Guidance for Pharmaceutical Industry - Adverse Drug Reaction Reporting Requirements

Version 1.1

Pharmacy and Poisons Board of Hong Kong

CONTENTS

1. Introduction 3

   1.1 Purpose 3
   1.2 Scope 3

2. What is Adverse Drug Reaction? 4

   2.1 Adverse Drug Reaction 4
   2.2 Serious Adverse Drug Reaction 4
   2.3 Unexpected Adverse Drug Reaction 4

3. What Report Format should be Used? 5

4. What should be included in the Adverse Drug Reaction Report? 5

   4.1 Follow-up Report 6

5. What and How to Report? 6

   5.1 Local Adverse Drug Reaction Reporting 6
   5.2 Pharmaceutical Products Used in Clinical Trials 8

6. Specific Considerations for Advanced Therapy Products 10

   6.1 Potential Adverse Drug Reactions of Concern 10
   6.2 Traceability of Reports 11

7. Contact Information 12

Appendix 1 Statement of Purposes 13

Appendix 2 Summary of Adverse Drug Reaction (ADR) Reporting Requirements 14

Document Information 15

1. Introduction

1.1 Purpose

This guidance sets out the requirements for reporting adverse drug reactions to the Drug Office, Department of Health (DH DO) by pharmaceutical industry. It covers the types of adverse drug reactions which should be reported, and the timelines and other requirements for reporting adverse drug reactions of pharmaceutical products.

1.2 Scope

This guidance applies to the reporting of adverse drug reactions of all pharmaceutical products in Hong Kong by pharmaceutical industry.

Pharmaceutical industry in this guidance includes:

- licensed wholesale dealers
- licensed manufacturers
- the holders of Certificate of Drug/Product Registration (the "Registration Certificate Holders")
- the holders of Certificate for Clinical Trial/Medicinal Test (the "Clinical Trial Certificate Holders")

Pharmaceutical industry should comply with the requirements set out in this guidance. In addition, pharmaceutical industry should observe requirements provided under the Personal Data (Privacy) Ordinance, Cap. 486 when reporting adverse drug reactions.

2. What is Adverse Drug Reaction?

2.1 Adverse Drug Reaction

An adverse drug reaction is a response, which is noxious and unintended, to a pharmaceutical product.

2.2 Serious Adverse Drug Reaction

A serious adverse drug reaction is any untoward medical occurrence that at any dose:

- results in death
- is life threatening
- requires inpatient hospitalization or results in prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- is a congenital anomaly/birth defect
- is a medically important event or reaction

2.3 Unexpected Adverse Drug Reaction

An unexpected adverse reaction is an adverse drug reaction whose nature, severity, specificity, or outcome is not consistent with the term or description used in the local product labelling.

3. What Report Format should be Used?

Adverse drug reaction report can be made on the Department of Health Adverse Drug Reaction Report Form or Council for International Organization of Medical Sciences (CIOMS) Form. A separate form should be used for each patient. Any follow-up information of an adverse drug reaction that has been reported to DH DO previously should be made on a new report form.

The Department of Health Adverse Drug Reaction Report Form is available at:
www.drugoffice.gov.hk/adr_industry.html
The CIOMS Form is available at the following link:
cioms.ch/index.php/cioms-form-i

4. What should be included in the Adverse Drug Reaction Report?

The form should be completed to the best of knowledge and information should be provided as much as possible.

The following items are considered essential for causality assessment and should be provided whenever possible:

- patient information[1] (**initials or reference number will be sufficient**; full name and other kinds of personal identifier of the patient, such as identity card number and hospital admission number, should **NOT** be provided on the report form)
- adverse reaction description (including the date of onset of reaction and, if related to a vaccine, adverse reaction category)

[1] Pharmaceutical industry should observe the requirements provided under the Personal Data (Privacy) Ordinance, Cap. 486 when reporting adverse drug reactions.

- drug therapy or vaccine including product name (particularly biological product and vaccine; or manufacturer's information) of the suspected and concomitant drug(s), batch number (particularly biological product and vaccine), dosage, route, dates of starting and stopping drug therapy, reason for use, etc.
- the interacting agent(s) (i.e. drugs, herbs or food) if suspected drug interaction is involved
- treatment of adverse drug reaction
- outcome of the reaction
- sequelae of the reaction
- comments (e.g. allergies, relevant information - hepatic and renal functions, alcohol use, smoking)
- reporter details (contact information should be provided for necessary follow-up; please read 'Statement of Purposes' (Appendix 1) in respect of the collection of personal data).

4.1 Follow-up Report

Any follow-up information of an adverse drug reaction that has been reported to DH DO previously should be made on a new report form. Please indicate that it is a follow-up report and quote the unique number of the previous adverse drug reaction report.

