LIST OF UPDATES FOR
DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021
(February 2021 Updates)

There are four (4) amendments for the February 2021 DRGD Updates as below:

Main Body of DRGD Third Edition

1. Amendment of Section B: Product Registration Process, 11.2 Product Registration Number, Page 43 and 44

Appendices of DRGD Third Edition

Appendix 3: Guideline on Registration of New Drug Products

2. Amendment of 1. Definition, Page 1

Appendix 5: Guideline on Registration of Generics

3. Amendment of 2. Generic Application, Page 2

Appendix 19: General Labelling Requirements

4. Amendment of Table 1 footnote, Page 3

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021

(February 2021 Updates)

1. Section B: Product Registration Process , 11.2 Product Registration Number, Page 43 and 44 is amended by -

(a) deleting administrative code "Y" since it is no longer applicable at the end of "e.g. MAL11070001ACERS" (page 43) and "Refers to administrative code used by NPRA i.e. C/ E/ R/ S" (page 44)

2. Appendix 3: Guideline on Registration of New Drug Products, Page 1 is amended by -

(a) inserting a new paragraph after *1.2 Hybrid (single/ combination products with registered active moieties)*:

"For medicinal gases classified as new drug products, please refer to Directive No. 8, 2021 and Guideline on Registration of Medicinal Gases.

Reference:

(i) Directive No. 8, 2021, NPRA.600-1/9/13 (18): *Direktif Berkenaan Pengukuhan Pelaksanaan Kawalan Regulatori Ke Atas Produk-Produk Gas Perubatan Dan Penggunaan Guideline on Registration of Medicinal Gases* (11 February 2021)*"*

3. Appendix 5: Guideline on Registration of Generics, Page 2 is amended by -

(a) inserting a new paragraph after (ii) (b) Abridge Evaluation

"For medicinal gases classified as generic products, please refer to Directive No. 8, 2021 and Guideline on Registration of Medicinal Gases.

Reference:

(i) Directive No. 8, 2021, NPRA.600-1/9/13 (18): *Direktif Berkenaan Pengukuhan Pelaksanaan Kawalan Regulatori Ke Atas Produk-Produk Gas Perubatan Dan Penggunaan Guideline on Registration of Medicinal Gases* (11 February 2021)*"*

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(February 2021 Updates)

4. Appendix 19: General Labelling Requirements, Table 1 footnote, (#) iii. The following are exempted from the security label requirement, Page 3 is amended by -

(a) inserting the words “radiopharmaceutical with short half-life” before the words “temperature-sensitive and cold chain products”.

(b) substituting the words “E.g. vaccines and biologicals” with the words “E.g. vaccines, etc.”.

LIST OF UPDATES FOR
DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021
(March 2021 Updates)

There are two (2) amendments for the March 2021 DRGD Updates as below:

Appendices of DRGD Third Edition

Appendix 4: Guideline on Registration of Biologics

1. Amendment of E. Lot Summary Protocol and Lot Release for Vaccine, Page 9

Appendix 21: Special Conditions for Registration of a Particular Product or Group of Products

2. Addition of 9. COVID-19 Vaccines, Page 3

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021

(March 2021 Updates)

1. **Appendix 4: Guideline on Registration of Biologics, Page 9** is amended by-

(a) inserting a new paragraph after "Submit Lot/ Batch Release Certificate issued by the competent authority." in *E. Lot Summary Protocol and Lot Release for Vaccine*:

"Every batch of registered vaccines and plasma products imported is required to undergo physical testing for Lot Release activity.

COVID-19 vaccine products imported and used during a pandemic are excluded from the requirement to conduct physical testing for Lot Release activity."

(b) inserting new references:

"References:

Directive No. 9, 2020, (9)dlm.BPFK/PPP/07/25Jld.4: *Direktif Keperluan Menjalankan Ujian Fizikal Untuk Aktiviti Lot Release Bagi Semua Vaksin dan Produk Plasma Berdaftar Yang Diimport* (12 May 2020)

Keputusan Pihak Berkuasa Kawalan Dadah (PBKD) Berkenaan Pengecualian Daripada Keperluan Menjalankan Ujian Fizikal Untuk Aktiviti Lot Release Bagi Semua Produk Vaksin COVID-19 Berdaftar Yang Diimport Dan Digunakan Semasa Situasi Pandemik, [NPRA.600-1/9/7(41)], (19 February 2021)"

2. **Appendix 21: Special Conditions for Registration of a Particular Product or Group of Products, Page 3** is amended by -

(a) adding a new entry after *8. VACCINES*:

" 9. COVID-19 VACCINES

a) The product registration holder shall ensure that the product shall only be sold or supplied to the government or other party authorized by the government only.

