Guidance for Healthcare Professionals – Adverse Drug Reaction Reporting

Version 2.0.1
(Draft for comment)

Drug Office
Department of Health

Contents

1. Introduction

Adverse drug reaction reporting is an integral element in drug safety surveillance and pharmacovigilance.

To enhance the post-market drug surveillance activities, the Drug Office of the Department of Health (DH DO) collects adverse drug reaction reports of pharmaceutical products for use in Hong Kong from healthcare professionals and conducts causality assessment to assist subsequent formulation of risk management strategies when necessary.

Healthcare professionals including doctors, Chinese medicine practitioners, dentists, pharmacists and nurses are encouraged to report suspected adverse drug reaction of their patients voluntarily.

This document serves as a guidance for reporting adverse drug reaction by healthcare professionals. It covers the types of adverse drug reactions which are encouraged to be reported, the information to be included in the report, and the manner of reporting.

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; or
- 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. Where to Get the Report Form?

Adverse drug reaction report can be made by completing the online report form at http://www.drugoffice.gov.hk/adr.html.

Alternatively, adverse drug reaction report can be made on DH DO Adverse Drug Reaction Report Form (Appendix 1). The form is also available at http://www.drugoffice.gov.hk/adr.html.

4. What to Report?

Healthcare professionals are encouraged to report the following adverse drug reaction cases:

- All suspected serious adverse drug reaction, even if the reaction is well known;
- Suspected drug interactions including drug-drug and drug-herb interactions;
- Non-serious adverse drug reactions but the reactions are deemed medically significant by the healthcare professional (e.g. increased frequency or unusual presentation of a known adverse drug reaction);
- Unexpected adverse drug reactions, i.e. the reactions are not found in the product information or labelling (e.g. an unknown side effect in a new drug).

If in doubt, please report.

You do not need to be certain that the adverse drug reaction is related to the suspected drug.

4.1 Special Considerations for Advanced Therapy Products

Due to their novelty, complexity and technical specificity, advanced therapy products[1] may raise some new and unexplored risks to and safety concerns which requires special attention. The reporting of adverse drug reactions and the monitoring of such reports could facilitate the early detection and management of the safety signal.

Some potential adverse drug reactions of concern are listed below –

- Adverse drug reactions related to quality characteristics of the product
  - Transmission of diseases (e.g. viral, bacterial, 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.

[1] "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. For detailed definition of each of the products, please refer to Appendix 2.

- Adverse drug reactions related to the storage and distribution of the product
  - For example, 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
  - For example, 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.

5. What should be Included in the Report?

Use a separate form for each patient. Please try to complete the form to the best of your knowledge and provide as much information as possible. The following items are considered essential for causality assessment and should be provided whenever possible:

- patient information (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*);
- details of drug therapy or vaccine (including the suspected and concomitant drug(s)) –

- product name;
- manufacturer's name if generic name is used in the report or the report involved the use of advanced therapy product, biological product or vaccine;
- supplier's name if different from manufacturer, particularly for advanced therapy products;
- batch number, particularly for biological product and vaccine;
- for advanced therapy products, batch number or ISBT128 code or Single European Code (SEC)[2] for identification of each container of the product to ensure the monitoring and tracing of product;
- dosage and route of administration;
- dates of starting and stopping drug therapy; and
- 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 the Statement of Purposes (Appendix 5) in respect of the collection of personal data).

* Note: Adverse drug reaction related to vaccine can be classified under one of the following Adverse Reaction Categories

Adverse Reaction Categories	**Descriptions**
Allergic reactions	Anaphylaxis is the severe reaction that characteristically evolves rapidly towards cardiovascular collapse requiring resuscitative therapy. Other examples of severe allergic reactions are wheezing or shortness of breath due to bronchospasm, swelling of mouth or throat, skin manifestation (e.g. hives, eczema, pruritus); or facial or generalized edema. Allergic reactions usually occur within 24 hours of immunization.
Local reaction	Local reactions, usually occurs within 5 days of immunization, of concern may include abscess (sterile or infected), or other severe local reactions, such as redness and swelling that extend beyond the nearest joint or last 4 days or more.

[2] Both ISBT 128 (maintained by the Council for Commonality in Blood Banking Automation ("ICCBBA")) and SEC (established under the Commission Directive (EU) 2015/565) are internationally recognized coding systems for identification of the medical products containing cells or tissues for tracing purpose. Some ATPs may use the ISBT 128 or SEC to encode the product and in such case, a unique ISBT 128 code or SEC could be found on the label of each container of the ATPs containing cells or tissues. The code on each container is different and unique. Samples of labels are appended in Appendices 3 (ISBT 128) and 4 (SEC). For ATPs encoded with a system other than ISBT 128 and SEC, batch number could be entered in the ATP record instead.

