

ORGANIZATION OF AMERICAN STATES



INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION

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FINAL REPORT
(Preliminary Version)

GROUP OF EXPERTS ON PHARMACEUTICAL
PRODUCTS
Buenos Aires, Argentina

ORGANIZATION OF AMERICAN STATES



INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION

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**GROUP OF EXPERTS ON
PHARMACEUTICAL PRODUCTS
August 24 - 26, 2005
Buenos Aires, Argentina**

**OEA/Ser.L/XIV.4
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August 29, 2005
Original: English**

FINAL REPORT

Preliminary Version

I. BACKGROUND

The Group of Experts on Pharmaceutical Products met on May 31 to June 2, 2004 in Brasilia, Brazil. Mr. Kleber Pessoa de Melo, Chief, Unit of Controlled Substances, ANVISA, Ministry of Health of Brazil chaired the meeting. The Executive Secretariat presented the report from this meeting for the consideration of the CICAD Commission during its thirty-sixth Regular Session in Washington, D.C. (December 7-9, 2004).

The Commission accepted the report and the recommendations offered by this Group of Experts. In doing so, the Commission directed that the Group should meet during 2005 to deal with the recommendations in the aforementioned report and possibly identify new issues related to the control of pharmaceutical products.

The Group of Experts met in Buenos Aires, Argentina from August 24 to 26, 2005.

II. PROCEEDINGS

A. PARTICIPANTS

1. MEMBER STATES OF CICAD

Forty-two experts from the following member states participated in this meeting: Argentina, Bahamas, Barbados, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, Guatemala, Haiti, Jamaica, Mexico, Panama, Peru, Trinidad and Tobago, United States and Uruguay.

B. SESSIONS AND ORGANIZATION OF THE MEETING

1. OPENING SESSION

The opening session for the meeting of this Group of Experts took place in the Hotel Madero In Buenos Aires on August 22, 2005. This was a joint opening session for this meeting and the meeting of the Group of Experts on Pharmaceutical Products - Dr. José Ramón Granero, Secretario de Programación para la Prevención de la Drogadicción y Lucha contra el Narcotráfico de SEDRONAR, welcomed the participants to the meeting and offered welcoming remarks.

2. WORKING SESSIONS

The Group of Experts on Pharmaceutical Products met during five (5) working sessions to review and finalize the model guide for industry and a second guide for inspection; to consider the control of products containing ephedrine and pseudoephedrine; to examine possible controls of the sale of drugs over the Internet. A copy of the schedule of activities is attached.

During the last meeting of the Group of Experts, the Executive Secretariat was asked to undertake consultation and other research related to a number of issues discussed during that meeting. The Executive Secretariat delivered a short report on the status of these assignments. Some of this information was used to facilitate discussions during this meeting and help to define a course of action for the Group.

At the beginning of the meeting, each participant was asked to identify one or two concerns that they had regarding the control of pharmaceutical products. These issues served as the basis for discussions during this meeting or for inclusion in the plan of action for future proposed meetings. The Group identified the following issues:

- Internet sales of drugs
- Pharmaceutical products containing Ephedrine and Pseudoephedrine
- Ketamine
- Counterfeit drugs, smuggling and effective border controls
- Synthetic drugs
- Awareness by the general public and health professionals regarding the problems of prescription drug abuse
- Inter-agency cooperation and coordination
- Computerized systems for the control of pharmaceutical products such as the National Drug Control System (NDS)

During the working sessions, participants delivered a number of presentations on various issues related to the control of pharmaceutical products.

The delegation of Mexico delivered a presentation on Pre-Export Notification for pharmaceutical products and the use of forged documents. The presentation included an overview of the system in place in Mexico to control the import and export of pharmaceutical products through the use of permits. In one actual case, Mexican officials discovered an attempt to use forged import documents for an export to the of pharmaceutical products to Dominican Republic.

Based on this case, Mexican officials implemented a procedure that includes the verification of import/export forms with the originating country. To this end, it is

important that officials are familiar with the permit forms used by trading partners. As such, the Mexican delegation offered to compile the import/export formats for psychotropic drugs used by all CICAD members. This compilation can then serve as a guide for the issuance of export permits which require a copy of the corresponding import permit. Once completed, the Executive Secretariat will assist with the distribution of this compilation to all member states.

Member states were asked to submit copies of their import and export permits to the following point of contact:

By Mail:

GRETA SPOTA
DIRECCION DE REGULACION DE ESTUPEFACIENTES Y
PSICOTRÓPICOS
Monterrey 33, col Roma
CP. 06700, México D.F.

By email:

prenotificacionmex@salud.gob.mx

The delegation of the United States delivered a presentation on the monitoring and investigating the sale of drugs on the Internet. This is a growing problem among CICAD member states that presents many new challenges for officials concerned with the control of drugs.

The presentation included basic information on how operations to sell drugs over the internet are structured and investigative mechanisms and procedures that law enforcement officials can implement to pursue these cases. In addition, the presentation included information concerning a large internet drug sales operation that was spread around the world. The successful conclusion of this case required cooperation, coordination and the exchange of information among law enforcement agencies and other organizations and officials in many countries. The presentation underlined the international character of this growing problem and the corresponding need for international cooperation to pursue these cases.