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DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021

(March 2021 Updates)

Reference:

Keputusan Pihak Berkuasa Kawalan Dadah (PBKD) Berkenaan Penetapan Syarat Pendaftaran Bagi Vaksin COVID-19 Yang Diluluskan Pendaftaran Bersyarat Hanya Boleh Dijual Dan Dibekal Kepada Pihak Kerajaan Atau Pihak Yang Dibenarkan Oleh Kerajaan, [NPRA.600-1/9/7 (43)], (10 March 2021)*"*

LIST OF UPDATES FOR
DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021
(April 2021 Updates)

There are four (4) amendments for the April 2021 DRGD Updates as below:

Main Body of DRGD Third Edition

SECTION E: POST-REGISTRATION PROCESS

1. Substitution in 21.2 Post-Market Surveillance, Page 61

Appendices of DRGD Third Edition

Appendix 20: Specific Labelling Requirements

2. Addition of new ingredient and safety information, No. 123, Mirtazapine, Page 119
3. Addition of new ingredient and safety information, No. 167, Rocuronium, Page 159
4. Addition of new ingredient and safety information, No. 202, Vascular Endothelial Growth Factor (VEGF) Inhibitors, Page 196

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021

(April 2021 Updates)

1. **SECTION E: POST-REGISTRATION PROCESS, Page 61** is amended by -

(a) substituting 418.4 with 418 in *Product Complaints* in *21.2 Post-Market Surveillance*.

Amendment of Appendix 20: Specific Labelling Requirements

2. **Addition of new ingredient 123. Mirtazapine and safety information on page 119** as follows in accordance with Directive No.12, 2021: *Direktif Untuk Semua Produk Yang Mengandungi Mirtazapine: Pengemaskinian Sisip Bungkusan Dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan Risiko Amnesia Dan Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS)* as decided in DCA Meeting No. 355, which takes effect on 1 May 2021 –

"123. MIRTAZAPINE

The following statements shall be included in the package insert and Consumer Medication Information Leaflet (RiMUP) for products containing Mirtazapine;

Package Insert

a) Adverse Effects/ Undesirable Effects:

Nervous system disorders

Frequency 'common': Amnesia

Skin and subcutaneous tissue disorders

Frequency 'not known': Drug reaction with eosinophilia and systemic symptoms (DRESS)

Consumer Medication Information Leaflet (RiMUP)

a) Side effects:

Frequency 'common': Memory problems

Frequency 'not known': Serious allergic reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). DRESS appears initially as flu-like symptoms with a rash on the face and then with an extended rash, high temperature and enlarged lymph nodes."

3. **Addition of new ingredient 167. Rocuronium and safety information on page 159** as follows in accordance with Directive No.11, 2021: *Direktif Untuk Semua Produk Yang Mengandungi Rocuronium: Pengemaskinian Sisip Bungkusan Dengan Maklumat Keselamatan Berkaitan Risiko Kounis Syndrome* as decided in DCA Meeting No. 355, which takes effect on 1 May 2021 –

"167. ROCURONIUM

The following statements shall be included in the package insert for products containing Rocuronium;

Package Insert

a) Adverse Effects/ Undesirable Effects:

Cardiac disorders

Frequency 'not known': Kounis Syndrome"

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(April 2021 Updates)

4. **Addition of new ingredient 202. Vascular Endothelial Growth Factor (VEGF) Inhibitors and safety information on page 196** as follows in accordance with Directive No.10, 2021: *Direktif Untuk Semua Produk Yang Mengandungi Vascular Endothelial Growth Factor (VEGF) Inhibitors Untuk Kegunaan Sistemik (Kecuali Kegunaan Pada Mata): Pengemaskinian Sisip Bungkusan Dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan Risiko Artery Dissections Dan Aneurysms* as decided in DCA Meeting No. 355, which takes effect on 1 May 2021 –

"**202. Vascular Endothelial Growth Factor (VEGF) Inhibitors**

The following statements shall be included in the package insert and Consumer Medication Information Leaflet (RiMUP) for products containing VEGF inhibitors for systemic use (except application on eyes);

Package Insert

a) Adverse Effects/ Undesirable Effects:

Vascular disorders

Frequency "not known": aneurysms and artery dissections

Consumer Medication Information Leaflet (RiMUP)

a) Side effects:

Frequency 'not known': An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)."

