Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

PRODUCT RESEARCH AND STANDARDS DEVELOPMENT DIVISION
Frequently Asked Questions (FAQs)
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1. POST-MARKETING SURVEILLANCE (PMS)

1.1. General Procedures

1.1.1. What are the requirements in submitting a complaint for suspected counterfeit drug?

I. If you are the Marketing Authorization Holder (MAH)/brand owner, you need to submit an affidavit of complaint which shall contain the following. The affidavit of complaint shall be accompanied by samples of counterfeit drug products duly marked for identification purposes:
   a. name of the product, the lot numbers and expiry date of the products he shall allege as counterfeit;
   b. name and address of the person and/or drug establishment or company he shall name as party-respondent; and
   c. specific acts that he shall allege as having been committed by the party-respondent; remedy or relief or action he shall intend FDA to take.

II. If you are a consumer or health care professional, you need to submit a letter of complaint containing the following. This shall be accompanied by the samples of suspected drug products duly marked for identification purposes:
   a. the name of the suspected product;
   b. the source or the name and address of the person from whom he/she acquired the suspected product;
   c. the mode of his acquisition; and
   d. the reason or fact giving rise to the suspicion that the drug product is counterfeit.

1.1.2. How can we report any sale or distribution of an unnotified product?

You may report any sale or distribution of unregistered products, through sending of an e-mail to ereport@fda.gov.ph, or you may proceed to the Food and Drug Action Center (FDAC) to submit the report with a sample, if possible.

1.1.3. Where to submit a complaint for a suspected counterfeit drug?

Complaint for a suspected counterfeit drug can be submitted at the FDAC.

1.1.4. How to notify or alert the FDA on a product recall?

The MAH is required to fill-out all of the required information in the Recall Notification template which can be accessed here: https://www.fda.gov.ph/cdrr-downloadables/ under "Marketing Surveillance". The Recall Notification including all relevant and necessary evidence and documents must be submitted to the FDAC in hard and soft copies, e.g., word document, excel file, and/or .pdf file.

Also, as per Section V, G. of the FDA Circular (F.C.) No. 2020-003 or the "Guidelines for Pharmaceutical Industry on Pharmacovigilance", the dissemination of Direct Healthcare Professional Communication (DHPC) letter is required whenever there are effects on the benefit-risk profile of a drug product, e.g., product recall, product defects. The issuance can be accessed in this link: https://www.fda.gov.ph/wp-content/uploads/2020/02/FDA-Circular-No.2020-003.pdf.

1.1.5. What are the requirements for the request of cancellation of a marketing authorization (MA)?

The MAH must submit a letter of intent through the letter lane at the FDAC containing the following:

a. reason for cancellation of MA, i.e., Certificate of Product Registration (CPR), Certificate of Listing of Identical Drug Product (CLIDP);
b. details of the last batch or lot distributed, i.e., batch/lot no., manufacturing date, expiry date, quantity, date distributed, and distribution list; and
c. original copy of the issued CPR or CLIDP, regardless if it is still valid or not.

1.1.6. What are the contact details of the PRSDD of the CDRR?

The landline number is (02) 8809-5596.

1.2. Product Verification

1.2.1. How long is the verification of a suspected counterfeit drug product?

The timeline for product verification of a drug product is fifty (50) calendar days.

1.2.2. What is issued if a drug product is verified as a counterfeit or not?

Upon verification, a Product Verification Certificate is issued to the requesting party. Subsequently, an FDA Advisory and FDA Order shall also be issued, if warranted.

1.2.3. How does the FDA coordinate with the MAH?

Once the Center receives the product requested for verification, an immediate communication is sent to the MAH, either by electronic mail or through phone conversation, containing the request for an authenticity certificate from the MAH whether they have manufactured, imported, or distributed the concerned product.

1.3. Product Recall

1.3.1. What is the legal basis of product recall?

F.C. No. 2016-012 that can be accessed in https://ww2.fda.gov.ph/attachments/article/349656/FDA%20Circular%20No.%202016-012.pdf.