This presentation generated a great deal of discussion. Most participants suspected that in some way or another, their country was affected by internet drug sales. Having said that, they were not in a position to assess the extent to which this was taking place, the problems it was causing or how to proceed to address the problem. As such, a working group was established to examine this issue in greater detail.

A. Review of Manuals/Guides

Model Reference Guide for Inspections for the Control of Pharmaceutical Products.

The guides developed by the Group of Experts are intended to serve as models that member states can modify and supplement based on limitations, requirements or circumstances that exist nationally.

The delegation of the United States presented a draft of the **Model Reference Guide for Inspections for the Control of Pharmaceutical Products.**

The Group of Experts reviewed, modified and finalized this draft guide (copy attached).

The Group submits this model guide for inspection to the Commission for its consideration. Further to review by the Commission and the inclusion of any changes that it requests, the final version of this model guide will be available for posting to the CICAD web page.

Model Reference Guide for the Pharmaceutical Industry

During the last meeting of the Group of Experts on Pharmaceutical Products, the delegations of Colombia and Costa Rica offered to draft a **Model Reference Guide for the Pharmaceutical Industry** .

The delegation of Colombia introduced the document to the Group. In doing so, the authors indicated that while the current draft was very comprehensive, they felt that there remained other elements that should be included in the document. While it might be possible for the plenary to undertake this task, in the interest of time, the authors proposed to continue their work on the draft and present it at the next meeting of the Group in 2006.

A. Ketamine

Ketamine is non-barbiturate, rapid-acting anesthetic that is used primarily in veterinary medicine. At the same time, it is increasingly being used by young people as a “club drug”. Because of its appearance, Ketamine is often mistaken for cocaine or crystal methamphetamine. Some reports indicate it is sometimes sold as MDMA (Ecstasy) and mixed with other drugs such as ephedrine and caffeine.

A number of participants in the Group identified a growing problem of abuse involving Ketamine. For this reason, a working group chaired by Argentina was formed to examine this problem further. The working group examined the problems of abuse presented by Ketamine in the CICAD member states. In many instances, member states were not clear on how best to deal with this problem. As such, the working group proposed to develop an information bulletin or notice of alert for the Executive Secretariat to distribute to CICAD member states and post on the web page. The note will outline the problems and dangers associated with the use or abuse of this drug to increase awareness among CICAD member states.

The working group, chaired by Argentina, offered to develop a self-evaluation questionnaire on the control of Ketamine. Once finalized, the Executive Secretariat will coordinate the distribution of the questionnaire to member states and compile the replies for presentation and discussion during the next meeting of the Group of Experts.

B. The Control of Drug Sales Over the Internet:

The illicit sale of drugs over the internet is a growing international problem. This includes the sale of pharmaceutical products and illicit drugs. Organized groups are establishing complex electronic “structures” to promote and sell these substances using the internet. These groups are able to circumvent traditional controls to make these substances available to users around the world. For the most part, in the case of the pharmaceutical drugs, there is no real patient-physician relationship or traditional prescription. In some instances the drugs may be outdated or counterfeit creating serious health implications for the users.

This is a new and growing problem against which most CICAD member states are ill prepared to deal with. There is little information as to the nature and scope of this problem in any give country. Further, most do not have the necessary systems, programs or procedures in place or trained officers to monitor, investigate and otherwise proceed with cases of illicit sales of drugs via the internet. More fundamental is the lack of necessary legislation or regulations providing the legal framework within which to execute the foregoing controls. As a starting point, the Group proposes to develop a guide or information bulletin, identifying the basic elements that countries must consider or have in place in order to effectively respond to the problem of internet sales of drugs. The delegation of the United States of America will prepare a draft for consideration by the Group at its next meeting.

Given that this is a complex and evolving problem, the Group of Experts proposes to include this issue as a standing item in its plan of action for future meetings.

Further to a very full discussion, the Group of Experts offers the following recommendations to member states regarding this issue:

- Member states are strongly urged to request training relating to the diversion and sales of pharmaceutical products via the Internet, and either on a regional or individual basis, from authorities in countries that have developed greater experience and expertise on this subject. Training should include the disciplines of investigation, customs controls, licensure, regulation and law. The CICAD Executive Secretariat should be contacted and included, as needed by the states involved, in the planning and coordination of training.
- Member states should give wide publicity and support for the education of the public and health care providers concerning the dangers and legal issues associated with Internet sales and diversion of pharmaceutical products. The CICAD Executive Secretariat is strongly encouraged to establish partnership with the pharmaceutical industry to provide resources and support for this venture.
- Member states should adopt laws and regulations that allow procedures for the investigation and enforcement of the laws that prohibit Internet sales of pharmaceutical controlled substances and precursor chemicals. Such laws should include, at a minimum, the authority and ability to intercept Internet communications, to provide for preservation of electronic communications, to make undercover purchases, and exchange information to other member states.
- Member states should establish a mechanism to grant preliminary approvals for business licenses and permits for Internet sales and business activities, assigning responsibility for implementing this process to one department or ministry such as the national ministry of health.
- Member states should respect the legislation and regulations of other member states by denying licenses and prohibiting operations by firms that violate, or are likely to violate, international law or the law of other states through illegal Internet sales.
- Member states should exchange information on Internet sales and diversion, and also provide relevant information to the INCB. This should include the timely completion and submission of the INCB survey on Internet sales and legislation, dated 25 July 2005.
- Member states should cooperate on investigations via information exchange and informal and formal legal assistance. Particular emphasis

should be placed on financial aspects of investigations and applicable administrative, civil and criminal proceedings.

