HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Controlled Drugs Documentation, Storage and Security Requirements for Operators

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

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1 ABBREVIATIONS

API is active pharmaceutical ingredient.
CD is controlled drug.
HPRA is the Health Products Regulatory Authority.
INCB is the International Control Board.
LONO is a letter of no objection.
MIA is a manufacturer's/importer's authorisation.
PHECC is the Pre-Hospital Emergency Care Council.
SOP is a standard operating procedure.
WDA is a wholesale distribution authorisation.
WHO is the World Health Organisation.

2 SCOPE

This document provides guidance to operators of controlled drugs located in Ireland regarding the requirements for documentation, storage and security that are set out in the Misuse of Drugs Act 1977 (as amended) (the 'Act'), and the various Orders and Regulations made thereunder, of which the Principal Regulations are the Misuse of Drugs Regulations 2017 (as amended) (the 'Regulations'). Additional requirements pertaining to the Medical Cannabis Access Programme are not outlined in this document and can be found on the Department of Health's website.

'Operator' is not a defined term with respect to controlled drugs under the Misuse of Drugs legal framework. For the purpose of this guide, 'operator' refers to an entity which holds or intends to hold a controlled drug annual licence or registration, including but not limited to manufacturers, wholesalers, research laboratories, forensic laboratories, pre-hospital emergency care providers (see Appendix 1 of this document for specific guidance), clinical trial sites (if applicable), and other entities which store controlled drugs, to which these guidelines apply.

It is ultimately the responsibility of the licensee or registrant to ensure that they comply with the requirements set out in the Act, and the various Orders and Regulations made thereunder.

The licensing authority for controlled drugs licenses and registrations in Ireland is the Department of Health. The HPRA manages the application process for controlled drug licenses and registrations on behalf of the Department of Health, who are the competent authority in this area.

A controlled drug annual licence is required for operators who produce a controlled drug, or a preparation containing a controlled drug, in any of the schedules of the Regulations. A controlled drug annual licence is also required for operators who possess, supply, import or export any controlled drug in Schedules 1 and 2. A controlled drug registration is required for

operators who possess, supply, import or export any controlled drug in Schedules 3, 4, and 5. See Table 1 for further information.

Table 1: Breakdown of the various licenses or registrations required for operators to manufacture, supply, possess, import, or export controlled drugs in Ireland

Activity	Regulatory requirements
Manufacture of any controlled drugs listed in the schedules	Annual licence, renewed each year
Supply, import, export or possess a controlled drug in Schedules 1 and 2	Annual licence, renewed each year
Supply, import, export or possess a controlled drug in schedules 3, 4 and 5	Registration, not subject to renewal*
In addition:	
Each import or export of controlled drugs in Schedules 1, 2, 3 and Schedule 4 part 1 into or out of Ireland	Import or export licence (as appropriate to accompany) the product
Each import or export of controlled drugs in Schedule 4 part 2 and Schedule 5 into or out of Ireland	Letter of no objection (LONO)

*Note: Renewal applications must be submitted if there are proposed amendments. If there are no proposed amendments, renewal applications are not required to be submitted however, the HPRA recommends that these be renewed at least every five years from the date of issuance.

It is emphasised that controlled drug licences and registrations are issued under specific national legislation in Ireland and are required in addition to other licensing requirements that may be applicable to the business operation (e.g. a manufacturer's/importer's authorisation (MIA), wholesale distribution authorisation (WDA), etc., under medicinal products legislation (human or veterinary)).

The operator must obtain the appropriate licence or registration for every controlled drug that it produces, possesses, supplies, import or exports, prior to commencing that activity. Production, possession, supply, importation or exportation of controlled drugs without the appropriate licence or registration is an offence under the Act.

Operators intending to apply for a controlled drug licence or registration should consult the Licences and registrations for controlled drugs page of the Controlled Drugs section of the HPRA website for information.

Operators must ensure that any activity involving controlled drugs, authorised by virtue of a controlled drug licence or registration, is undertaken only within the period of validity of the licence or registration. Any activity undertaken once the period of validity has lapsed, in the

absence of a valid licence or registration, is unauthorised and is an offence under the Act. Controlled drug annual licences must be renewed on an annual basis, and controlled drug registrations are recommended to be renewed at least every five years or before if changes occur at the site. Applications to renew controlled drug licences should be submitted four to six weeks in advance of the expiry date.

3 INTRODUCTION

A controlled drug is any substance, product or preparation specified in the Schedule of the Misuse of Drugs Act 1977 (the 'Act'). The Misuse of Drugs Act 1977 has been amended on several occasions by subsequent legislation. The main objective of the Act is to ensure the availability of controlled drugs for licit uses including medical and scientific purposes while preventing illicit uses of controlled drugs, including their abuse, misuse and diversion for non-medical and non-scientific purposes.

The Act prohibits the import, export, production, possession, sale and supply of controlled drugs unless carried out in accordance with the terms outlined in Regulations made under the Act.

Since September 2005, the HPRA has managed the application process for controlled drug licences and registrations on behalf of the Department of Health. As part of this process, the HPRA carries out inspections of manufacturers and wholesalers of controlled drugs, as well as other types of operators as required, ensuring compliance with the relevant requirements. Information about inspections relating to controlled drugs can be located at the Inspections relating to controlled drugs page of the HPRA website.

4 LEGISLATIVE BASIS

4.1 At international level

At the international level, the legislative basis for the control of controlled drugs is the Single Convention on Narcotic Drugs, 1961 and the Convention on Psychotropic Substances,1971. As a party to both conventions, Ireland is required to establish strict controls around any drugs scheduled in either Convention to prevent the diversion of the licit movement of controlled drugs into the illicit market. The international body that monitors and supports governments' compliance with the international controlled drug Conventions is called the International Narcotics Control Board (INCB).