1.3.2. What are the products that can be recalled as per F.C. No. 2016-012?

All health products registered or notified with the different Centers of the FDA, i.e., Center for Cosmetics Regulation and Research (CCRR), Center for Drug Regulation and Research (CDRR), Center for Device Regulation, Radiation Health and Research (CDRRHR), and Center for Food Regulation and Research (CFRR), can be recalled.

1.3.3. Who is responsible to do a recall?

The MAH is responsible to conduct a recall with proper coordination with all the stakeholders involved, e.g., clients, distributors, retail outlets, etc. The FDA oversees the recall done by the MAH.

1.3.4. What is a voluntary recall?

This is when the MAH on its own volition explicitly intends to conduct a recall of their drug product due to any of the following: violations on labeling information and/or issues on quality, safety, and efficacy which were discovered through their post-marketing surveillance activities or other official means.

1.3.5. Is there such a thing as an "FDA-initiated recall"?

As per F.C. No. 2016-012, there is no definition for FDA-initiated recall. However, a trigger for recall may come from any post-marketing surveillance activities of the FDA which shall be relayed by the FDA to the MAH for the commencement of a recall.

1.3.6. What are the other reasons when a recall is deemed as needed?

You may refer to Section 5.2 of F.C. No. 2016-012. It must be noted that all received triggers by the agency for recall shall be appropriately evaluated or investigated by the FDA to verify the need for recall.

1.3.7. What is a recall strategy?

It is a plan in line with a recall made by the MAH and its partners, e.g., manufacturer, showing chronological actions to be done and containing all of the information as stated in Section 5.4.1 of F.C. No. 2016-012. Upon receipt of the recall notification from the MAH, a proposed recall strategy may also be drafted by the FDA when the recall strategy made by the MAH is insufficient.

1.3.8. What happens in the conference of recall between the FDA and MAH?

Only two (2) representatives from each company shall be invited for a conference. Details of the said conference, i.e., date, time, and venue, shall all be relayed by the CDRR to the MAH through a formal letter, e-mail correspondence, and telephone call. On the actual day of the conference, there will be a discussion of the best recall strategy to be implemented, and presentation of recall actions and media announcement following Section 5.6 of F.C. No. 2016-012. Representatives of the MAH are encouraged to bring supporting documents regarding their recall. A PowerPoint presentation of the actions done by the company is optional.

1.3.9. If I do voluntary recall, will I be given a Product Recall Order (PRO)?

No. There will be due process as per F.C. No. 2016-012. The MAH will be called for a conference to determine the best recall strategy to be implemented by the MAH. If there is no agreement on this strategy between the FDA and MAH or the MAH declines to do any recall after it has been established that there is a need for recall, there will be a referral to the Legal Services Support Center (LSSC) for the appropriate issuance of a PRO. This PRO will be personally issued by the Regulatory Enforcement Unit (REU).

1.3.10. If I do voluntary recall, do I need to wait for any instructions from the FDA on when to start?

No. The MAH may commence with their recall once recall notification (link: https://www.fda.gov.ph/cdrr-downloadables/ under "Marketing Surveillance") is submitted to the FDA. Thereafter, the FDA shall follow-up on the recall actions of the MAH through the stated conference or through recall status reports.

1.3.11. What is a Media Announcement?

This is a posting, publication, or announcement done by the MAH through any of the quad media, i.e., print/newspaper, radio, television, social media/online (official website) and/or through the FDA website, relaying the recall of their product. This is required to be done by the MAH for all recalls as part of protecting the public.

1.3.12. What happens to the recalled products after complete retrieval in rural and urban areas of affected stocks?

Stocks are subjected to preferred disposition of the MAH. Refer to Annex D of F.C. No. 2016-012.

1.3.13. What if I prefer to locally destroy the stocks of a recalled product?

At a minimum of one (1) week before the scheduled activity, the MAH is required to submit to the letter lane or counter at the FDAC, your notification on the destruction. The following information must be provided:

a. Date, time, and venue of disposal;
b. Identity of the DENR accredited third-party waste treater who shall facilitate the disposal; and
c. Contact details (e.g., telephone no., mobile no., e-mail address) of the focal person to whom the FDA shall coordinate the activity.