- Member States should encourage various sectors of industry to voluntarily support efforts to prohibit illegal sales of pharmaceutical products and precursor chemicals via the Internet. These should include, but are not limited to transportation services, financial services, ISP's, manufacturers and distributors.

C. Diversion and Control of Pharmaceutical Products containing Ephedrine and Pseudoephedrine:

The delegation of Mexico delivered a presentation, joint prepared with Canada and the United States on problems related to the control of raw materials and pharmaceutical products containing ephedrine and pseudoephedrine.

Ephedrine and pseudoephedrine are commonly found in cold products, which are readily available over-the-counter in most countries. At the same time, these drugs are precursors in the illicit production of methamphetamine. While controls are in place for the raw materials of ephedrine and pseudoephedrine and single entity products, there are no controls over combination products. As such, traffickers are diverting large quantities of "combination" pharmaceutical products containing pseudoephedrine.

The production and illicit use of methamphetamine is of particular concern to a number of CICAD member states. Having said that, this drug and other chemical-based drugs represent a growing problem among other CICAD member states. Through their presentation, the delegations in question offered some suggestions for action by this group, the Commission and the CICAD member states. The presentation generated considerable discussion that led to the formation of a special working group to examine this matter further.

The working group noted the need to balance controls and availability or access to these drugs. It is clear that the illicit production and use of methamphetamine is not apparent or clearly defined in some member states. It is also clear that some member states do not have controls in place to avoid exploitation by criminal groups seeking products containing ephedrine and pseudoephedrine. In an effort to increase awareness regarding the problems presented by these combination products, the working group prepared a short background paper and a checklist (copy attached) that CICAD member states might use to help minimize the diversion of these products.

The Group submits this background paper and checklist to the Commission for

its consideration. If approved and accepted by the Commission, the final version of this paper will be posted to the CICAD web page.

The pre-export notification (PEN) process is an effective way to minimize the diversion of drugs and chemicals. While PEN's can be requested for ephedrine and pseudoephedrine in the raw, bulk form, there are no similar provisions for combination products. The most appropriate forum in which to raise this issue is the Commission on Narcotic Drugs (CND). In discussing this issue further, the Group of Experts agreed on the need to take this issue to the CND in the form of a resolution. The delegations of Argentina, Brazil, Colombia, Mexico and the United States of America agreed to work together on drafting a resolution to require or allow requests for PEN's for combination products containing ephedrine and pseudoephedrine. This resolution would be presented at the next CND meeting in March 2006. The Group also agreed that member states would work within the regional groups of the CND of which they are members to promote acceptance of the proposed draft resolution. The Executive Secretariat agreed to assist with this effort prior to and during the CND meeting.

Further to discussions by the working group and the plenary, the Group of Experts offers the following recommendations:

- That CICAD member states use the checklist provided by the Group of Experts including the promotion of implementing the PEN mechanism for pharmaceutical products containing ephedrine or pseudoephedrine.
- Building on the checklist developed by the Group of Experts, that the Executive Secretariat support its member states in developing a national capacity to identify the diversion of pharmaceutical products containing ephedrine or pseudoephedrine.
- That CICAD Commission propose a resolution to the OAS General Assembly which directs its member states to reinforce or develop and implement control mechanisms regarding single entity and combination pharmaceutical products containing ephedrine and pseudoephedrine.
- That CICAD's Executive Secretariat raise the issues and recommendations brought forward in the report to the next INCB meeting with the intention of products containing ephedrine and pseudoephedrine being included within the scope of Project Prism.

D. Issues for future consideration by the Group of Experts

Further to the round table discussion of issues of concern and those identified during the course of the meeting, the Group of Experts recommends that it meet

during 2006 to consider the following issues as part of its proposed plan of action:

- Internet sales of drugs
 - o Guide/information bulletin on the Control of Internet sales of drugs
- Synthetic (chemical-based) drugs
- Review of the Ketamine questionnaire results
- Counterfeit drugs, smuggling and effective border controls
- Finalize the draft Model Reference Guide for the Pharmaceutical Industry .
- Public awareness regarding the problems of abuse/misuse of pharmaceutical products
- Guide for health professionals on the rationale use of pharmaceutical products
- Inter-agency cooperation in the control of pharmaceutical products
- Computerized systems for the control of pharmaceutical products such as the National Drug Control System (NDS)

3. CLOSING SESSION

The Group of Experts concluded its work at 18:00 on August 26. The Executive Secretariat thanked the Chair and the Government of Argentina for their support and expressed appreciation to the members for their participation.

