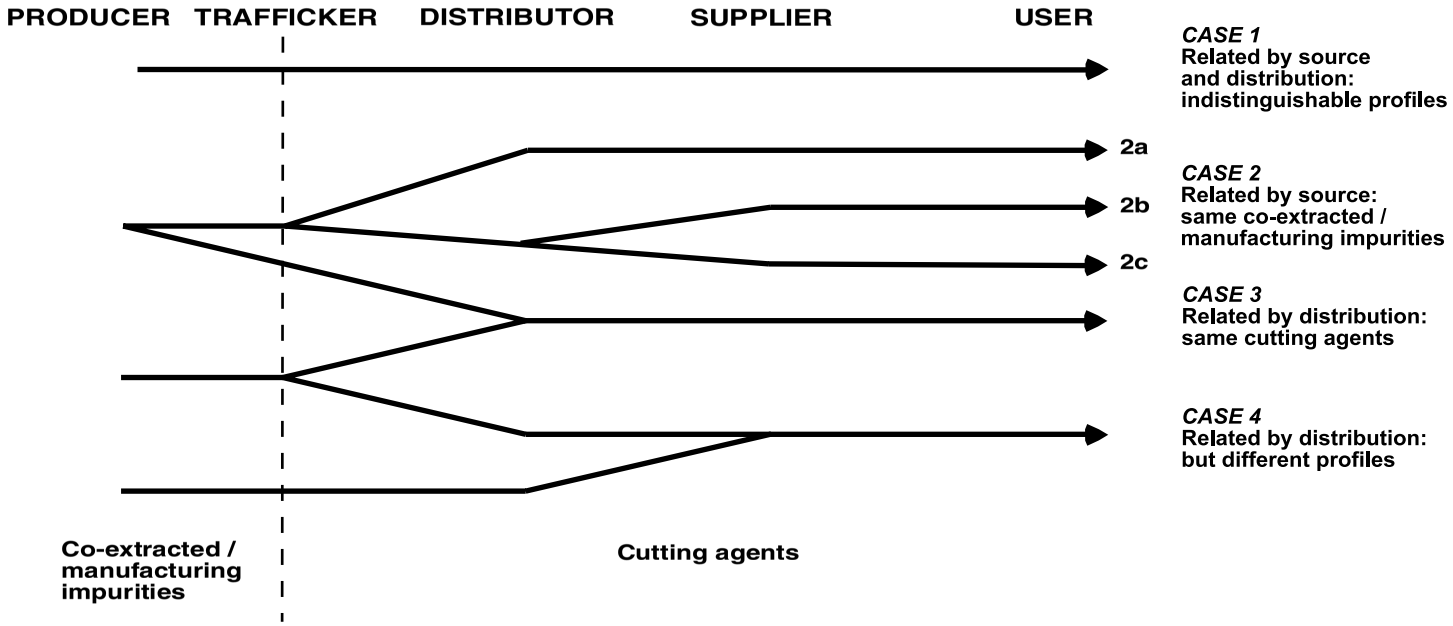
19. In cases where chemical profiles are significantly different, it is clear that there is no chemical link between the samples. However, there is always the possibility that the samples may be related (case 4): they may have been sold by a local dealer who has diluted his drug supply using different cutting agents or who has obtained his supplies from more than one wholesale source. At the international level, the samples may represent products from different manufacturers brought together for final processing and/or distribution as a single consignment.

20. Chemical profiles of samples from a common source may differ if the samples are seized at different levels in the distribution chain, or if the samples are distributed in different chains. Cutting agents may be added at different stages of distribution, and different cutting agents may be added by different dealers. Consequently, samples will have the same relative proportions of co-extracted and/or manufacturing impurities but are likely to contain different cutting agents (cases 2a-2c). While such samples are probably related by source, they are unrelated by distribution and do not have the same "history". Caution should be exercised when interpreting such results, because chemical profiles may suggest that they are not linked.

[1]The chemical profile of a sample is understood to be the profile of the co-extracted and manufacturing impurities (impurity profile), and the cutting agents.

01-83778_1.p65 9 23/01/2004, 11:11

Figure 1. The drug supply chain and its impact on chemical profiles



21. It is also difficult to establish a connection between samples which are shown to contain similar proportions of the same cutting agents but which differ in the relative proportions of co-extracted and/or manufacturing impurities (case 3). Consequently, while the samples are related by distribution, chemical profiles may again suggest that the samples are not linked. This situation is unlikely at the major distributor level where "wholesalers" are likely to obtain supplies from a single source. It is more common at the local level where a dealer may obtain drugs from a number of sources and then dilute the different types of sample with the same cutting agents.