It is imperative that the notification of destruction is submitted to the FDA, at least one (1) week before the activity, to give ample time for coordination of this request by the Center to the field officers from the FROO for appropriate witnessing. The MAH may follow-up on the status of this request through calling (02) 8809-5596 or e-mailing cdrr_postmarketsurveillance@fda.gov.ph.

1.3.14. What is a termination of recall?

A recall may be terminated if all affected stocks (specific batches or lots) of a product deemed for recall are retrieved both in urban and rural areas, appropriately disposed or destroyed, complied with the necessary requirements as stated in Annex D of F.C. No. 2016-012, and are never again made available to the consuming public.

1.3.15. How does the FDA terminate a recall?

Evaluation of required documents for termination of recall (refer to Annex D of F.C. No. 2016-012) is done and must be deemed sufficient, and complete. Appropriate advisory on the termination of recall shall be posted at the FDA website if deemed necessary by the agency.

1.3.16. For unregistered or counterfeit products, is recall applicable?

No, seizure of stocks by regulatory field officers is done for this case.

1.4. Cancellation of Marketing Authorization (MA)

1.4.1. What is an MA?

As per Administrative Order (A.O.) No. 2016-0008, this is an official document issued by the competent drug regulatory authority (DRA), i.e., Philippines FDA, for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy, and quality, and containing, *inter alia*: the name of the product; the pharmaceutical dosage form; the quantitative formula (including excipients) per unit dose; the shelf-life and storage condition(s); and packaging characteristics; specific information on which authorization is based [e.g., "The product(s) must conform with all the details provided in the application and as modified in subsequent correspondence."]; the product information approved for health professionals and the public, the sales category, the name and address of the holder of the authorization, and the period of validity of the authorization. In the Philippines, the MA is in the form of a CPR or CLIDP.

1.4.2. What is the difference between the cancellation and revocation of MA?

Cancellation of MA is the delisting of a certain product from the active pool of registered products in the database, FDA website, and FDA inventory system, requested by the MAH not because of issues on quality, safety, and efficacy but may be due to commercial reasons, e.g., slow moving stocks, or non-renewal of an MA. Cancellation is synonymous to delisting or deregistration. On the other hand, revocation of MA is one of the sanctions given, depending on the severity of violation, as a consequence for committing prohibited acts that are listed in Section 11 of Republic Act (R.A.) No. 3720 and later amended to R.A. No. 9711 and its implementing rules and regulations (IRR).

1.4.3. When should an MAH request for the cancellation of its MA?

For an expired MA with no intention to renew its registration, the MAH at all times must submit its request for cancellation in not more than one (1) year from the expiration of the MA. For a valid MA, it shall depend on the decision of the company regarding the commercial disposition of its drug product in the market, excluding cases of issues on quality, safety, and efficacy of a drug product.

1.4.4. Can stocks of the concerned product be sold or exhausted in the market if the MA is for cancellation?

No. Only registered products, meaning those with valid MAs and with no intentions to cancel their registration, are allowed to be distributed or sold in the market. In cases of a submitted request to the FDA of cancellation of a valid MA, the company is prohibited to release new stocks from the manufacturer, importer, trader, distributor, etc. and also forbidden to sell or offer for sale stocks in the market after said request is submitted to the FDA. Otherwise, these are directed by the FDA to be retrieved fully from the market within one (1) month from releasing of such stocks.

1.4.5. If a Principal Certificate of Product Registration (PCPR) has been cancelled, what is the fate of all its corresponding CLIDP/s?

All CLIDPs of the cancelled PCPR are automatically cancelled and delisted from the registered products in the FDA database, FDA website, and FDA inventory system. There shall be no communication given by the FDA to the MAH/s of the CLIDP/s. In this regard, it is the responsibility of the MAH of the PCPR to convey to the owner/s of its CLIDP/s that such request for the PCPR shall be provided to the FDA.

1.4.6. If a specific CLIDP has been cancelled, what is the fate of its PCPR and other CLIDPs?

The specific CLIDP shall be cancelled or delisted from the registered products in the FDA database, FDA website, and FDA inventory system while its PCPR and other CLIDPs will not be affected.

Also, before submission of the request for cancellation to the FDA, the MAH of this specific CLIDP is required to notify accordingly the MAH of the PCPR on the intention and submission to the FDA of the request for deregistration of its corresponding CLIDP.