III. CONCLUSIONS AND RECOMMENDATIONS OF THE GROUP OF EXPERTS

RECOMMENDATIONS TO CICAD IN ITS THIRTY-SEVENTH REGULAR SESSION:

The Group of Experts on Pharmaceutical Products recommends that the Commission:

1. Consider and accept the guide or documents and direct the Executive Secretariat to post them to the CICAD web page:
 - **“Model Reference Guide for Inspections for the Control of Pharmaceutical Products”**
 - **“Ephedrine and Pseudoephedrine Use in the Illicit Production of Methamphetamine”**
2. Consider proposing a resolution to the OAS General Assembly that would direct its member states to reinforce or develop and implement control mechanisms regarding single entity and combination pharmaceutical products containing ephedrine and pseudoephedrine.
3. Direct the Executive Secretariat to raise with the INCB the issues and recommendations identified in this report concerning products containing ephedrine and pseudoephedrine with a view to including these products within the scope of Project Prism.
4. Consider and accept the plan of action proposed by the Group of Experts and directs that the Group meets in 2006 to consider the issues in the plan as well as other new trends or threats identified in the area of chemical control

ORGANIZATION OF AMERICAN STATES



INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION



MEETING OF THE GROUP OF EXPERTS CONCERNING PHARMACEUTICAL PRODUCTS

August 24 - 26, 2005
Buenos Aires, Argentina

SCHEDULE OF ACTIVITIES

Wednesday, August 24

- | | |
|---------------|--|
| 13h00 – 14h00 | Registration |
| 14h00 – 14h30 | Introduction and Review <ul style="list-style-type: none">• Background• Objectives and CICAD Commission expectations• Schedule of work• Proposed work methodology• Status report on Recommendations• Other issues |
| 14h30 – 15h15 | Roundtable introductions and identification of new issues |
| 15h15 – 15h30 | Break |
| 15h30 – 16h00 | Discussion of new issues |
| 16h00 – 17h00 | Presentation on Pre-Export Notification for pharmaceutical products (Mexico) and the use of forged documents |

Thursday, August 25

- 09h00 – 10h45** **Review and finalize the draft guides:**
- Inspection
- Industry
- 10h45 – 11h00** **Break**
- 11h00 – 12h30** **Review and finalize the draft guides (con't)**
- 12h30 – 14h00** **Lunch**
- 14h00 – 15h45** **Review and finalize the draft guides (con't)**
- 15h45 – 16h00** **Break**
- 16h00 – 17h00** **Presentation on issue of Internet sales of drugs**

Friday, August 26

- 09h00 – 10h45** **Working group discussions:**
- Internet sales
- training
- Other issues
- 10h45 – 11h00** **Break**
- 10h45 – 12h00** **Working group discussions (con't)**
- 12h30 – 14h00** **Lunch**
- 14h00 – 15h00** **Working group discussions (con't)**
- 15h00 – 15h15** **Break**
- 15h15 – 16h30** **Conclusions, commitments and recommendations for
action by the Expert Group**
- 16h30** **Closing**



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INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION

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Guide for Best Practices for Investigations of Handlers of Pharmaceutical Products



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Best Practices Guidelines for Investigation of Pharmaceutical Products

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I. Introduction

A. Background

The diversion and abuse of pharmaceutical products containing narcotic and psychotropic substances is a major and growing concern among CICAD member states. Effective control over these substances requires a strong legislative base and regulatory framework as well as comprehensive administrative and monitoring processes and procedures. This last element should include a well organized and professional inspection and investigative component.

The objective of this document is to serve as a guide to help in establishing or strengthening inspection and investigative activities related to the control of pharmaceutical products. This guide is a summary of best practices that builds on the document entitled "Elements for a National System to Control Pharmaceutical Products" adopted by the CICAD Commission in 2003. These Best Practices Guidelines presume that states either have in place or plan to adopt a legal and regulatory system generally along the lines of the Elements document.

B. Purpose

Inspections and investigations of handlers of pharmaceutical products are conducted to prevent and detect the diversion of controlled substances from legitimate to illicit channels. These inspections and investigations should be part of a national system that at the same time ensures an adequate and uninterrupted supply of pharmaceutical substances required to meet legitimate medical, commercial and scientific needs.

II. Profile of an Inspector/Investigator

The investigative team must be constituted by personnel specialized in the different areas related to the administrative, technical and investigative control of pharmaceutical drugs.

At the minimum, the team should be made up of one pharmaceutical specialist (chemist, pharmacist, pharmacologist) with knowledge in evidence gathering, and a specialist in accounting, with emphasis in documentation analysis and bookkeeping (control books, raw material logs, import, export, etc.).

Additionally, control institutions should propose and implement training

programs for investigators on the different analytical and auditing methodologies, as well as the information exchange related to the diversion of chemical substances.

III. Common Elements of an On-Site Inspection

Scope. An on-site inspection is central to any investigation of an applicant for licensure or a licensee. All on-site visits should include certain common elements and practices. This part discusses those common elements. Later parts will address additional aspects of the on-site inspection that relate to a particular type or stage of investigation.

A. Preparing

Before conducting the on-site inspection, the Inspector should check all available criminal information records and other appropriate information systems concerning the applicant. These should include a search of all required business licenses.

B. Staffing

At least two Inspectors should participate in all aspects of the on-site portion of the inspection.

C. Notice Prior to Inspection.

Except in the case of a pre-registration inspection, no advance notice should be required by law or given by the competent authority. In fact, advance notice may hamper the integrity of a periodic or complaint investigation.

D. Introduction of Inspectors

To initiate the on-site inspection, the Inspectors should present their identification to a representative of the business and state the purpose of the visit.