4.2 At national level

The Act is designed to prevent the abuse of certain substances that are considered to be dangerous, with a strong potential for abuse and misuse while at the same time ensuring

appropriate access to controlled drugs for medical and scientific purposes, by regulating the various professional activities associated with these substances. The Act prohibits the possession, sale and/or supply, importation, exportation and production of controlled drugs. However, these activities are permitted if carried out under strict conditions that are set out in legislation if specifically authorised or exempted from these prohibitions. Under the Act, a number of Regulations and Orders have been made which describe the requirements for controlled drug operators. The Principal Regulations made under the Misuse of Drugs Acts are the Misuse of Drugs Regulations 2017 (the 'Regulations'). These Regulations have been amended on several occasions since 2017.
The Regulations divide controlled drugs into five schedules according to their potential for abuse and their therapeutic usefulness. The Regulations also apply varying controls to these substances such as imposing restrictions on the production, supply, importation and exportation, depending on the schedule in which they are listed. Schedule 1 controlled drugs have the most restrictions imposed due to their strong potential for abuse and little, if any, therapeutic value. Schedule 5 substances and preparations, however, have the least number of restrictions.

Together the Act and the various Regulations and Orders made thereunder are referred to as the Misuse of Drugs Legal Framework.

Additional detail in relation to the legislation governing controlled drugs in Ireland can be found on the 'About controlled drugs legislation' page of the HPRA website.

5 GUIDANCE FOR OPERATORS OF CONTROLLED DRUGS

5.1 Controlled Drugs Register

5.1.1 Controlled Drugs Register requirements

Operators that produce, supply, import, export or possess a controlled drug in Schedule 1 or 2 of the Principal Regulations are required to keep a Controlled Drugs Register. (Note: operators that produce controlled drugs in all Schedules of the Principal Regulations are required to keep a record of all amounts of drug(s) produced in pursuance of the licence.) The Controlled Drugs Register should be completed chronologically and must show a running stock balance of every quantity of controlled drug obtained or supplied by them to, or from a person within, or outside of Ireland. A separate Controlled Drugs Register, or separate part of the same Register should be used for entries of each class of controlled drug.

For the purposes of this guidance document, a 'class' of controlled drug refers to controlled drugs specified in either paragraph 1 and 3 of Schedule 1 of the Principal Regulations, or paragraphs 1, 3 and 6 of Schedule 2 of the Principal Regulations. Any stereoisomeric forms, or salt forms of a controlled drug should be considered as being in the same class of the controlled drug.

Entries in the Controlled Drugs Register should be made in the form that is specified in either Schedule 6 of the Principal Regulations, or Schedule 7 Part 1 and Part 2 as applicable to the relevant operation.

In the case of a manufacturer or wholesaler of medicinal products, the Controlled Drugs Register may be an electronic register which shall be based on a computerised system, such as a validated warehouse management system, equivalent to the requirements for a bound book register as set out in Schedule 6 of the Principal Regulations, or Schedule 7 Part 1 and Part 2, as applicable to the relevant operation. The electronic register shall be validated in line with good manufacturing practice (GMP), or good distribution practice (GDP), as appropriate to the activities performed. The exact format of the electronic register may vary by operator depending on the computerised system used.

The Principal Regulations state that a Controlled Drugs Register should comply with the following requirements:

- The class of controlled drug to which the entry on any page of the register relates should be specified in the header of that page.
- Every entry should be made (where reasonably practicable) on the day on which the controlled drug is obtained or supplied; or if not, on the following day.
- Cancellations, obliterations or alterations of any entry in the register should not be made. Corrections to an entry can be made by way of a marginal note or footnote which should specify the date that the correction was made. Corrections should also be initialled.
- Every entry and every correction should be made in ink so that it cannot be removed.
- The Controlled Drugs Register should not be used for any purpose other than the purpose described in the Principal Regulations.
- A separate register should be kept for each premises at which the person required to keep the register carries on their business. (Note: a separate annual licence and/or registration is also required for each premises.)
- A manufacture or wholesaler using an electronic register may use the same validated computerised system for different premises; however, it should be possible to discern the quantities of controlled drugs held at each distinct premises.
- Every Controlled Drugs Register should be kept in the premises to which it relates and should be available for inspection under Section 24 of the Act.

The Controlled Drugs Register should be periodically checked by the licence or registration holder to ensure that there are no discrepancies, or failures to comply with the requirements listed above. Any discrepancies or non-conformances identified should be investigated thoroughly to identify the cause. This process should be described within a standard operating procedure (SOP). Any theft or unaccounted loss of controlled drugs that is identified should be reported to the HPRA, and to An Garda Síochána as described in the section relating to 'Reporting of Theft or Unaccounted Loss' of this guidance.

For controlled drugs in Schedules, 3, 4, and 5, the company should keep a record of each quantity of the drug(s) which it receives or supplies. Such records should include the date of each transaction, the necessary qualitative and quantitative details, the name of the supplier or the consignee and the country of origin or destination as the case may be.

5.1.2 Stock inventory checks of controlled drugs

The operator should conduct frequent stock inventory checks of the controlled drugs held at the site, including controlled drugs destined for destruction. The methodology used for the cycle checks should be documented in an SOP. The methodology used, and frequency of checks should be determined by the operator and should be based on the complexity of the operations, the schedule that the controlled drug is in, and the quantity of controlled drugs that are received and supplied. It would be recommended to conduct blind cycle checks. (A blind cycle check is where the person conducting the count does not know in advance the quantity that is expected.) Where possible, cycle checks should be timed in line with the storage of surveillance camera footage, to make sure that footage can be reviewed if any discrepancies are identified.

Stock inventory checks should be documented, and any discrepancies identified should be thoroughly investigated as this may indicate either an unaccounted loss or theft of a controlled drug. Unaccounted losses or thefts of controlled drug should be immediately reported to the Controlled Drugs team of the HPRA at controlleddrugs@hpra.ie using the 'Report of theft or unaccounted loss of controlled drugs and precursor chemicals' form available on the HPRA website. Any suspected theft or unaccounted loss should also be reported to An Garda Síochána.