1.4.7. Can cancellation/deregistration/delisting of an MA be reverted?

No. Once the response letter from the FDA on the cancellation is duly signed by the Center Director, then the drug product is no longer registered with the FDA. Thereafter, if the company still wishes to market the drug product despite the cancellation of its MA, then the company will need to apply for initial registration.

In cases of withdrawal of request for cancellation of MA, the MAH must both submit a letter of non-pursuance of the said request and appropriate notification via telephone call or e-mail correspondence to the FDA the soonest possible time. Accordingly, the processing of said withdrawal request shall entail the releasing of an acknowledgement letter with the attached CPR/CLIDP at the FDAC.

1.4.8. What are the other responsibilities of an MAH if a product registration is cancelled and/or stocks are withdrawn from the market?

As per F.C. No. 2020-003 or the "Guidelines for Pharmaceutical Industry on Pharmacovigilance", the MAH is mandated to continue collecting and reporting for adverse reactions up to three (3) years from the date of the last release of the product into the market.

1.5. Destruction

1.5.1. When does a company need to notify the FDA on the destruction or disposal of its products?

A notification letter containing the following must always be submitted to the FDAC (letter lane) at least one (1) week before the schedule of the activity when there is intention to destroy or dispose drug products:

a. DENR accredited third party waste treater who shall facilitate the destruction or disposal activity;
b. List of drug products, e.g., expired, damaged, recalled, etc., with quantities per unit, batch or lot nos., mfg. and exp. dates;
c. Venue, date, and time of destruction or disposal activity; and

d. Contact details (e.g., telephone no., mobile no., e-mail address) of the focal person to whom the FDA shall coordinate the activity.

1.5.2. What are needed to be notified for destruction or disposal?

Any of the following which are intended for destruction:

a. Empty vials, bottles, or packaging materials of drug products that may be subjected to refills or counterfeiting activities;
b. Expired and/or damaged drug products, labeling materials, packaging materials; and
c. Recalled products.

1.5.3. What are the cases when the presence of an FDA Representative is needed to witness a destruction or disposal?

An FDA representative is always needed to witness the destruction or disposal of any recalled drug product. However, for the other items mentioned above, the presence of such representative from the FDA shall be evaluated by the agency depending on the necessity of the presence of such witness.

1.5.4. What are the documents needed to be submitted in line with the destruction or disposal of the abovementioned items (except recalled drug products)?

For all destruction or disposal, regardless if the activity was witnessed by an FDA representative or not, the MAH is required to submit the following to the FDA, within thirty (30) calendar days since date of destruction or disposal:

a. Certificate of Destruction or Certificate of Treatment issued by a third-party waste treater duly accredited by the DENR;
b. List of destroyed or disposed drug products, labeling materials, or packaging materials with stated quantities, batch/lot number, etc.;
c. FDA Report of the FDA representative, *if applicable*; and
d. Photographs of the destruction or disposal activity from loading of stocks to actual destruction or treatment, e.g., incineration.

2. PHARMACOVIGILANCE (PV)

2.1. General Procedures

2.1.1. Where can I report an Adverse Drug Reaction (ADR)?

For the consumers and healthcare professionals, you may directly report to our website at https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=PH or download the suspected ADR form at https://ww2.fda.gov.ph/attachments/article/150840/ADR%20Form.pdf and email it to pharmacovigilance@fda.gov.ph.

For the pharmaceutical industry, you may report using the Council for International Organizations of Medical Sciences (CIOMS) I form and email it to pharmacovigilance@fda.gov.ph or if capable with E2B (R2 or R3), you may inform us accordingly to facilitate electronic transmission of Individual Case Safety Report (ICSR).

2.1.2. What are the contact details of the Pharmacovigilance Section of the CDRR?

The landline number is (02) 8809-5596 and the e-mail address is pharmacovigilance@fda.gov.ph.

2.1.3. What are the guidelines for Pharmacovigilance?

The FDA Circular No. 2020-003 or the "Guidelines for Pharmaceutical Industry on Pharmacovigilance" is the issuance published last 07 April 2020 in newspapers of general circulation and has become effective on 22 April 2020.

