



ORGANIZATION OF AMERICAN STATES

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 a 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 on document analysis and bookkeeping (control books, raw material logs, import, export, etc.).

Additionally, national pharmaceutical control entities should propose and implement training programs for investigators on the different

analytical and auditing methodologies, as well as indicators and evidence suggesting 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.

<p>“Total drugs responsible for” =</p> <p>Initial inventory of drug stock</p> <p>+</p> <p>Purchases and Acquisition by licensee</p> <p>+</p> <p>Returns by customers</p>	<p>“Total drugs accounted for” =</p> <p>Inventory on date of audit</p> <p>+</p> <p>Sales</p> <p>+</p> <p>Returns by Vendors</p>
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	+
	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

[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).

§ 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;
- 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.