5.2 Security

The licence or registration holder should take whatever steps are necessary to prevent unauthorised access to the controlled drugs. Security requirements should be considered carefully and should be commensurate to the size, complexity and risk of the operation that is being conducted. This section of the guidance describes security requirements that should at a minimum be in place at the site, and the mandatory safe custody requirements for stocks of controlled drugs in Schedule 1, 2, or 3.

5.2.1 Safe custody requirements

All stocks of controlled drugs in Schedule 1, 2, or 3 (including controlled drugs requiring low temperature handling) must be kept in a locked fixed receptacle which is so constructed or maintained as to prevent unauthorised access to the controlled drugs. The Misuse of Drugs (Safe Custody) Regulations 1982 state that a person lawfully having any controlled drug in Schedule 1, 2, or 3 in their possession should ensure that the controlled drug is kept in a locked, fixed receptacle which can be opened only by them, or a person authorised by them.

Any safe, cabinet, or locked receptacle in which controlled drugs are kept should be constructed and maintained in accordance with a standard which is at least equivalent to the requirements set out in the Schedule to the Misuse of Drugs (Safe Custody) Regulations 1982. To demonstrate this, the operator must obtain a certificate issued by an Garda Síochána Superintendent certifying that the safe, cabinet, or locked receptacle complies with the requirements set out in the Schedule.

Nothing should be displayed outside the storage area to indicate that controlled drugs are kept in it.

All stocks of controlled drugs in Schedule 4 Part 1, 4 Part 2, or 5 must be stored in an appropriately secure manner to prevent unauthorised access to the drug(s) and, where applicable, in accordance with the requirements of the Act. The company must be able to demonstrate that the controlled drugs are being stored in an appropriately secure manner and that unauthorised access to the controlled drug is being ensured.

Where possible, the area where controlled drugs, in any schedule, are being stored should be comprehensively monitored by surveillance cameras at all times.

5.2.2 Access, combination locks, keys and keyholders

Swipe/fob access
If the operator uses swipes/fobs to control access to relevant controlled drugs areas for staff, the access control system should be able to provide a clear audit trail at all times. Access should be provided to authorised persons only, and access should be removed as soon as possible if that staff member's employment is terminated, or if they begin working in an area that no longer requires access to controlled drugs. Access to swipe cards/fob keys should be controlled.

Access codes
Access and PIN codes should be changed at defined intervals and provided only to authorised persons. Access and PIN codes should be changed if an authorised person's employment is terminated, or if they begin working in an area that no longer requires them to access controlled drugs.

Combination locks
An operator may wish to use combination locks as a system to control access to controlled drugs to authorised persons only. The following guidance should be considered as best practice in this case:

- Combinations should be changed periodically, as defined in a procedure.
- Combinations should be changed as soon as possible if a staff member's employment is terminated, or if they begin working in an area that no longer requires access to controlled drugs.
- Codes to combination locks should be kept confidential and should not be written down.
- Combination codes should be issued only to the individual that requires them.

- A system that provides an audit trail should be considered whereby access to controlled drugs using combination locks is controlled and recorded with a witnessed signing-in and out procedure (for example, two combination locks whereby no individual has knowledge of both codes could be used).

Keys and keyholders
If keys are used by the operator to control access to relevant controlled drugs areas for staff, a similar level of security that is applied to the storage of controlled drugs should be applied to the storage of the keys. For example,

- Keys should be kept in a safe, or key box which itself requires access, either by key, or by combination lock.
- Key boxes used to store keys that provide access to controlled drug storage areas should not be constructed out of weak materials that can easily be broken.
- Access to keys should be limited to authorised persons only.
- An audit trail system should be in place whereby access to individual keys should be controlled and recorded with a witnessed signing-in and out procedure.
- Access to keys should be removed from personnel that no longer are employed at the operator's site, or that no longer work in an area that requires access to controlled drugs.

5.2.3 Security requirements

External security
This section describes a number of external security arrangements that would be considered good practice for operators to consider when designing their security arrangements for controlled drugs.

Camera surveillance: Ensure that all relevant external areas are monitored by camera surveillance. Consider how these areas will be monitored during nighttime, for example, by using motion-activated lights and cameras.

Footage maintenance: Camera footage should be maintained for a justified period of time. Ensure there is an off-site or restricted access to backup of this footage.

Facility construction: The facility should be constructed in such a way as to minimise the risk of unauthorised access. Attention should be given to potential unauthorised routes of access to the building. Physical deterrents such as shutters on doors and windows could also be considered. The facility should be maintained on an ongoing basis to ensure that no risks to unauthorised access develop over time due to deterioration.

Intruder alarm system: Install an intruder alarm system to alert in the event of unauthorised access to the external site. It is recommended that this alarm system is monitored and the footage backed up by an off-site company. Alarm systems should be maintained on a regular basis and tested frequently.

Access control: A system should be in place to control access to the site to prevent unauthorised entry. Ideally a system that provides an audit trail of access to the site should be used, such as swipe card access. Alternatively, combination locks, or key based systems could be used. Specific guidance around the use of swipe cards, combination locks and keys is included above.

Unauthorised access routes: Ensure there are no possible unauthorised access routes from the external area into the building. For example, external doors and windows should be locked.

Controlled drug deliveries: Implement a system to manage deliveries of controlled drugs to and from the site, minimising the risk of unauthorised access during these instances.

Internal security
This section describes a number of internal security arrangements that would be considered to be good practice for operators to consider when designing their security arrangements for controlled drugs.

Camera surveillance should be in place for all relevant internal areas of the site, including the receipt area, dispatch area, general warehouse, storage area, waste, quarantine and reject areas. There should be systems in place for the maintenance of footage. A backup of footage should be maintained off-site. Access to surveillance footage should be restricted.

Receipt and put away: A system should be in place to control access to controlled drugs during receipt to authorised persons only. The processing and put away of receipts of controlled drugs into their appropriate storage location should be prioritised over other products. The operator should verify that the consignment was received from the approved supplier, and that what was received matches what was ordered. The operator should check whether there are any signs of tampering or damage to the product. Receipt checks should be documented and maintained by the operator. Entries into the Controlled Drugs Register (where applicable) could be completed at this point.