2.2. FDA Circular No. 2020-003

2.2.1. What is the effectivity date of the FDA Circular No. 2020-003?

The Circular was published in a newspaper last 07 April 2020 and thus effective last 22 April 2020.

2.2.2. In local case reports from scientific literature, it was stated that the product as identified by its brand is reportable. What if the local journal used the generic name or Active Pharmaceutical Ingredient (API) of the product and there is only one MAH for that product, should the MAH still report this product considering that all other reporting elements are complete?

The purpose of the identifiable brand in the Circular is to avoid duplication of reports from several MAHs. However, being the sole MAH, you should assume that the product is owned by your company. Therefore, it is your responsibility to report adverse drug reactions to such product.

2.2.3. What is the expectation from an MAH if a certain product, e.g., old product or product marketed for a long time, does not have reported Adverse Events (AEs)? Also, may you provide examples of evidence of actions taken to "facilitate reporting".

The PV system of an MAH should always encourage the reporting of adverse reactions and may be done through the few examples stated below to facilitate reporting:

- During product presentations of medical representatives, ADR reporting may be included in their lectures by showing how healthcare professionals (HCP) could report ADRs; or
- Providing information in reporting ADRs through the website of an MAH.

2.2.4. In the submission of a Periodic Benefit-Risk Evaluation Report (PBRER), is the length of the covered period dictated by what is available from the MAH and what is the mechanism for the submission?

The FDA will notify the MAH through official communications regarding the required submission of the PBRER and also including the covered data lock points.

2.2.5. Are all New Drug Products (NDP) required to submit a PBRER?

No. Only an NDP with new active substance that has not been previously registered in the Philippines shall provide a PBRER. Therefore, for other NDPs as defined in F.C. No. 2020-003, such as new mode of administration, new dosage strength, new dosage form, etc., a PBRER is not needed to be submitted.

2.2.6. AEs found from literature search of literature reports, published or unpublished studies and from surveys or market research are reported as ICSRs through submissions via E2B to pharmacovigilance@fda.gov.ph. Are the journals or market research summary reports also needed to be submitted to update-safety-info@fda.gov.ph?

It is through your discernment if the information from journals or market survey reports affect the benefit-risk balance of your product. If yes, these documents must be submitted to the FDA through update-safety-info@fda.gov.ph. It must be noted that ICSRs from journals or literature do not require the submission of the copies of these journals or literature but may be requested by the FDA, if needed.

2.2.7. Do reported AEs from non-interventional studies follow the spontaneous or CT reporting time frames?

ADR reported from non-interventional studies must follow the reporting time frames as indicated in F.C. No. 2020-003.

2.2.8. In the reporting requirements for a PBRER of an NDP, what are the timelines to be followed for the submission?

A PBRER of an NDP must comply with the required submission timelines of seventy (70) calendar days from the data lock point for each submission for the whole duration of five (5) years. For example, if a PBRER is based on its International Birth Date (IBD) and covered the period of 15 January 2020 to 15 July 2020, the said PBRER must be submitted to the FDA within seventy (70) days from 15 July 2020.

2.2.9. It was stated that records of products that were suspended, withdrawn, or canceled may only be disposed after ten (10) years from its removal from the registration. What does "registration" mean?

The registration is the Philippine registration status.

2.2.10. In reporting significant safety updates, is a PBRER sufficient in the absence of a signal detection report?

No. A PBRER is different from signal detection. A significant safety update is any information that could affect or change the benefit-risk balance of your registered product and depending on your system, a PBRER may be a part of your signal detection procedure.

It must be noted by the MAH that if a PBRER is the source of such significant safety update or information, a communication letter and the PBRER must be provided to the FDA.

2.2.11. Where can the Risk Management Plan (RMP) Philippine-specific Annex Template be downloaded?

It can be accessed through this link: https://www.fda.gov.ph/cdrr-downloadables/ under "Pharmacovigilance".

2.2.12. Is an MAH exempted in the submission of a Philippine-specific RMP, if its RMP follows the latest Guideline on Good Pharmacovigilance Practices (GVP) Module V-Risk Management Systems and the company declared on the document that it is intended for the Philippine market?