5. What and How to Report?

5.1 Local Adverse Drug Reaction Reporting

5.1.1 Local Serious Adverse Drug Reactions

Pharmaceutical industry should report all serious adverse drug reactions occurring in Hong Kong to DH DO.

For Advanced Therapy Products (ATPs)[2], considering their complicated nature and our limited knowledge and experience, all serious or unexpected adverse drug reactions occurring in Hong Kong should be reported. Please refer to section 6 for special considerations for reporting of adverse drug reactions in relation to ATPs.

Reports should be submitted to DH DO as soon as possible and no later than 15 calendar days of receipt of information. Follow-up reports should also be submitted as required.

For other reporting requirements as the conditions for registration approval, Registration Certificate Holders should refer to the conditions specified on the Certificate of Drug/Product Registration for details.

5.1.2 How to Report

Local reports should be submitted to the Clinical Trials and Pharmacovigilance Unit of DH DO by:

- email to adr@dh.gov.hk
- completing the report form online at: www.drugoffice.gov.hk/adr_industry.html

Electronic submission is always the preferred means. If electronic means are not feasible, please return the completed form by:

- fax to 2319 6319
- mail or delivery to the Clinical Trials and Pharmacovigilance Unit at Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East, 100 How Ming Street, Kwun Tong, Kowloon, Hong Kong

[2] 'Advanced therapy product' means any of the following products that is for human use – (a) a gene therapy product; (b) a somatic cell therapy product; and (c) a tissue engineered product. Definitions of gene therapy product, somatic cell therapy product and tissue engineered product are set out in section 2 of the Pharmacy and Poisons Ordinance, Cap. 138.

If the adverse drug reactions are related to the pharmaceutical products used in clinical trial, please refer to section 5.2 of this guidance. Pharmaceutical industry may refer to the table summarizing those scenarios at Appendix 2 of this guidance for easy reference.

5.2 Pharmaceutical Products Used in Clinical Trials

5.2.1 Adverse Drug Reactions

Clinical Trial Certificate Holders should report all local adverse drug reactions that are serious and unexpected as soon as possible to Clinical Trials and Pharmacovigilance Unit of DH DO.

Fatal or life-threatening unexpected adverse drug reactions should be reported as soon as possible but no later than 7 calendar days after first knowledge by the sponsor that a case qualifies, followed by a report as complete as possible within 8 additional calendar days. This report must include an assessment of the importance and implication of the findings, including relevant previous experience with the same or similar pharmaceutical products.

Other serious, unexpected adverse drug reactions that are not fatal or life-threatening, it should be reported as soon as possible but no later than 15 calendar days after first knowledge by the sponsor that the case meets the minimum criteria for expedited reporting.

For non-serious adverse drug reactions and serious adverse drug reactions that are expected, it should be reported in a brief summary at the conclusion of the trial.

For more details concerning safety reporting related to clinical trial, please refer to the 'Notice of Requirement on Reporting of Local Drug Related Safety Report, Progress Report and Final Study Report in Clinical Trial' available at:
www.drugoffice.gov.hk/eps/do/en/pharmaceutical_trade/guidelines_forms/clinicalTrial.html

5.2.2 How to Report

Clinical Trial Certificate Holders should submit the reports to the Clinical Trials and Pharmacovigilance Unit of DH DO by email to: ct@dh.gov.hk.

Email is the preferred means. If email is not feasible, please return the completed form by:

- fax to 2803 4962
- mail or delivery to the Clinical Trials and Pharmacovigilance Unit at Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East, 100 How Ming Street, Kwun Tong, Kowloon, Hong Kong

6. Specific Considerations for Advanced Therapy Products

Due to their novelty, complexity and technical specificity, ATPs may raise some new and unexplored risks and safety concerns which require special attention. Reporting of adverse drug reactions and monitoring of such reports could facilitate early detection and management of the safety signal.

6.1 Potential Adverse Drug Reactions of Concern

Some potential adverse drug reactions of concern are listed below. Nevertheless, not all of the adverse drug reactions listed below are unique to ATPs. The list serves to provide examples to stimulate further considerations.