If the product received was imported, the associated import licence should be endorsed within no more than seven days of the receipt of the consignment (detailed guidance on this is included further on in this document).

Storage: During storage, the operator should comply with the safe custody requirements described in the relevant section above for all controlled drugs in Schedules 1, 2, and 3 (including controlled drugs required to be stored at low temperatures). Controlled drugs in Schedule 4 Part 1, 4 Part 2, or 5 must be stored in an appropriately secure manner to prevent unauthorised access to the drug(s). Periodic cycle checks of controlled drugs should be carried out as described above.

Picking and dispatch: A system should be in place to control access to controlled drugs during picking and dispatch to authorised persons only. The operator should ensure that deliveries of controlled drugs waiting to be dispatched are not left sitting in the dispatch area for prolonged

periods of time. The operator should confirm that deliveries are to be made to an approved customer only. Entries into the Controlled Drugs Register (where applicable) could be completed at this point.

If the product dispatched is to be exported, the associated export licence should be endorsed within no more than seven days of the export of the consignment (detailed guidance on this is included below).

Intruder alarm system: Depending on the size, complexity and Schedules of controlled drugs, consider installing an intruder alarm system to alert in the event of unauthorised access to the internal site and to the secure controlled drugs storage area. It is recommended that the alarm system should be monitored and the footage backed up by an off-site company. Alarm systems should be maintained on a regular basis and tested frequently.

Access control: A system should be in place to control access to the controlled drugs storage area. If codes or keys are used, these should be periodically changed. Codes/keys should be changed if staff involved in controlled drugs terminate employment. Specific guidance on the usage of code and key access is included above.

Quarantine, production, reject, returns, and waste disposal areas for controlled drugs should be subject to the same security requirements as the controlled drug storage area. During the manufacturing process a system should be in place that ensures that all reasonable steps are taken to prevent unauthorised access to the controlled drugs.

Personnel: The operator should put processes in place to control the return of identification cards, keys, swipe cards, and uniforms, as well as the deactivation of access cards and/or the changing of codes/combinations as quickly as possible when staff change roles or terminate employment.

Consideration should be given to the management of staff such as cleaning staff, maintenance staff, or contractors who may require access to areas where controlled drugs are stored.

The operator should have a method for assessing the suitability and appropriateness of personnel involved in the handling of controlled drugs, to ensure that no staff member may pose a risk to the security of controlled drugs. The exact method may vary between operators and may include but is not limited to a review of recent employment history and references, relevant training and experience, and restricting immediate access to controlled drugs upon commencement of employment.

5.3 Disposal/destruction of controlled drugs

5.3.1 Destruction of controlled drugs

A controlled drug in Schedule 1, 2, 3, or 4 should not be destroyed unless in the presence of, and in accordance with the directions of a person authorised for this purpose by the Minister for Health.

When a Schedule 1, 2, 3, or 4 controlled drug is destroyed, a record should be kept of the date of destruction, the name of the controlled drug, and the quantity destroyed, and this should be signed by the authorised person who was present for the destruction.

5.3.2 Waste management programme

The operator should have a dedicated waste management programme for controlled drugs, and this should be described within an SOP. The following security considerations should be taken into account when designing the waste management programme at the site:

Storage of rejected/waste product
Rejected and/or waste-controlled drug stock should be treated with the same level of security as sellable controlled drug stock. The same safe custody requirements described in the guidance apply, and the operator should take every step necessary to prevent unauthorised access to the rejected/waste-controlled drug product. An inventory should be kept of rejected/waste product. Rejected/waste-controlled drugs awaiting disposal should not be kept on site for an excessive period of time.

Method of destruction used
The operator should consider the method of destruction used for the controlled drug to make sure that the drug is irretrievable once destroyed. If dedicated controlled drug disposal kits are to be used, the manufacturer's instructions must be followed.

Adherence to import/export licensing requirements
If the waste management programme involves controlled drugs being shipped to another country for destruction, the operator should ensure that import and/or export requirements for controlled drugs are adhered to.

Third-party service provider
If a third-party service provider is to be used for the destruction of controlled drugs, the operator should assess whether they also require a controlled drug licence and/or registration (if they are to store controlled drugs retrievable from waste, at their premises prior to destruction). A contract should be in place between the operator and the third-party service provider to ensure that the activities are defined and controlled between both entities.
The operator should maintain a certification of destruction.

5.4 Transportation

Operators must have a system in place to take whatever steps are necessary to prevent unauthorised access to the controlled drugs during transportation. Equivalent levels of security should be considered for stocks of controlled drugs being transported, as is given for stocks of controlled drugs being stored at the operator's premises. Security measures adopted for stocks of controlled drugs during transport should take into consideration factors such as the quantity of controlled drugs, the Schedule that the controlled drug is in, and the transportation method and route.

The operator and any third-party transport provider used for transportation should have procedures in place that describe the roles and responsibilities for all transport related activities.

The following security considerations should be considered at a minimum when organising transport of controlled drugs:

- A record of the driver should be kept for road transport.
- Vehicles used for road transport should be maintained regularly and should have appropriate anti-theft devices, such as alarms, locks, or immobilisers.
- Drivers should have clear instructions described in procedures for routine and emergency situations during transport and should receive regular training in these procedures.
- If a vehicle is ever required to be left unattended, the duration of this should be reduced to the minimum amount of time possible. The vehicle should be secured at all times when left unattended.
- Deliveries should be made to the address stated on the delivery note and into the care or the premises of the consignee. Controlled Drugs should not be left on alternative premises.
- Products that have specific additional storage requirements, such as low temperature handling, are subject to safe custody requirements, and the operator should take all reasonable steps to ensure the security of the controlled drug during transport.