All RMP must be compliant with the European Medicines Agency (EMA) Guideline on Good Pharmacovigilance Practices (GVP) Module V, i.e., EMA/838713/2011). Therefore, if an RMP which is compliant with the latest EMA/838713/2011 Guideline on GVP Module V is made or intended for the Philippine market, there is no need to submit an RMP Philippine-specific annex. Otherwise, if the said RMP doesn't specify that it is intended for implementation in the Philippine market, the MAH is required to provide an RMP Philippine-specific annex. Also, if there is no attached Philippine-specific Annex with your RMP, this specific RMP shall be regarded as intended and to be implemented in the Philippines.

2.2.13. Is the global PV plan, e.g., Pharmacovigilance Site Master File (PSMF), sufficient in the absence of an RMP?

No. A PSMF is different from an RMP. The PV plans and activities stated in an RMP or Philippine-specific annex are expected to be implemented in the Philippines.

2.2.14. Is the Post-Authorisation Safety Study (PASS) the new term of Post-Marketing Surveillance?

The Post-Marketing Surveillance is a broad term and as per the IRR of R.A. No. 9711, "Post-Marketing Surveillance" refers to the activities involved in safety, efficacy, and quality monitoring of health products. However, the PASS is a term more appropriately used in PV and shall be used regularly when referring to such PV activities.

2.2.15. Is it still required to conduct local Phase IV Clinical Trials for Monitored Release applications as mandated in the F.C. No. 2018-012?

If a certain PASS (i.e., foreign studies) already addresses or characterizes a safety concern, the conduct of a local Phase IV Clinical Trial is not needed, unless required by the FDA.

2.2.16. Is the MAH required to monitor other reference drug regulatory authorities (DRAs)?

The MAH is not required by the FDA to monitor other DRAs unlike in the Health Sciences Authority in Singapore which directs the MAH to monitor the United States FDA,

Medicines and Healthcare product Regulatory Agency, Health Canada, and Therapeutic Goods Administration. However, it is still expected from the MAH to monitor its products in countries where it is marketed.

2.3. Development Safety Update Report (DSUR)

2.3.1. What is the format and content of a DSUR submission?

The guidance on the format and content of a DSUR can be accessed from the latest version of the International Conference on Harmonization (ICH) E2F Development Safety Update Report.

A sponsor should prepare a single DSUR for a single investigational drug. However, if a sponsor makes multiple DSURs for a single investigational drug (e.g., covers different indications, development programmes, or formulations), this section should summarize significant findings from the other DSURs if they are not presented elsewhere within this report. When available, the sponsor should summarize significant findings from DSURs provided by other sponsors who are conducting clinical trials with the same investigational drug during the reporting period.

2.3.2. What is the timeline for the submission of a DSUR?

It should be submitted not later than sixty (60) calendar days from the DSUR data lock point.

2.3.3. When is the data lock point (DLP) of a DSUR?

The data lock point of a DSUR should be the last day of the one (1)-year reporting period.

2.3.4. What is the frequency for the submission of a DSUR?

DSURs should be continuously submitted as long as indicated by national and/or regional laws or regulations. When the submission of an annual report is no longer required in an individual country or region, the sponsor should indicate that the final DSUR serves as the last annual report for the investigational drug in that country or region. Also, the sponsor should indicate whether or not clinical trials are continuing elsewhere.

3. CLINICAL RESEARCH

3.1. General Procedures

3.1.1. Where to apply for a Clinical Research Section (CRS) application?

The application for a CRS document, e.g., Compassionate Special Permit, Import License, must be made at the FDAC through the receiving lane or counter.

3.1.2. How to pay the required fees for a CRS application?

Download the Assessment Slip from the FDA website, fill-out the document, and present this to the Cashier. Refer to https://ww2.fda.gov.ph/attachments/article/343801/Assessment%20Slip%20for%20Clinical-related%20Applications.pdf for the Assessment Slip.

3.1.3. How will the CRS receive the applications?

Applications received through the FDAC will be forwarded to the CDRR-Central Receiving and Releasing Section and thereafter, shall be provided to the CRS of the Center.