22. Practical experience shows that the chemical profiles of samples with the same history (i.e., samples from the same source and distributed in the same chain) are often very similar, but rarely indistinguishable. Variability in profiles is generally related to inter- and intra-batch variations introduced during drug manufacture. Homogeneity of samples can also be affected by poor mixing or addition of cutting agents. This, again, makes comparison studies more complex.

23. In many cases, physical inspection of samples (e.g. an examination of punch marks) can provide additional evidence of direct links between samples. However, in cases of tableted drugs where drug production and tableting do not necessarily take place in the same location, similarities in physical characteristics between different tablet seizures simply suggest a relationship at the level of the tableting laboratory, while the drug powders may be from different sources. Conversely, different physical shapes do not necessarily mean that there is no relationship between two samples; drug powders manufactured in the same batch may be tableted in different batches using different moulds or different tableting machines.

B. Establishing specific links between two or more samples

24. Irrespective of the equipment and software available in a laboratory carrying out profiling studies, the results of such studies have to be interpreted carefully by an experienced analyst, especially if those results are to be presented in court. A measure for the validity/quality of the results and the conclusions drawn from them is the **strength of evidence**.

25. The strength of evidence of a link between samples, as assessed by examination of profiles of those samples, is determined by two factors, the closeness of their correlation and the frequency of the particular pattern of the profile. The strength of evidence may be increased, if it can be shown that the pattern of the particular profiles is of an unusual type, i.e., of low frequency, compared to the patterns of previously analysed samples. The strength of evidence may also be increased by an assessment of how common or unusual various individual components are. For example, the presence of unusual cutting agents may provide a critical source of information to help compare and link samples, and provide evidence of direct (immediate) links in conspiracy or dealer/user cases. In addition, the overall strength of evidence may be further improved by combining information from chemical profiling studies with information from other investigative approaches (e.g., that provided by examination of packaging materials, etc.).

26. Several factors may complicate the establishment of specific links between drug samples. One such factor, independent of source or distribution, is the "ageing" of drug samples, i.e., a change in the impurity content of a drug sample due to decomposition of the main drug and/or accompanying impurities as a result of the

01-83778_1.p65 11 23/01/2004, 11:11

conditions to which the sample is subjected, in particular exposure to light, heat and/or air. Chemical comparison of drug samples related by source, yet exposed to different environments during the supply chain, could thus suggest that the samples are not linked. In a similar way, certain aggressive cutting agents (e.g., ascorbic acid) may alter the composition of a drug sample over time so that the impurity profiles of samples related by source but seized at different stages of the supply chain may no longer be the same. The net result is that the chemical comparison of older samples may not provide any useful information to help link samples together.

C. Establishing drug distribution patterns

27. For *natural and semi-synthetic drugs*, the prospects of establishing distribution patterns and networks associated with specific drug manufacturers or trafficking organizations are limited if they are only based on chemical profiles. This is largely due to the fact that there is little or no information on what constitutes a "batch" of a natural/semi-synthetic drug. Moreover, it is by no means certain that large illicit consignments of such drugs constitute the product of a single batch (or even of one drug-producing region). There is also only a limited amount of information on the extent of variation of manufacturing impurities across batches, countries or geographic regions with drugs of this type. Consequently, it is extremely difficult to link together those samples manufactured by the same producer in different batches, while at the same time discriminating against those samples manufactured by a different producer in the same region. However, using multiple analytical techniques with at least one independent method and with support of intelligence information and physical properties, such a task is not impossible.

28. In addition to difficulties in grouping natural and semi-synthetic drugs based on the presence of co-extracted and manufacturing impurities, the nature of international trafficking in such drugs further complicates attempts to build up major national or international distribution networks: samples from the same "batch" (i.e., the product of a laboratory operation at a given time) are likely to be distributed in different supply chains (likely to be reflected by the use of different cutting agents or packaging) to a variety of destinations. Consequently, in building up major national or international distribution networks, the presence of unusual cutting agents, and any other relevant information, may therefore be used to group related samples, in addition to the presence of the manufacturing impurities.

29. Moreover, in attempts to build up major international distribution networks, the presence of some characteristic cutting agents may also be of further significance, because it is believed that some of these substances are added to the illicit drug material close to the source of drug manufacture. Consequently, those groups which are made up of samples containing the same characteristic cutting agents may be associated with specific production or trafficking organizations.

30. For *synthetic drugs*, provided there is no change in the method or the conditions of drug synthesis, it is possible to build up a network of related samples (i.e., a series of samples produced by the same illicit chemist and/or at the same laboratory) over a period of time, because inter-batch variations in impurity content of samples are believed to be relatively small. Similar to the situation with natural and semi-synthetic drugs, the presence of some characteristic cutting agents in synthetic drugs may be indicative for specific production or trafficking organizations.