5.4.1 Use of third party-service providers for transport

This section is applicable if a third-party services provider is to be used for the transport of controlled drugs. In relation to outsourced activities, wholesalers and manufacturers of human medicinal products should comply with Chapter 7 of the EU GDP Guidelines for medicinal products for human use. Wholesalers and manufacturers of veterinary medicinal products should comply with Chapter 8 of the EU GDP Guidelines for medicinal products for veterinary use.

For all other entities that are not wholesalers or manufacturers, conduct due diligence checks to assess the reputation, competence and suitability of the service provider. It would be considered best practice for the operator to enter into a contract with the third-party service provider to define in detail the arrangements between both parties.

As part of the due diligence checks, operator should conduct an audit of the third-party service provider. The purpose of the audit is for the operator to satisfy itself that the third-party service provider is suitably competent to perform the task. The operator should at a minimum assess the following points:

- Any additional control systems in place for delivery of controlled drugs.
- Training of drivers in transport procedures.
- SOPs covering all aspects of transport , including handling emergency situations, and reporting of thefts or unaccounted losses during transport.
- Maintenance of vehicles used for transport.
- The suitability of the vehicles used for transport of controlled drugs.
- The arrangements around subcontracting activities.
- The suitability of the arrangements around the use of transport hubs and temporary storage during transport.

5.4.2 Reporting of theft or unaccounted loss during transport

Any theft or unaccounted loss of controlled drug during transport should be immediately reported to the Controlled Drugs Section of the HPRA at controlleddrugs@hpra.ie using the 'Report of theft or unaccounted loss of controlled drugs and precursor chemicals' form available on the HPRA website. Any suspected theft should also be reported to An Garda Síochána.

5.4.3 Temporary storage during transport

Operators must have a system in place to take whatever steps are necessary to prevent unauthorised access to the controlled drugs during temporary storage during transportation. In Ireland, temporary storage of controlled drugs for over 48 hours at a premises is considered to be storage, and a controlled drug licence or registration would be required for that particular premises. The authorisation requirement for temporary storage of controlled drugs during transport may differ depending on each country's national legislation. It is the responsibility of the operator to ensure that any premises used to temporarily store controlled drugs are appropriately authorised for this activity.

5.5 Orders, suppliers and customers

Requirements for verifying the authority of suppliers to supply controlled drugs, and customers to receive controlled drugs are described below. It is emphasised that controlled drug licences and/or registrations are issued under specific national legislation in each country and are a requirement that is in addition to other licensing requirements that may be applicable to the business operation (e.g. a manufacturer's/importer's authorisation (MIA), wholesale distribution authorisation (WDA), etc., under medicinal products legislation (human or veterinary)).

The operator must ensure that their system for qualifying suppliers and customers considers all legislative requirements that are applicable. This guidance is specifically given in relation to controlled drugs and does not encompass additional legislative requirements.

5.5.1 Suppliers

Operators of controlled drugs should only receive supplies of controlled drugs from an entity that is authorised to supply them with controlled drugs. Prior to the purchase and receipt of any controlled drug, the operator must verify that the supplying entity is authorised to supply the specific controlled drug in question. It is the responsibility of the operator to establish this, and to obtain appropriate documentary evidence. (Note: controlled drugs may be subject to different levels of control in different states. For example, a substance that is a controlled drug in Ireland may not be controlled in another country. It is the responsibility of the operator to establish what the requirements are for the controlled drug in the relevant country, and to obtain appropriate documentary evidence of this.)

Checks may include requesting copies of the supplier's authorisation, licence or registration that entitles them to supply controlled drugs. Printouts should be obtained and retained as records of such checks. The content and detail of each authorisation should be reviewed, such as but not limited to the company name, address, specific controlled drug listed on the authorisation, and authorised operation. If the original document is not in English, the operator must ensure it is translated into English. It is expected that translations are carried out by an independent and certified translator. Information obtained from the supplier should be independently verified with the relevant competent authority in that country. This can be achieved either through the competent authority's website, or by contacting the competent authority directly. All communications related to this must be documented.

Contact information for competent authorities is published by the United Nations Office on Drugs and Crime (UNODC) in an online directory available on its website. Operators may wish to consult the 'Competent National Authorities under the International Drug Control Treaties' directory for this purpose.

If the operator becomes aware that their supplier no longer holds a current controlled drug authorisation, or other authorisation that is required to permit supply, the operator should confirm the reason with the supplier and independently verify the reason and document any communication.

Periodic checks on existing suppliers should be performed to ensure that they maintain an authorised status.

There should be a system in place to ensure that the operator cannot place an order for a controlled drug with a supplier until the supplier has been approved. For wholesalers and manufacturers, a clear link between the quality and purchasing department should exist to facilitate this.

For operators that are organisations that hold a controlled drug annual licence or registration for the purpose of providing pre-hospital emergency care services, and that are regulated by the Pre-Hospital Emergency Care Council, in pursuance of the condition of the licence, all stocks of

controlled drugs should be obtained from a person operating a retail pharmacy business, on foot of a requisition provided for in the Principal Regulations. The requisition must be raised by a medical practitioner, as described in Regulation 14 of the Principal Regulations. Specific guidance for these operators is included in Appendix 1 of this document.

Operators are requested to report to the HPRA issues which they consider suspicious or unusual with respect to the sourcing of controlled drugs. Operators may be assured that all such matters will be investigated confidentially.

5.5.2 Customers

Operators of controlled drugs should only supply them to entities that are authorised to receive the specific controlled drug. The operator must obtain documentary evidence to support this. The approval system should ensure that each customer is legally entitled to receive the specific controlled drug that is to be supplied. (For example, a customer authorised to receive a Schedule 5 controlled drug may not be authorised to receive a Schedule 2 controlled drug.)

Ongoing periodic checks should be performed to verify the continued authority of the customer to receive the particular controlled drug. If documentation is not in English, the operator must ensure that it is translated into English. It is expected that translations are carried out by an independent and certified translator.