3.2. Compassionate Special Permit (CSP)

3.2.1. What are the requirements for a CSP?

The list of requirements is enumerated in the A.O. No. 2020-0028, Roman II and A.O. No. 2005-0008, Roman IV B for Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) unregistered Drug and Test Kits. The following can be accessed through these links:

- https://law.upd.edu.ph/wp-content/uploads/2020/07/DOH-AO-No-2020-0028.pdf (A.O. No. 2020-0028); and
- https://ww2.fda.gov.ph/attachments/article/15918/ao%208%20s%202005.pdf (A.O. No. 2005-0008).

3.2.2. Who can apply for a CSP?

Based on the A.O. No. 2020-0028, unregistered and investigational drug products can only be accessed through a CSP by patients suffering with the following conditions:

a. AIDS;
b. Cancer;
c. Life-threatening conditions; and
d. Emerging or re-emerging infectious diseases considered as Public Health Emergencies or Public Health Treats.

Furthermore, it must be noted by the applicant that if a product intended to be applied for a CSP has a generic counterpart with a valid CPR, this application is prohibited.

3.2.3. How much is the payment for a CSP application?

The fee + Legal Research Fund (LRF) is ₱ 510.00 per patient. For institutional use, the fee + LRF is ₱ 510.00 per product.

3.2.4. What is the turnaround time on the processing of a CSP application?

The processing time of a CSP application is seventy-two (72) hours upon receipt of the complete requirements by the CRS.

3.2.5. What is the validity of a CSP?

A CSP is valid for one (1) year from the date of its issuance and must only be used once throughout its validity.

3.3. Product Classification

3.3.1. What are the guidelines for a Product Classification?

a. R.A. No. 9711, where Drug, Device, Food and Cosmetics were defined. Refer to this link: https://ww2.fda.gov.ph/index.php/issuances-2/others-laws-and-regulations-not-applicable-to-the-above-categories/others-republic-act/29052-republic-act-no-9711.
b. Office Order No. 22 s. 1991: Guidelines for the Classification of Vitamins and Minerals as Drug or as Food. Refer to this link: (link: https://ww2.fda.gov.ph/attachments/article/29021/OO%2022%20s%201991.pdf.
c. A.O. No. 23-C s. 2000: Policies and Guidelines on the Over-the-Counter (OTC) Drug Products. Refer to this link: https://ww2.fda.gov.ph/attachments/article/16557/ao%2023c%202000.pdf.

3.3.2. What are the requirements for a Product Classification?

a. Letter of Intent
b. Complete Technical Profile of the Product and must include the following:
    - Description;
    - Formulation/List of ingredients with corresponding amount per unit dose, expressed in the metric system;
    - Indication;
    - Direction for use;
    - Claims (if any); and
    - Labeling materials/Brochure.
c. Classification of the product in the country of origin
d. List of countries where the product is currently marketed and the corresponding classification of the product in these countries
e. Representative sample
f. Proof of payment + LRF (₱ 510.00)

3.3.3. What is the turnaround time on the processing of a Product Classification application?

The processing time is sixty (60) calendar days upon receipt of the application by the CRS.

3.4. Clinical Trial (CT) Application

3.4.1. What are the requirements for an Initial CT Protocol application?

The list of documentary requirements for an application for a CT is enumerated in Appendix C of the A.O. No. 2020-0010 which can be accessed through this link: https://www.fda.gov.ph/wp-content/uploads/2020/05/Administrative-Order-2020-0010.pdf.

Also, all of the forms are available for download at the FDA website. Refer to this link: https://ww2.fda.gov.ph/industry-corner/downloadables/343801-clinical-trial-requirements

3.4.2. What are the requirements for an Import License (IL) application?

The requirements for an IL application are enumerated in Appendix C of the A.O. No. 2020-0010 and can be accessed through this link: https://www.fda.gov.ph/wp-content/uploads/2020/05/Administrative-Order-2020-0010.pdf.

3.4.3. How much is the payment for a CT Protocol application?

The following are the fees:

- Clinical review + LRF is ₱ 2,525.00;
- Import License + LRF is ₱ 510.00; and
- Regulatory Review is ₱ 60,000.00.

3.4.4. What is the turnaround time on the processing of a CT Protocol application?

The processing time is sixty (60) calendar days upon receipt of the application by CRS; the said timeline includes the forty-five (45) calendar days of review to be done by the regulatory reviewer that will start when they receive all of the requirements.