E. Obtaining Lawful Access

As a condition of application for licensure and for retaining a license, national laws and regulations should provide for the licensee's consent to inspection by regulatory and law enforcement authorities at reasonable times to ensure compliance or to investigate complaints. Nonetheless, access in each particular case should be through an established, lawful means.

The process is simplest in the case of a pre-registration inspection, where the applicant should welcome the visit as a pre-condition to licensure. If an applicant denies access, then the competent authority should deny the license. In other cases,

including periodic inspection and complaint investigations, the bases for gaining lawful access will vary by national law.

A reasonable series of options for obtaining lawful access is described below.

1. A Notice of Inspection, prepared on a form by the investigating entity, is the simplest means of gaining access. The Notice should contain a statement of rights and an acknowledgement of consent to inspection.

2. The representative of the business at the premises should sign the Notice form as evidence of consent. In some cases, a firm will give only verbal consent. In such cases, the Inspector should so indicate on the form. In either case, a copy of the form should be given to a responsible representative at the firm.

3. If the Notice is not effective to gain consent to enter, the Inspector may seek an Administrative Inspection Warrant (AIW) signed by a judge. The AIW allows no greater right of inspection, but the judicial backing affirms that the inspection is in fact legally authorized.

Note: A judicial order of this kind should be obtained at the outset if the Investigators suspect non-compliance, and especially criminal activity, at the premises. The basis for such warrants does not need to be suspicion or wrongdoing, but merely a valid public interest in the effective enforcement of laws and regulations. (This is called “administrative probable cause.”)

IV. Pre-Registration Inspections

Scope. A pre-registration inspection is more than a pre-condition for licensure – although that is its central legal / regulatory function. It should also try to set the applicant on a course towards full compliance with the letter and spirit of applicable laws and regulations. A good corps of licensees can even assist regulatory and law enforcement officials in doing their job to assure compliance and protect the public.

During the on-site pre-registration inspection, the Inspector should examine the following areas.

1. Accuracy and Completeness of Application

The Inspectors should review the application with the firm’s management to determine that all information regarding the proposed activity has been accurately presented. They should explain that only those activities stated on the application may be conducted, and only at the business address in the application.

2. Identification of Responsible Individuals

The Inspectors should determine who has ultimate responsibility for the operation of the firm, as well as those who will have direct control over the record keeping, security and handling of pharmaceutical substances. Sufficient information (name, address, date of birth) should be solicited to permit a follow-up review of law enforcement records.

3. Interviews

The Inspectors should interview the individual(s) with overall responsibility for the proposed operation and those persons who will be directly maintaining records and handling the pharmaceutical products.

4. Familiarization with Regulatory System

The Inspectors should ensure that the applicant is aware of and is able to comply with all provisions of the country's applicable laws and regulations. They should clarify common errors and misunderstandings of the law, and may explain any national and regional trends in diversion. For example, an applicant should be informed that a complete and accurate count of pharmaceutical products required to be taken on the date of licensure (even if zero) and every two (two) years thereafter. Requirements of other types of records, including reports of theft or loss and maintenance and retention of records, should be discussed.

5. Review of Other Relevant Licenses

The Inspectors should examine any licenses or permits otherwise required for the applicant to conduct the proposed activity (e.g., medical license, pharmacy or hospital registration, as well as general business licenses). Documents at the firm should be cross-checked with those obtained – preferably in advance -- from official public records.

6. Security

The Inspectors should perform an in-depth review of both physical security and handling procedures to determine if there are safeguards to prevent unexplained loss of the regulated products. A review of vaults, safes and storage areas is necessary to determine that they meet existing regulations. Alarm systems and alarm lines should be thoroughly tested. The effectiveness of the system as well as the security should be discussed in detail with representatives of the firm and (if necessary) the alarm company. Day to day handling procedures should be reviewed to ensure that employee theft and in-transit loss is minimized.

V. Periodic Inspections

Scope. This section covers inspections that are not for initial licensure (see Part III) or as part of a complaint investigation (see Part V). All licensed manufacturers, distributors, practitioners, importers, exporters, researchers and dispensing pharmacies should be subject to periodic on-site inspections to ensure compliance with laws and regulations. A satisfactory inspection entitles the licensee to continued licensure. An unsatisfactory inspection may lead to further action, including sanctions. This section will first review the types of periodic inspection and then discuss how the inspections are conducted.

A. Types of Periodic Inspections

1. New Licensee Re-Inspection

Licensees should be inspected within one year of initial licensure to ensure they have established good systems and patterns for compliance with the law and preventing diversion of pharmaceutical products.

2. Cyclical Investigation

A full inspection of the registrant of should occur on a cyclical basis, but not less than once every five years, for all licensees, *i.e.*, importers, exporters, manufacturers, distributors, practitioners, pharmacies, researchers and, if applicable in the national system, transporters. The inspection should include a full security, record keeping and drug accountability audit.

3. Secondary/Follow-up Inspections

A secondary or follow-up inspection occurs when an Inspector documents actionable items, (*e.g.*, by a citation or administrative action) against a licensee as a result of findings from the firm's periodic inspection. Secondary inspections are also appropriate where another inspection results in administrative action other than a resolution fully in favor of the licensee.