The operator should independently verify the information provided by a customer in relation to their authority to receive the particular controlled drug. Depending on the type of customer, this could involve contacting the local competent authority or verifying the registration status of a retail pharmacy business or healthcare professional with the appropriate body. In all cases, documentary evidence should be kept of such checks.

There should be a system in place to ensure that a customer cannot order a controlled drug from the operator until they have been approved. A clear link between the quality and sales department should exist to facilitate this, where applicable.

Wholesalers and manufacturers of human/veterinary medicinal products that must comply with the respective GDP guidelines for human/veterinary medicines must monitor their transactions of controlled drugs and investigate any irregularity in the sales patterns of controlled drugs. Unusual sales patterns that may constitute diversion or misuse of medicinal products should be investigated and reported to competent authorities where necessary.

5.6 Documentation requirements

5.6.1 Standard operating procedures

Standard operating procedures (SOPs) are a crucial part of ensuring that there are robust consistent processes in place throughout the operator's system to ensure that the

documentation, storage and security requirements for controlled drugs are adhered to. Documentation and records relating to controlled drug operations should be maintained by the operator for at least two years. The exception to this is documentation and records relating to controlled drug operations of products or preparations specified in Schedule 1 to the Misuse of Drugs (Prescription and Control of Supply of Cannabis for Medical Use) Regulations, which should be maintained for at least five years.

At a minimum, procedures should be in place that cover the following activities:
- Licensing requirements including the application process for controlled drug annual licences, registrations, import and export licences (including endorsements), as appropriate
- Cycle count checks including investigation and communication requirements when discrepancies are identified
- Verification of the authority of the suppliers and customers to supply controlled drugs
- Access, management of keys/combination locks, and security restrictions
- Annual statistical returns (for manufacturers and wholesalers)
- Quarterly statistical returns (for importers and exporters)
- Maintenance of Controlled Drugs Registers (waste, quarantine, usage, etc.)
- Requirements placed on the operator under the Regulations, and conditions of controlled drug licences/registrations
- Theft/unaccounted loss including investigation and communication requirements
- Certification of the controlled drugs safe, cabinet, or locked receptacle by An Garda Síochána
- Destruction/disposal of controlled drugs
- Transport of controlled drugs (if applicable)
- Training of personnel in controlled drugs requirements
- Provision of new information to the HPRA, e.g. appointment of a new responsible officer, change of premises

SOPs should be reviewed regularly to ensure that they are accurate, appropriate in scope and up to date with the operator's activities and legislation.

5.6.2 Maintenance of records relating to controlled drugs

The requirements for the maintenance of records relating to controlled drugs will depend on the activities that the operator is authorised to conduct, and the schedule of controlled drugs that are authorised under the controlled drug licence or registration. The requirements are stated on the licence and/or registration that is held by the operator.

The operator should have a system in place to ensure that records are kept in line with the requirements stated on the licence or registration, as well as the requirements set out in the Regulations.

5.6.3 Furnishing of information with respect to controlled drugs

On demand by the Minister for Health or by any person authorised in writing by the Minister, the operator must provide:

- Records in respect of producing, obtaining or supplying any controlled drugs or in respect of any stock of such drugs in their possession
- Any stock of such drugs in their possession
- Any register, book or document in their possession which is required to be kept in respect of any dealings in controlled drugs.

5.7 Personnel

5.7.1 Responsible officer

The operator should appoint a person to be responsible for ensuring that the licensee and/or registrant complies with the conditions of the controlled drug licence and/or registration, and the requirements of the Act, and various Orders and Regulations made thereunder. There is no legal definition for 'responsible officer' with respect to controlled drugs. For the purpose of this guide, 'responsible officer' is the term used to refer to such a person.

This controlled drug responsible officer should be given appropriate authority by the operator to perform their duties. The written job description of the responsible officer should define their roles and responsibilities relating to controlled drugs. They should receive initial and continuing training relevant to their role, including all relevant national legislation and HPRA guidance documents relating to controlled drugs, and procedures (SOPs) specific to the operator's processes. Training records should be documented and retained by the operator.

5.7.2 Other personnel

The operator should have a clear understanding of the roles, responsibilities and interrelationships between all personnel involved in controlled drug operations. Roles and responsibilities relating to controlled drugs for each personnel should be documented in a written job description or role profile.

The operator should have a procedure relating to the initial and ongoing controlled drugs specific training of personnel. Personnel involved in controlled drug operations should receive training on awareness around the requirements of controlled drugs, as well as on all relevant procedures.

5.8 Import/export requirements for controlled drugs

As well as requiring a controlled drug licence or registration to produce/manufacture, supply or possess any controlled drug in the Schedules to the Regulations, each import or export of controlled drugs into or out of Ireland requires a controlled drug import or export licence or

letter of no objection (LONO) to accompany the consignment. The import or export of controlled drugs in Schedules 1, 2, 3 and Schedule 4 Part 1 into or out of Ireland requires a controlled drug import or export licence. The import or export of controlled drugs in Schedules 4 Part 2 and Schedule 5 requires a controlled drug LONO. Controlled drug import or export licences for controlled drugs in Schedules 1, 2, 3 or Schedule 4 Part 1, as well as LONOs for controlled drugs in Schedule 4 Part 2 must be applied for through a secure, electronic portal called NDSWeb Extranet. LONOs for controlled drugs in Schedule 5 must be applied for by contacting the Controlled Drugs team at the HPRA at controlleddrugs@hpra.ie.

Detailed guidance specific to the import and export requirements for controlled drugs is described in the guidance document 'Guide to Import and Export Licences and Letters of No Objection for Controlled Drugs (Including the import of cannabis products for medical use)' available on the HPRA website.

Detailed guidance for operators that are required to use NDSWeb Extranet to apply for controlled drug import or export licences, or LONOs (for Schedule 4 Part 2 controlled drugs) can be found in the 'Guide to NDSWeb Extranet', also available on the HPRA website.