01-83778_1.p65 12 23/01/2004, 11:11

D. Identifying the source of drug samples

31. Natural and semi-synthetic drugs on the one hand, and synthetic drugs on the other, differ in their manufacturing processes as well as in the nature of the starting materials, i.e., natural raw materials bound to certain geographic regions, or chemical precursors, respectively. As a consequence, conclusions which can be drawn from the detailed chemical analysis of either drug type are different: while for natural and semi-synthetic drugs, at least in theory, an assignment of geographic origin is possible, this is not the case for synthetic drugs.

32. In general, in characterization studies aimed at identifying the source or geographic origin of drug samples, it is not necessary to examine the pattern of cutting agents in the sample as these (in most cases) will bear little or no relation to the source. Particular efforts have to be directed at concentrating on the examination of impurity profiles of co-extracted and/or manufacturing impurities in different samples.

1. Natural and semi-synthetic drugs

33. The chemical characteristics of natural and semi-synthetic drugs are relatively specific to particular **geographic areas** of the world because, within any one region, the factors which influence the natural impurity content of drug samples (e.g., soil, climatic conditions, etc) may be sufficiently consistent. In addition, clandestine production methods in any one region are believed to be closely related. Consequently, samples of drugs of the same type made by different manufacturers in the same country or region contain similar proportions of the same core manufacturing impurities and may therefore, in theory, be classified together (the basis of assigning regions of origin).

34. As a consequence, where a drug sample exhibits the impurity pattern of a known manufacturing process, and that pattern is characteristic, the origin of the sample may be attributed to the geographic region or regions where the process is known to be employed. More specifically, a given sample may be assigned to a specific region of origin, if its impurity profile has the characteristic impurity pattern of a sample known to be from that region. A prerequisite to this is the existence of a well maintained, representative and up-to-date collection of samples of authenticated origin. In the same way, the origin of samples of the raw materials (e.g., coca leaves, opium) may be identified.

35. However, it is important to recognize that the chemical characteristics of a given natural or semi-synthetic product could be altered or disguised if, for example, seedstock was internationally exchanged, or if significant changes to the drug manufacturing process were introduced by drug producers. As a result, chemical profiles would bear little or no relationship to previous samples from the same regional source or drug producing organization, which would, in turn, severely complicate the interpretation of chemical profiles and correlation with geographic origin. Obviously it then becomes difficult if not impossible to classify samples from chemical profiles alone. The same would be true if the different manufacturing methods were used freely around the world.

36. In contrast to the identification of the geographic region of origin for natural and semi-synthetic drugs, it is not possible in practice to relate a series of batches

01-83778_1.p65 13 23/01/2004, 11:11

of such drugs to a single **source of drug production** (i.e., the production site or specific "batch"). This is a consequence of the nature of the clandestine production process of such drugs and the limited knowledge about batch variation with this type of drugs (see Section 3.B of this *Annex*). However, as noted above, in cases where it is known that certain cutting agents are added to natural drug materials close to the source of drug manufacture, the presence of some characteristic cutting agents may be of significance and may help to relate samples to specific production organizations.

2. Synthetic drugs

37. For *synthetic drugs*, practical experience has shown that the impurity profiles of products from one illicit laboratory are characteristic, at least for some drugs. Consequently, samples can be classified into groups identified by their chemical profiles; a given sample or group of samples may be associated with an individual illicit chemist or laboratory, thus enabling samples from the same source to be linked together. While such chemical profiling information cannot help to identify the geographic origin of a synthetic drug sample (i.e., the location of the illicit laboratory), it may be used to relate samples from a series of batches to a single chemist or laboratory, and to identify the source of supply or distribution.

E. Identifying and characterizing the specific starting materials employed in clandestine drug manufacture

38. In a similar way to the chemical characteristics of finished drug products, the corresponding starting materials (natural raw products and precursor chemicals) used in the clandestine production process may also contain certain impurities. The impurity content and the type of impurity may vary depending on the nature of the starting material (e.g., raw opium or a chemical substance), on whether a precursor chemical was diverted from legitimate sources, or was itself manufactured clandestinely. The identification of characteristic impurities (or patterns of impurities) in precursors may, therefore, help to relate them to a clandestine (or commercial) source.

39. In addition, knowledge about the presence of certain impurities in starting materials may also help to relate finished drug products to the corresponding starting materials (and ultimately to their source). To this end, an understanding of the mechanisms leading to the presence of impurities in clandestine drugs is important: impurities may already be present in the starting materials, and may be carried over unchanged to the final product; they may arise from reactions of original impurities present in starting materials; or they may be generated *de novo*, as by-products during drug manufacture (they are thus indicative of certain manufacturing routes, but less useful for the identification of the sources of starting materials). It is this knowledge which enables the forensic chemist to draw correct conclusions about the use of certain starting materials, or specific "batches" of them, in clandestine manufacturing processes.

01-83778_1.p65 14 23/01/2004, 11:11