B. Elements of a Periodic Inspection

A periodic inspection should be divided into three phases: preparation, on-site visit and follow-up.

1. Preparation

The Investigator should examine all available information pertinent to the licensee to determine past history and complaints submitted concerning the licensee or its products. If the applicant currently operates or has operated in other states, provinces or countries, the Inspectors should check available information including through contacts with regulatory authorities of such jurisdictions to determine the applicant's history of compliance.

2. Walk-Through Visit

The Investigators should conduct a walk-through inspection of the firm's facility, gaining an initial familiarity with the firm's general procedures for handling pharmaceutical products. Also during the walk-through inspection, the Inspectors should take note of storage protocol for pharmaceutical products and the location of security devices installed by the licensee.

3. Interviews

In addition to a general review of compliance practices, the interviewing Inspectors should ask the licensee about any known or suspected diversion of pharmaceutical products or substances.

4. Additional Background Information

Inspectors should obtain on-site, or verify information from advance off-site research, the following information:

- Names, addresses, dates of birth, etc. of corporate owners and officers of the firm, as well as persons responsible for record keeping and security.
- Information concerning the location(s) of the firm, length of time in business, and length of time at the current location.
- Percentage of the firm's business in pharmaceutical products.
- Number of employees and the type of work they perform.
- Whether the firm has had any losses or thefts of pharmaceutical substances since the last investigation (if any) or since they began business, if a new firm.
- The firm's procedures and systems for:
 - pre-employment checks;
 - verification that customers are properly licensed, and for obtaining customers' license numbers; and
 - identifying suspicious and excessive orders.

4. Accountability audit of pharmaceutical products

A time-consuming but critical element of a periodic inspection is an accountability audit. A minimum of eight pharmaceutical products should be audited (assuming the firm is licensed to handle that many products). The Inspectors should select

pharmaceutical products typically found in the illicit market. The audit period should be for a minimum of one year.

The basic principle of a drug accountability audit is simple: A licensee's accounts are in order if, and only if, Initial stock + Additions to stock during the audit period = Remaining stock + Subtractions from stock during the audit period. More specifically, the right and left sides of the following table should be counted and should equal each other.

"Total drugs responsible for" =	"Total drugs accounted for" =
Initial inventory of drug stock	Inventory on date of audit
+	+
Purchases and Acquisition by licensee	Sales
+	+
Returns by customers	Returns by Vendors
	+
	Theft or Losses
	+
	Disposal or destruction of drugs

If "total drugs accounted for" is less than "total drugs responsible for," the discrepancy is known as a "shortage." If it is more, the discrepancy is an "overage." Discrepancies may be represented by either a percentage or a numerical deviation. In the case of a significant discrepancy, further investigation should be conducted in an attempt to determine the cause (e.g., inadequate record keeping, theft or intentional diversion).

5. Security

A security evaluation should include the following:

- a general review of security of the firm;
- a description of all controlled substances storage areas;
- an evaluation of the alarm lines or any backup systems, the alarm central station, police response time and other integrity devices; and
- a test of the alarm system to ensure that all controlled areas are covered with functioning intrusion and protection devices.

6. Follow-up to Inspections (Verifications)

After the on-site inspection is completed, verifications of purchases and sales should be performed with the firm's suppliers and/or customers. The extent of the verifications will depend on what is found during the on-site inspection and drug accountability audit.

V. Investigation of Complaints

Scope. A "complaint investigation" is any targeted or in-depth investigation of a licensee or non-licensee other than a pre-registration or periodic inspection. A complaint investigation may be triggered by a tip from law enforcement (e.g., based on an investigation of a known drug diverting organization), a complaint by a citizen or customer or as a result of "flags" from a database that tracks pharmaceutical products.

A. Objective

A complaint investigation program should focus limited national resources on priority targets. The complaint investigation should seek to determine whether the target has violated the law. In appropriate cases, the investigation may also assist other countries.

B. Setting Priorities for Complaint Investigations

1. The government should prioritize its efforts based on the threat, risks and challenges relative to their country. Different agencies may focus on varying targets or types of targets. These priorities should be periodically reevaluated.

2. The greatest emphasis should be placed on licensees who, through their position in an organization, are suspected of diverting large quantities of pharmaceutical products.

C. Inter-Agency Cooperation and Flexibility

Generally, countries manage the regulation of pharmaceutical products, health professionals and the application of the penal legislation in different ministries or entities. Such national systems have to elaborate an inter-institutional mechanism that enables the exchange of information between the entities, encouraging good communication, cooperation and coordination, avoiding the duplication of efforts and rivalry between them.

In such national systems, a highly integrated inter-agency mechanism should be developed that, for example, allows the regulatory authority to refer individuals suspected of criminal conduct to the criminal enforcement authority. This might include shared databases, cooperative investigations, co-location of personnel and other arrangements that foster the greatest permissible communication and coordination will help avoid gaps, duplication of effort and inter-agency rivalry.

Pharmaceutical diversion cases tend to be complex because of the review of extensive paperwork necessary to prove certain violations. The types and ranges of sanctions available add another layer of complexity to the investigation. These tendencies make it critical that countries adopt a flexible approach and develop a system that avoids unnecessary institutional barriers or divisions.