The operator should have procedures in place that incorporate the requirements set out in the guidance documents referenced above. In particular, consideration should be given to the following points:

- The procedure should clearly describe how to apply for the relevant controlled drug import or export licence or LONO.
- The operator should have a method for verifying that the import/export licence has not expired or is not close to expiring before using it.
- The operator should have a method for ensuring that a controlled drug import/export licence or LONO is not used to import or export a quantity that is greater than what is permitted on the licence or LONO.
- The procedure should clearly describe how to endorse a controlled drug import or export licence or LONO (for Schedule 4 part 2) both physically and on NDSWeb Extranet.
- The procedure should include a requirement to endorse controlled drug import or export licences within seven days of the date of import or export.
- Personnel involved in applying for and handling controlled drug import or export licences or LONOs should be appropriately trained on the procedure and the relevant HPRA guidance documents.

In relation to the export of controlled drugs, Regulation 18 of the Principal Regulations describes specific documentation requirements for the export of controlled drugs that must be adhered to. The transactions relating to the export must be properly documented and the commercial documents such as invoices, cargo manifests, customs, transport and other shipping documentation accompanying the drug must include the name of the controlled drug as set out in the relevant schedule, or where such a name would not identify the drug, the international non-proprietary name for the drug as recommended by the World Health Organisation (WHO).

This documentation should be dated and should include the total quantity being exported, the name and address of the exporter and of the importer, and when available that of the ultimate consignee.

5.9 Statistical reporting requirements for controlled drugs

To fulfil the requirement for Ireland to report statistics relating to controlled drugs to the INCB, operators such as manufacturers or wholesalers are required to submit statistical returns to the HPRA on a quarterly and annual basis.

5.9.1 Annual statistical returns

On an annual basis, typically at the start of the year in January, the HPRA contacts manufacturers and wholesalers of controlled drugs by email on behalf of the Minister for Health in relation to the annual statistical reporting requirements of controlled drug operators.

The HPRA will circulate annual statistical reporting forms to manufacturers and wholesalers of controlled drugs which contain detailed guidance notes for their completion.

Manufacturers
For annual statistical returns for manufacturers, the manufacturer should have a procedure around furnishing the following information to the HPRA within the deadline requested:

- Opening stock: quantity of all controlled drugs held on site in that year (as of 1 January).
- Quantity of CD imported in that year.
- Quantity of CD obtained domestically in that year.
- Quantity of API produced in that year.
- Quantity of CD used in manufacture in that year.
- Quantity of CD supplied domestically in that year.
- Quantity of CD exported in that year.
- Quantity of CD lost and/or destroyed in that year.
- Closing stock: quantity of CD left on site in that year (as of 31 December).

Wholesalers
For annual statistical returns for wholesalers, the wholesaler should have a procedure around furnishing the following information to the HPRA within the deadline requested:

- Details of all controlled drug products held in stock as of 31 December of a given year. The following details should be provided:
  - Product name
  - Pack size
  - Number of packs
  - Name of controlled drug in salt form and anhydrous base form
  - Quantity per dosage unit (g) in salt form and anhydrous base form (Note: guidance in relation to calculating the quantity of the salt form and the anhydrous base form is included in Appendix 2 of this document.)

5.9.2 Quarterly statistical returns

On a quarterly basis, after the end of each quarter, the HPRA (on behalf of the Minister for Health) contacts importers and exporters of controlled drugs that hold any controlled drug import/export licence or LONOs (for Schedule 4 Part 2 controlled drugs) that have not yet been endorsed at the end of the quarter.

Importers and exporters of controlled drugs that hold any licences or LONOs that have not yet been accounted for at the end of the relevant quarter should have a procedure that covers the furnishing of the following information to the HPRA:

- The date that a particular import/export licence or LONO was used to import/export a consignment
- The quantity of controlled drug product/substance that was imported/exported under a particular import/export licence or LONO
- If the import/export licence or LONO has not yet been used, confirmation of same.

The operator should have a process in place to ensure that the requested information is furnished accurately to the HPRA within the deadline requested, regardless of personnel leave.

5.10 Withdrawal of controlled drug annual licence and registrations

In the event of the operator no longer requiring a controlled drug annual licence or registration, or ceasing to carry on business at the address listed on the annual licence or registration, the operator must withdraw the annual licence or registration and return it immediately to the HPRA. Information on what steps to follow to withdraw an annual licence or registration are included on the 'Application to withdraw a controlled drug or precursor chemical registration or annual licence' form which can be found on the HPRA website under 'Make a submission'.

Appendix 1 Pre-Hospital Emergency Care Council (PHECC)

The Pre-Hospital Emergency Care Council (PHECC) is an independent statutory body that sets standards for education and training in pre-hospital emergency care in Ireland. PHECC publishes Clinical Practice Guidelines (CPGs) and accredits institutions to deliver training and education. It also maintains a statutory register of practitioners and approves service providers to implement CPGs.

Practitioner registration
During the course of duty and in the immediate and necessary treatment of a sick or injured person, pre-hospital emergency care practitioners may administer controlled drugs, depending on their registration status.

There are three registration levels:
- Emergency Medical Technician (EMT)
- Paramedic (P)
- Advanced Paramedic (AP)

Each registered practitioner receives a unique personal identification number (PIN). Registration status determines which controlled drugs they may possess and administer, as outlined in the 'Pre-Hospital Emergency Care Scope of Practice' booklet found on the PHECC website. Definitions of 'Paramedic' and 'Advanced Paramedic' are also provided in Regulation 4(1) of the Medicinal Products (Prescription and Control of Supply) Regulations 2003 (as amended).

Controlled drugs and licensing
- An annual licence is required to supply, offer to supply, or possess controlled drugs listed in Schedule 2 of the Misuse of Drugs Regulations 2017.
- A registration is required for controlled drugs in Schedules 3, 4, and 5.
- The licensee/registrant is responsible for ensuring the site is appropriately authorised.

Storage and security
All stocks must be under the control of the licensee/registrant, an Advanced Paramedic, or a Paramedic employed by the licensee/registrant.