Systemic reaction	Systemic reactions usually occur within 5 days but may occur up to 3 months after immunization. Early onset ones of concern include toxic shock syndrome, hypotonic-hyporesponsive episode, persistent crying or screaming episodes, high fever (greater than 39 °C or 102.2 °F), sepsis, or rash (especially those lasts for 4 days or more or requires hospitalization). Thrombocytopaenia (with platelet < 50,000/mm^3) may have a delayed onset.
Neurological disorders	Some neurological adverse reactions may be related to vaccination. Seizures (usually generalized convulsion), encephalopathy, meningitis or encephalitis, if occurred, may have an onset within 15 days of immunization. Brachial neuritis or Guillain-Barré Syndrome, if occurred within 3 months of immunization, may be related to the immunization.

5.1 Follow-up Reports

Acknowledgement with a unique reference number will be issued to each report received. Any follow-up information of an adverse drug reaction that has been reported to DH DO previously can be made on a new report form. Please indicate that it is a follow-up report and quote the unique reference number from the previous report.

6. How to Report?

- Report online by completing the online report form at http://www.drugoffice.gov.hk/adr.html; **OR**
- Download the report form (available at http://www.drugoffice.gov.hk/adr.html) and return the completed report by:
  - email to adr@dh.gov.hk;
  - fax to 2319 6319; or
  - mail or delivery to the Undesirable Medical Advertisements and Adverse Drug Reaction Unit, Drug Office, Department of Health at Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East, 100 How Ming Street, Kwun Tong, Kowloon.

7. What Happen to the Report?

Any information related to the identities of the reporter and the patient will be kept in strict confidence.

All adverse drug reaction reports are reviewed by a team of professional staff. Serious adverse drug reaction reports may be reviewed by expert advisors if indicated.

Information of the report will be entered into the adverse drug reaction database system for analysis.

Through monitoring and analysis of adverse drug reaction reports, signals related to safety profile of medicines such as unexpected adverse drug reactions, unusual presentation of a known adverse drug reaction, or a susceptible patient group may be identified. These findings will initiate further evaluation to establish the possible role of a medicine in causing the reaction and provide important information for the DH DO to conduct necessary actions such as changes in marketing authorization or providing early warnings to healthcare professionals.

8. Contact Information for Further Information

Undesirable Medical Advertisements and Adverse Drug Reaction Unit

Drug Office, Department of Health

Suite 2002-05, 20/F, AIA Kowloon Tower

Landmark East, 100 How Ming Street, Kwun Tong

Kowloon

Phone: 2319 2920

Fax: 2319 6319

Email: adr@dh.gov.hk

Appendix 1 DH DO Adverse Drug Reaction Report Form

Report can be returned by fax to 2319 6319
For Follow-up report (see Guidance),
Please provide previous case Ref. No.:_____

Department of Health
Adverse Drug Reactions (ADR) Report Form

Please read the following instructions:

1. Please read the Guidance for Healthcare Professionals (http://www.drugoffice.gov.hk/adr.html); and Guidance for Pharmaceutical Industry (http://www.drugoffice.gov.hk/adr_industry.html) before completing the ADR report form.
2. ADR can be briefly described as a noxious and unintended response to a pharmaceutical product (i.e. drug or vaccine).
3. If the ADR of a newborn/child may be related to the mother, please submit a separate report for the mother.
4. Please provide information to every section.
5. **Full name and any kind of personal identifier of the patient**, such as identity card number and hospital admission number, **should not be provided** on the report form.
6. Information of individual reporter will be treated in strict confidence. Please read the Statement of Purposes overleaf in respect of the collection of your personal data.
7. As limited space is provided, please use another page for additional information if necessary.
8. For further enquiries, please contact the Undesirable Medical Advertisements and Adverse Drug Reaction Unit of Drug Office of the DH at 2319 2920.

Section (A): Patient Information

Patient initials or ref. no.: _____ **(Please read instruction 5 above)**
Sex: ❑M ❑ F ❑ Unknown For woman, is she pregnant? ❑ No ❑ Yes ❑ Unknown
Weight (if known): _____ kg Date of birth: (dd/mm/yyyy) _____/_____/_____ or age (at last birthday):_____
Ethnic group: ❑ Chinese ❑ Asian (Not Chinese) ❑ African ❑ Caucasian ❑ Eurasian ❑ Unknown ❑ Others_____

Section (B): About the Adverse Drug Reaction

Date of onset of ADR: (dd/mm/yyyy) _____/_____/_____

Description of event: _____

_____

ADR category (for vaccine related ADR only):
❑ Allergic reaction ❑ Local reaction ❑ Systemic reaction ❑ Neurological disorders
Severity (can tick more than 1 box if appropriate):
❑ Life threatening ❑ Prolonged Hospitalization ❑ Hospitalized on: (dd/mm/yyyy) _____/_____/_____
❑ Hospitalization NOT required
Laboratory result (if applicable):_____