D. Investigative Techniques

The type of investigation and the desired action may dictate the techniques to be used, which may include:

- searches of the controlled premises and other places where records and evidence may be located;
- accountability audits of controlled substance;
- interviewing patients of the pharmacy and/or physician;
- interviewing employees;
- undercover drug purchases; and
- video, audio and wiretap surveillance.

E. Preparing a Report of Investigation

The Investigator should prepare a detailed report documenting all areas of non-compliance and/or criminal conduct. A good format for the report would include both an organized analysis of findings by subject-area and a listing of which applicable laws and regulations were violated, together with a summary of the evidence to prove each violation. Further documentation may include any history of past violations.

VI. **Actions against Licensees**

Scope. This part discusses the handling of a case after the complaint investigation is completed – at least in its initial phase. It reviews the legal bases for sanctions (drawing on the CICAD “Elements” document that was the antecedent of this Guide) and the choice of appropriate sanctions with specific examples of possible options.

A. Moving from Investigation to Sanctions or Referral for Action

The Investigator should discuss his report with his supervisors and determine the most appropriate type of action or actions; this will dictate whether and how the case is referred. The possible actions or sanctions could be administrative, civil or criminal in nature or a combination depending on the circumstances. Upon determining the course of action, the Investigator is responsible for preparing the referral documents for transmission to the appropriate entity or entities for further action. The importance of interagency cooperation and communication in pursuing these cases cannot be understated..

At any point in an investigation when a determination is made that significant violations, possibly warranting civil or criminal prosecution, have occurred, a prosecuting attorney should be contacted and apprised of the findings. The attorney may then help direct the organization of evidence and the course of any further investigation.

B. Bases for Sanctions

Bases for all types of sanctions include those in the CICAD “Elements” document.[1] The following acts could be the basis for various types of sanctions.

- Unlawful import, export or transit;
- Unlawful manufacture, distribution or possession for the purpose of distribution;
- Unlawful distribution [and transportation];
- Unlawful prescribing or dispensing of pharmaceutical products --
 - § for other than a legitimate medical purpose, or
 - § outside the usual course of professional practice or scope of license of the prescriber or dispenser;
- Unlawful possession for purposes other than for trafficking (an act subject to reduced penalties, including treatment as an alternative to punishment);
- For a licensed person, firm or institution to engage in activities that exceed those permitted by the applicable license;

[1] “Elements for the Control of Pharmaceutical Products Containing Narcotics and Psychoactive Substances,” especially Part IV.B. – Administration and Enforcement – Corrective Actions and Sanctions and Part II.A. – Legislative Foundation and Regulatory Framework – Legislation (Measures).

- To refuse make or maintain any information or documents required by law or regulations;
- To furnish false or fraudulent information or omit any information required by law or regulations;
- To refuse lawful entry for inspection of premises as permitted by law or regulation; or
- To distribute, seek to acquire or to acquire a pharmaceutical product by misrepresentation, fraud, forgery, deception or theft.

Particularly when considering criminal actions, the Investigator and prosecutor should consider whether licensees or non-licensees have engaged in the following activities, which support substantive criminal acts in which pharmaceutical products are involved:

- organization, management, direction and financing;
- indictment, inducement, or advice;
- conspiracy, collusion, participation or aiding and abetting;
- harboring, association and accessory after the fact;
- attempt; and
- facilitation.

C. Choice of Appropriate Sanctions

Competent authorities (and the attorneys representing them) should consider the range of available administrative, civil and corrective actions and sanctions. Generally, lesser corrective actions and sanctions should be applied in the following circumstances:

- Relatively minor and technical violations/
- First-time violations; and
- Violations that have not resulted, or are less likely to result, in diversion of pharmaceutical products

Stricter sanctions should be applied in the following circumstances:

- Relatively significant violations;
- Repeated violations, especially if the licensee has been previously notified or warned;
- Violations that have resulted in, or significantly increase the possibility of, diversion;
- Violations that result in death or serious injury; and
- Violations engaged in knowingly, intentionally or willfully.

For a criminal prosecution, the investigative report should set forth sufficient evidence to show knowing or intentional facilitation of illegal activities with pharmaceutical controlled substances. If a physician, pharmacist or other health professional was involved, it will be necessary to prove that controlled substances were dispensed or distributed outside the usual course of professional practice and not for a legitimate medical purpose in order to be prosecuted.

Civil fines or monetary penalties are an effective tool in sanctioning licensees who show an egregious pattern and/or history of failure to comply with controlled substances laws and regulations. Civil penalties should be used where it appears that the violator lacked criminal intent to violate the law

Administrative sanctions are penalties against the license or registration. They can range from a private (non-public) reprimand to revocation of the license; intermediate sanctions could range from a public reprimand to supervision of practice by a monitoring body to temporary suspension of the license, subject to conditions on reinstatement. Administrative sanctions should be used when and to the extent necessary to protect the public. When it is clear that a licensee's continued practice threatens the public health and welfare, administrative sanctions are appropriate. When such actions pose an immediate threat to public health and welfare, an immediate, emergency revocation – if provided for by law – is the best course. Emergency suspension should be used sparingly, as it could deprive a licensee of a business or livelihood even before affording the opportunity for due process.