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(May 2021 Updates)

There are three (3) amendments for the May 2021 DRGD Updates as below:

Main Body of DRGD Third Edition

Section B: Product Registration Process

1. Amendment of 7.12 Product Authentication, Page 37

Appendices of DRGD Third Edition

Appendix 4: Guideline on Registration of Biologics

2. Amendment of E. Lot Summary Protocol and Lot Release for Vaccine, Page 9

Appendix 19: General Labelling Requirements

3. Amendment of Table 1 footnote, Page 3

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021

(May 2021 Updates)

1. Section B: Product Registration Process, 7.12 Product Authentication, Page 37 is amended by-

(a) substituting the words “security device” with the words “security label (hologram)”.

(b) substituting the word “will” with the word “shall” before the words “be affixed to” in the second statement of the first paragraph.

(c) substituting the words “each unit pack” with the words “the secondary packaging or immediate label” before the words “of the product” in the second statement of the first paragraph.

(d) substituting the word “outer” with the word “secondary” in the first statement of the second paragraph.

(e) substituting the word “packaging” with the word “label” in the first statement of the second paragraph.

(f) substituting the statement “None of the product particulars on the label shall be covered by the security device” with the new statement, “The security label (hologram) shall cover none of the product particulars on the label.”

2. Appendix 4: Guideline on Registration of Biologics, Page 9 is amended by-

(a) inserting a new statement after “Submit Lot/ Batch Release Certificate issued by the competent authority.” in *E. Lot Summary Protocol and Lot Release for Vaccine*:

“Lot Release activity is implemented for biological products manufactured in Malaysia.”

(b) inserting a new reference:

“Reference:

Directive No. 13, 2021, NPRA.600-1/9/13(23): *Direktif Berkenaan Pelaksanaan Aktiviti Lot Release Ke Atas Produk Vaksin dan Produk Plasma Yang Dikilangkan Di Malaysia* (28 April 2021)”

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021

(May 2021 Updates)

3. Appendix 19: General Labelling Requirements, Table 1 footnote, Page 3 is amended by –

(a) inserting a new statement " ii. For large volume parenteral (LVP) products defined as containers labelled as containing more than 100mL [based on the United States Pharmacopeia (USP)], the security label (hologram) shall be affixed on the immediate label of each unit of the product." after statement i.
(b) moving the word "shall" from before the word "however" to after it in the statement, "The security label shall, however, not be affixed to the outer shrink wrap of the product."
(c) inserting a new statement "It is sufficient for the security label (hologram) to be affixed to the outer carton / unit of sale for small volume parenteral (SVP) products [defined as packaged in containers and labelled as containing 100mL or less based on the United States Pharmacopeia (USP)]. in "The following are exempted from the security label requirement:"

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DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021
(June 2021 Updates)

There is one (1) amendment for the June 2021 DRGD Updates as below:

Appendices of DRGD Third Edition

Appendix 20: Specific Labelling Requirements

1. Amendment of existing safety information, No. 37, Ceftriaxone, Page 39

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(June 2021 Updates)

Amendment of Appendix 20: Specific Labelling Requirements

1. **The specific labelling requirements for existing ingredient, No. 37 Ceftriaxone on page 39** is amended in accordance with Directive No.14, 2021: *Direktif Untuk Semua Produk Yang Mengandungi Ceftriaxone: Pengemaskinian Sisip Bungkusan Dengan Maklumat Keselamatan Berkaitan Risiko Encephalopathy* as decided in DCA Meeting No. 358, which takes effect on 1 July 2021 –

(a) by inserting the following statement:

"CEFTRIAXONE

The following statements shall be included in the package insert for products containing Ceftriaxone;

Package Insert

Adverse Effects/ Undesirable Effects:

Nervous system disorders
*Frequency 'not known': Encephalopathy**

**Reversible encephalopathy has been reported with the use of ceftriaxone, particularly when high doses are administered in patients with renal impairment and additional predisposing factors such as older age, pre-existing central nervous system disorders."*

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(July 2021 Updates)

There is one (1) amendment for the July 2021 DRGD Updates as below:

Appendices of DRGD Third Edition

Appendix 14: Evaluation Routes

1. Amendment of 2) Full Evaluation (Conditional Registration), Page 1

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DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIRST REVISION JULY 2021

(July 2021 Updates)

1. Appendix 14: Evaluation Routes, Page 1 is amended by -

(a) inserting a new reference in *2) Full Evaluation (Conditional Registration)*:

"References:

i. Directive No. 15, 2021, *NPRA.600-1/9/13(25)*: *Direktif Berkenaan Pelaksanaan Pendaftaran Bersyarat Produk Farmaseutikal Semasa Bencana Secara Recognition* (12 July 2021)"