All Drug Therapies/Vaccines Prior to ADR (Please use trade names and, for vaccine, indicate batch number. Please circle the suspected drug.)	**Daily Dosage** (dose number for vaccines e.g. 1st DTP)	**Route**	**Date Begun**	**Date Stopped**	**Reason for Use**

Section (C): Treatment & Outcome

Treatment for ADR: ❑ No ❑ Yes. Details (including dosage, frequency, route, duration) _____

Laboratory result (if applicable): _____

Outcome:❑ Recovered on: (dd/mm/yyyy) / / ❑ Not yet recovered ❑ Unknown ❑ Died on: (dd/mm/yyyy) / /

Sequelae: ❑ No ❑ Yes: ❑ Persistent disability ❑ Birth defect ❑ Medically significant events Details:_____

Allergies or other relevant history (including medical history, liver/kidney problems, smoking, alcohol use etc)

_____

Section (D): Reporter Details (Please read instruction 6 above)

Name of Reporter and Organization:_____ Sector of service: ❑ Private ❑ Public

Occupation: ❑ Doctor ❑ Chinese medicine practitioner ❑ Dentist ❑ Pharmacist ❑ Nurse ❑ Others_____

Correspondence Address:_____

Tel. no.: _____Fax. no.: _____ Email: _____

Also report to: ❑Manufacturer ❑Distributor/Importer ❑Others_____ Date of this report:_____

Please fold inside along the dotted line and seal the edge

Please Affix Stamp

To: Undesirable Medical Advertisements and Adverse Drug Reaction Unit
Drug Office
Department of Health
Suites 2002-05, 20/F, AIA Kowloon Tower,
Landmark East, 100 How Ming Street, Kwun Tong, Kowloon

Please seal the edge

Please seal the edge

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
Undesirable Medical Advertisements and Adverse Drug Reaction Unit
Drug Information and Pharmacovigilance Division
Drug Office
Department of Health
Suites 2002-05, 20/F, AIA Kowloon Tower,
Landmark East, 100 How Ming Street, Kwun Tong, Kowloon
Tel: 2319 2920

Appendix 2 Definitions of Gene Therapy Products, Somatic Cell Therapy Product and Tissue Engineered Products (Proposed)

Gene Therapy Product

Gene therapy product—

(a) means a product—

(1) that contains an active substance containing or consisting of a recombinant nucleic acid that may be used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence; and

(2) the therapeutic, prophylactic or diagnostic effect of which relates directly to—

(A) the recombinant nucleic acid sequence it contains; or

(B) the product of genetic expression of that sequence; but

(b) does not include a vaccine against an infectious disease.

Somatic Cell Therapy Product

Somatic cell therapy product means a product that—

(a) contains or consists of any of the following cells or tissues—

(1) cells or tissues that have been subject to substantial manipulation so that their biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered;

(2) cells or tissues that are not intended to be used for the same essential functions in their recipient as in their donor; and

(b) is presented as having properties for, or may be used in or administered to human beings with a view to—

(1) treating, preventing or diagnosing a disease; or

(2) restoring, correcting or modifying physiological functions,

through the pharmacological, immunological or metabolic action of those cells or tissues.

Tissue Engineered Product

Tissue engineered product—

(a) means a product that—

(1) contains or consists of any of the following cells or tissues—

(A) cells or tissues that have been subject to substantial manipulation so that their biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement have been altered;

(B) cells or tissues that are not intended to be used for the same essential functions in their recipient as in their donor; and

(2) is presented as having properties for, or may be used in or administered to human beings with a view to, regenerating, repairing or replacing a human tissue; but

(b) does not include a product that—

(1) contains or consists of exclusively non-viable human or animal cells or tissues; and

(2) does not act principally by pharmacological, immunological or metabolic action.