- adverse drug reactions related to quality characteristics of the product
    - transmission of diseases (e.g. viral, bacterial or parasitical infections and infestations) in relation to the origin of cells or tissues
    - tumourigenesis due to the alteration of differentiation capacity of the cells during the manufacturing process, "off target" mutations and unintended "on target" mutations in relation to gene editing, etc.
- adverse drug reactions related to the storage and distribution of the product
    - treatment failure due to impact on the biologic activity in related to preservation, freezing and thawing and breaking the controlled temperature conditions
- adverse drug reactions related to patient associated conditions/disease or underlying disease, or concomitant treatment/ interactions with other medicinal products
    - unwanted immunogenicity and the consequences
    - adverse drug reactions related to conditioning of patient, e.g. chemotherapy in case of CAR T-cell therapy
    - adverse drug reactions related to both intended and unintended genetic modification of the patient's cells

- early and late consequences of homing, grafting, differentiation, migration and proliferation
- infection with vectors used in gene therapy medicinal products
- adverse drug reactions related to clinical follow-up, e.g. immunosuppression associated with the co-medication

- adverse drug reactions related to reconstitution procedures
  - dosing errors and maladministration
- adverse drug reactions related to administration procedures and re-administration
- adverse drug reactions related to persistence of the product in the patient
  - later complications (e.g. malignancies and autoimmunity)
  - adverse drug reactions related to non-specific integration into other cells with the potential of tumourigenicity
  - adverse drug reactions related to germ line integration of transgene or other genetic transformation of the germ line
- transmission of virus or vector to healthcare professionals, care givers, offspring and other close contacts
- adverse drug reactions occurring in offspring due to:
  - foetal transmission of vectors, biologically active substances, cells, infectious agents, etc.
  - transmammary exposure of children for lactating women (to vectors, biologically active substances, cells, infectious agents, etc.)

6.2 Traceability of Reports

To enable traceability of adverse drug reaction reports to the product, reports which do not contain the batch number of the ATP used should be followed up to obtain such information. Batch number should be included in the report to DH DO.

For ATPs, pharmaceutical industry should ensure that database or other record system capable of linking the adverse drug reaction reports with other traceability data is in place. Such linkage could be established via the batch number of the ATPs used or other traceable data.

7. Contact Information

Clinical Trials and Pharmacovigilance Unit

Drug Office, Department of Health
Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East,
100 How Ming Street, Kwun Tong, Kowloon, Hong Kong

For enquiries on reporting adverse drug reaction:
Phone: 2319 2920
Fax: 2319 6319
Email: adr@dh.gov.hk

For enquiries from Clinical Trial Certificate Holders:
Phone: 3974 4180
Fax: 2803 4962
Email: ct@dh.gov.hk

Appendix 1 Statement of Purposes

Purpose of Collection

This personal data are provided by reporter for the purposes of reporting adverse drug reaction of the patient to the Department of Health (DH). The personal data provided will be used by DH for the following purposes:

(a) follow-up of the case report; and

(b) surveillance of drug-related events.

2. The provision of personal data is voluntary. If you do not provide sufficient information, we may not be able to assess the report properly.

Classes of Transferees

3. The personal data you provide are mainly for use within DH. Apart from this, the data may only be disclosed to parties where you have given consent to such disclosure or where such disclosure is allowed under the Personal Data (Privacy) Ordinance.

Access to Personal Data

4. You have a right of access and correction with respect to personal data as provided for in sections 18 and 22 and Principle 6 of Schedule 1 of the Personal Data (Privacy) Ordinance. Your right of access includes the right to obtain a copy of your personal data. A fee may be imposed for complying with a data access request.

Enquiries

5. Enquiries concerning the personal data provided, including the making access and corrections, should be addressed to:

Senior Pharmacist
Clinical Trials and Pharmacovigilance Unit
Drug Office
Department of Health
Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East,
100 How Ming Street, Kwun Tong, Kowloon, Hong Kong
Tel: 2319 2920

Appendix 2 Summary of Adverse Drug Reaction (ADR) Reporting Requirements

Who to Report	Type of Pharmaceutical Product	Type of ADR Report	Reporting Time-frame	Reporting Office
Licensed wholesale dealers / Licensed manufacturers / Registration certificate holders	All pharmaceutical products* other than advanced therapy products	Local serious ADR	As soon as possible and no later than 15 calendar days	Clinical Trials and Pharmacovigilance Unit, Drug Office, Department of Health
	Advanced therapy products*	Local serious or unexpected ADR		
Clinical trial certificate holders	Pharmaceutical products used in clinical trials	Fatal or life-threatening unexpected ADR	As soon as possible and no later than 7 calendar days, followed by a report as complete as possible within 8 additional calendar days	
		Other serious and unexpected ADR	As soon as possible and no later than 15 calendar days	
		Non-serious ADR / Serious expected ADR	At the conclusion of the trial (reported in brief summary)	

*Additional reporting requirements may be specified on the Certificate of Drug/Product Registration.

Document Information

Version	Date	Description of Change
1.0	1 August 2021	(First version issued in June 2021)
1.1	25 January 2024	Updates contact information

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