Drugs in Schedules 2 and 3 must be stored at the licensed premises in a locked safe designed to prevent unauthorised access, in compliance with the Misuse of Drugs Act 1977. Drugs in Schedule 4 must be stored in an appropriately secure manner to prevent unauthorised access to the drug(s).

Obtaining supplies of controlled drugs
- All stocks of controlled drugs must only be obtained from a person operating a retail pharmacy business, on foot of a requisition provided for in the Principal Regulations.

- The requisition must be raised by a medical practitioner, as described in Regulation 14 of the Principal Regulations.

Quantity limits
For Schedule 2 drugs, the quantity an individual Advanced Paramedic or Paramedic may possess must not exceed the amount specified on the annual licence.

Licence or registration validity
- The licence or registration applies only to the named licensee/registrant and the specified business premises (not a domestic dwelling).
- If the licensee/registrant ceases business or the licence is revoked, it must be returned immediately to the HPRA acting on behalf of the Minister for Health.

Returning unused stock
If controlled drugs are no longer required for administration by Advanced Paramedics or Paramedics, they must be returned to the supplying pharmacy. A record of the return must be retained, in accordance with Regulation 20(8) of the Medicinal Products (Prescription and Control of Supply) Regulations 2003 (as amended).

APPENDIX 2 GUIDANCE ON CALCULATING THE QUANTITY OF A SALT AND ITS ANHYDROUS BASE FORM

Base substance vs salt substance

A controlled substance may be present in its base form, e.g. 10 mg of midazolam where there is 10 mg of midazolam base in the preparation. Alternatively, the controlled substance may be present within the preparation in a salt form, e.g. 10 mg of midazolam hydrochloride. In this instance a conversion factor must be applied in the calculation of the total controlled substance quantity to account for the percentage of the 10 mg which is made up by the presence of the salt molecules. In the description given above the conversion factor for midazolam hydrochloride is 89.9. Therefore, there is 8.99* mg of midazolam base present in the preparation.

*10 mg x (89.9/100) = 8.99 mg

Information regarding the active substance in the preparation can be found in the Summary of Product Characteristics (SPC) for the medicinal product. Please see examples detailed below. The conversion factors on a substance can be found on the Green List (for psychotropic substances) and the Yellow List (for narcotic drugs) on the INCB website.

Please contact controlleddrugs@hpra.ie should you require further clarification on the controlled substance.

Examples

Example 1
Base substance.

1. NAME OF THE MEDICINAL PRODUCT
Controlled Drug 10 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 10 mg of midazolam

For this preparation/product, the anhydrous base substance is midazolam. The anhydrous base quantity of midazolam in grams is 0.01 g.

Calculation: 10 mg (*quantity of the anhydrous base form in mg*) ÷1000 = 0.01 g (*quantity of the anhydrous base form in g*)

Example 2
The salt of the substance is stated in brackets.

1. NAME OF THE MEDICINAL PRODUCT
Controlled Drug 10 mg/2 ml Solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ml contains 5 mg of midazolam (as midazolam hydrochloride)
One ampoule of 2 ml contains 10 mg of midazolam

As the salt is referenced in brackets for the product in the SPC, this means a conversion factor has already been applied in the calculation of the product strength. For this preparation/product, the salt is midazolam hydrochloride, and the anhydrous base substance is midazolam. The quantity of the anhydrous base substance in grams is 0.01 g of midazolam in each 2 ml ampoules.

Calculation: 10 mg (quantity of the anhydrous base form in mg in 2 ml) ÷1000 = 0.01 g (quantity of the anhydrous base form in g in 2 ml)

Example 3
The substance is listed in its salt form.

1. NAME OF THE MEDICINAL PRODUCT
Controlled Drug 15 mg/ml Solution for injection 1 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ml contains 15 mg of midazolam hydrochloride

The product contains 15 mg midazolam hydrochloride. For this preparation/product, the conversion factor has not yet been applied as the salt is not referenced in brackets in the SPC. The salt is midazolam hydrochloride, and the anhydrous base substance is midazolam. The quantity of the anhydrous base substance midazolam in grams is 0.0135 grams in each 1 ml.

Calculation:
15 mg (quantity of the salt form in mg in 1 ml) ÷1000 = 0.015 g (quantity of the salt form in g in 1 ml)
0.015g ×0.899 (conversion factor for midazolam hydrochloride to midazolam) = 0.0135 g (quantity of the anhydrous base form in g in 1 ml)

Example 4
Calculating the strength of a liquid preparation with a volume of 120 ml.

1. NAME OF THE MEDICINAL PRODUCT
Controlled Drug 20 mg/ml Oral solution 120 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ml contains 20 mg of midazolam hydrochloride

For this preparation/product, the conversion factor has not yet been applied, as the salt is not referenced in brackets in the SPC. The salt is midazolam hydrochloride, and the anhydrous base substance is midazolam. The quantity of the anhydrous base substance midazolam in grams is 2.158 g in each 120 ml bottle.

Calculation:
20 mg (quantity of the salt form in mg in 1 ml) ÷1000 = 0.02 g (quantity of the salt form in g in 1 ml)
0.02g × 120 ml (volume of the product) = 2.4 g (quantity of the salt form in g in 120 ml)
2.4 g ×0.899 (conversion factor for midazolam hydrochloride to midazolam) = 2.158 g (quantity of the anhydrous base form in g in 120 ml)

Example 5
Calculating the total base quantity in a transdermal patch

1. NAME OF THE MEDICINAL PRODUCT
Controlled Drug 25 micrograms/hour Transdermal Patch

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each transdermal patch contains 4.2 mg of fentanyl

For transdermal patches, the SPC should be consulted to determine the total quantity of controlled drug contained within one transdermal patch.

For this preparation/product, the anhydrous base substance is fentanyl. The anhydrous base quantity of fentanyl in grams is 0.0042 g.

Calculation: 4.2 mg (quantity of the anhydrous base form in mg) ÷1000 = 0.0042 g (quantity of the anhydrous base form in g)