Substantial Manipulation

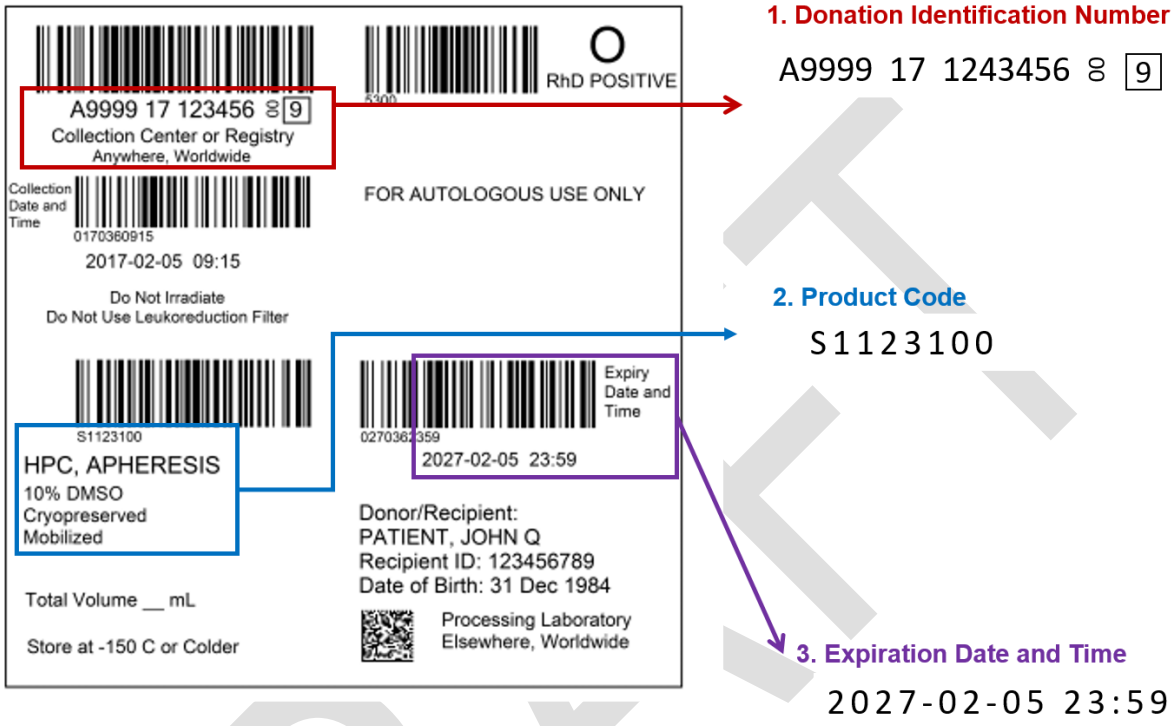
Substantial manipulation, in relation to cells or tissues, does not include the manipulation processes set out in the Schedule of the Pharmacy and Poisons Ordinance (Cap. 138).

Under the Schedule of Cap. 138, the following manipulation processes are not substantial manipulations—

1. Cutting
2. Grinding
3. Shaping
4. Centrifugation
5. Soaking in antibiotic or antimicrobial solutions
6. Sterilization
7. Irradiation
8. Cell separation, concentration or purification
9. Filtering
10. Lyophilization
11. Freezing
12. Cryopreservation
13. Vitrification

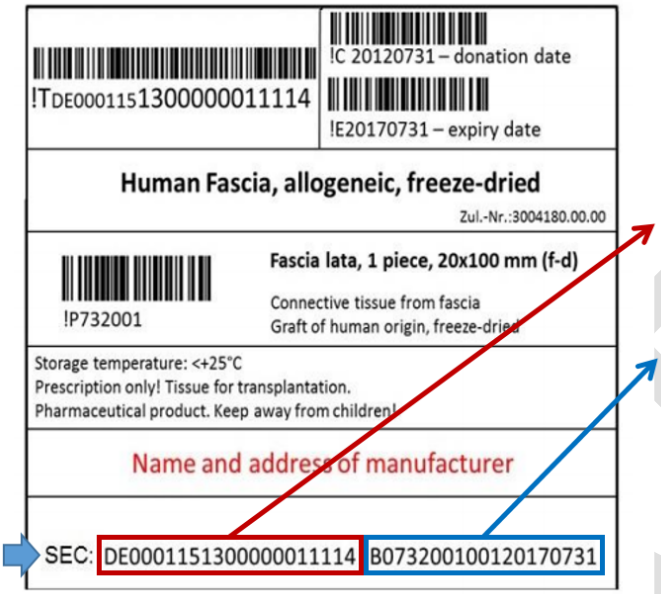
Appendix 3 Sample of Labels containing ISBT 128 Code

ISBT 128 code contains three components – Donation Identification Number (DIN), product code and expiration date and time. Sample label below shows the location where the three components of the ISBT 128 code could be found.



Appendix 4 Sample of Labels containing Single European Code (SEC)

SEC contains two components – Donation identification sequence and product identification sequence. SEC on the product label precedes with the letters "SEC:" and follows with two alphanumeric sequences. Sample label below shows the location where the two components of the SEC could be found.



1. Donation Identification Sequence

DE 000115 1300000011114

2. Product Identification Sequence

B 0732001 001 20170731

Appendix 5 Statement of Purposes

Purpose of Collection

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

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Landmark East, 100 How Ming Street
Kwun Tong, Kowloon
Tel: 2319 2920

Document Information

Version	Date	Description of Change
1.0	Jan 2015	Previous version (Final)
1.1	Dec 2019	Previous version (Final) • Update of contact information
2.0	29.10.2019	Second version (Draft for comment) • Included specific considerations for reporting adverse drug reactions concerning advanced therapy products
2.0.1	13.1.2020	Second version (Draft for comment) • Update of contact information