The choice between civil penalties and administrative sanctions requires the exercise of judgment on a case-by-case basis. A firm, as opposed to an individual, may be a more appropriate defendant for civil penalties because it is able to hire different people or change its systems to correct past violations, its continued licensure serves the community, and a business typically has a greater ability to pay a substantial penalty. An individual may be a more appropriate target for sanctions against the license because a person may lack professional judgment, skill or competence, and may simply be motivated to break the law.

D. Examples of Administrative Actions

The following paragraphs supply examples of administrative sanctions and processes (subject to legal / regulatory authority).

1. Letter of Admonition

A letter of admonition advises the licensee of any violations which are alleged to have occurred and documents these violations in written form, with specific citations to the laws and regulations. The letter should require a response by the licensee within a specified time period (for example, 30 days), which should describe the corrective actions taken.

2. Administrative Hearing

An administrative hearing provides the opportunity for both the competent regulatory authority and the licensee to explain their respective views on the apparent violations and to discuss the necessary remedial or corrective actions. At the conclusion of the hearing, an agreement will usually be prepared either confirming that

the violations did, in fact, occur or finding that they did not. Proposed corrective action should be discussed. Some record should be made of the hearing, whether by recording, transcription or careful note-taking.

Hearings of this type may serve two distinct purposes. An administrative hearing may be part of the due process afforded under the administrative sanction process. In other situations, the hearing is itself the administrative action. In either case, the notice asking the licensee to attend a hearing should clearly state its purpose.

3. Administrative Charges

The administrative charge should include a summary of the violations alleged together with the supporting evidence. This initial charging document should trigger whatever due process and hearing rights are available under the national law. The person or firm charged should have the opportunity to show why it should retain its license to handle pharmaceutical products. The competent authority should make and retain a formal or informal record of proceedings.

If the charges seek an immediate suspension because the activity or violative conduct is continuing, making the suspension necessary to prevent imminent danger to the public health and safety, the charges should so state. In addition, reflective of the urgency of the matter, the charges should be filed as soon as possible after the competent authority learns of the violative conduct. Whatever procedural process is otherwise available to licensees should be provided – or at least offered -- on an expedited basis in such cases, and the competent authority and its attorneys should be prepared to go forward to prove the case. A license to handle controlled substances is a privilege rather than a right, but an immediate suspension reverses the normal expectation that a license, once issued, will remain in full force and effect.

4. Voluntary Surrender

A license may be voluntarily surrendered by the licensee at any time. A voluntary surrender should be accompanied by the original license, unused government forms and pharmaceutical products. The licensee should also complete a form indicating whether the surrender is due to failure to comply with the state's laws and regulations or due to a voluntary desire to discontinue business. The form should be signed by the licensee and witnessed by an Investigator.

Where the license surrender is due to failure to comply with the state's laws and regulations, the competent authority should make a record of this fact. The licensee's file should reflect the circumstances of the surrender, and the state's database should include that information for reference in case the surrendering licensee later seeks registration.



ORGANIZATION OF AMERICAN STATES

INTER-AMERICAN DRUG ABUSE CONTROL COMMISSION

cicad

Ephedrine and Pseudoephedrine Use in the Illicit Production of Methamphetamine

Ephedrine and Pseudoephedrine Use in the Illicit Production of Methamphetamine

Background

Effective actions to fight the traffic of substances such as heroin, cocaine, etc, have led to the emergence of the so called “*synthetic drugs*” such as methamphetamine. Methamphetamine can be easily produced domestically using ingredients such as ephedrine and pseudoephedrine which are commonly found in cold products. Its low cost and ease of synthesis make it an attractive and easy drug to produce and sell. This phenomenon has become a profitable alternative for multinational organized crime.

Ephedrine and pseudoephedrine are included in Table I of the 1988 UN Convention. As signatories to this Convention, countries in this region have implemented controls for the import, export and production of pseudoephedrine and ephedrine as bulk chemicals (raw materials) and single entity pharmaceutical products.

Since there are controls in place for raw material and single entity products, the clandestine laboratory operators are using combination products containing pseudoephedrine to produce methamphetamine. This has been seen in countries such as the United States, Mexico and Canada.

The illicit production of methamphetamine has been a concern in the United States for some time. In recent years, it has spread to its neighbouring countries, Canada and Mexico. This has led to an increase in the diversion of “combination” pharmaceutical products containing pseudoephedrine. Diversion generally migrates from region to region seeking voids in legislation. Therefore as imports may decrease in some countries, they may increase in others. This is a serious concern for CICAD member states.

Checklist to avoid the diversion of ephedrine and pseudoephedrine

In order to avoid the diversion of pharmaceutical products which contain ephedrine and pseudoephedrine at the national level, consideration should be given to the following steps:

1. Limit the quantity which can be sold at the retail level;
2. Limit the access of OTC cold products containing pseudoephedrine or ephedrine;
3. Encourage industry to examine ways to formulate their pseudoephedrine and ephedrine products so they cannot be used in the illicit production of methamphetamine;
4. Rationalization of the imports so that they are in balance with legitimate domestic demands; and,
5. Promote the pre-export notification of pharmaceutical products which contain pseudoephedrine/ephedrine, including combination products, by all CICAD member states and encourage third countries shipping to this hemisphere to do likewise