3.4.5. Should the IL application be submitted together with the CT application?

For an initial CT application:

i. An IL application shall be filed simultaneously with the CT application. Therefore, documentary requirements must be provided for both.
ii. A single Document Tracking Number (DTN) will be both assigned to the CT and IL application.
iii. Consequently, any decision on the initial CT application and IL application will be released together.

For an ongoing CT:

i. An IL may be applied separately for the following reasons: extension of validity, addition of quantity of investigational product/s or ancillary supplies to be imported, and amendment.
ii. A different DTN will be assigned to the IL application. Refer to this link: https://www.fda.gov.ph/wp-content/uploads/2019/05/FDA-Circular-No.2012-007-A.pdf.

3.4.6. What are the requirements for a CT Amendment application?

The requirements can be accessed through this link: https://www.fda.gov.ph/wp-content/uploads/2020/05/Administrative-Order-2020-0010.pdf or as follows:

a. Cover Letter
b. Application Form (Appendix D1), available at: https://ww2.fda.gov.ph/industry-corner/downloadables/343801-clinical-trial-requirements
c. Original version, corresponding amendment/s, and rationale in a tabulated format
d. Supporting data
e. Proof of payment + LRF (₱ 1,010.00)

3.4.7. What is the turnaround time on the processing of a CT Amendment application?

The processing time is thirty (30) calendar days upon receipt of the application by the CRS.

3.4.8. What license should I apply before I conduct any CT?

It depends on the roles, duties, and/or responsibilities of the applicant in the clinical trial. Refer to the ICH E6 for the responsibilities of a Contract Research Organization (CRO) or Sponsor at this link: https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4_2016_1109.pdf) and F.C. No. 2015-003 under General Guidelines (link: https://ww2.fda.gov.ph/attachments/article/238083/FDA%20Circular%20No.%202015-003.pdf).

3.4.9. Who can apply to conduct a CT Protocol (Phase I to IV) and IL?

Establishments with a License to Operate (LTO) as a Sponsor or a CRO may apply for CT and IL. Since the submission of applications for initial CT and IL is done simultaneously, the applicant for the initial CT application must be the same with the applicant of the IL application. In cases where the applicant is not the Importer, a separate Cover Letter for the IL application must be submitted with the inclusion of the name and details of the Importer.

3.5. PMS Protocol or Local Phase IV Studies

3.5.1. What are the requirements for a PMS Protocol application?

The requirements for a PMS Protocol application can be accessed through this link: https://ww2.fda.gov.ph/attachments/article/15912/bc%205%20s%201997.pdf or as follows:

a. Letter of Intent
b. Copy of Protocol which includes items enumerated in the B.C. No. 5 s. 1997: Protocol for Local Clinical Trial
c. Proof of payment + LRF (₱ 2,525.00)

3.5.2. What are the products needed to be conducted for a local Phase IV CT (PMS)?

The drug products that are classified as Monitored Release (MR) and stated under the Scope of the F.C. No. 2018-012. This issuance can be accessed through this link: https://ww2.fda.gov.ph/attachments/article/525777/FDA%20Circular%20No.%202018-012.pdf.

3.5.3. How many subjects are required in the Phase IV CT (PMS)?

Based on the B.C. No. 5 s. 1997, one thousand (1,000) patients per year or three thousand (3,000) patients over three (3) years are needed. However, for a drug product with very limited therapeutic indication, ten percent (10%) of the total patients are required as subjects. Refer to 3.7 of the B.C. No. 5 s. 1997. (link: https://ww2.fda.gov.ph/attachments/article/15912/bc%205%20s%201997.pdf)

3.6. Administrative Order No. 2020-0010

3.6.1. Who are allowed to import Investigational Products (IP)?

Based on the A.O. No. 2020-0010, only an establishment with a valid LTO as an Importer is allowed to import IPs. This LTO is not the same with the Bureau of Customs (BOC) License as Importer.

3.6.2. Who has the obligation to notify the FDA of the clinical trial-related inspections by other national or drug regulatory authorities?

The sponsor, CRO, investigator, or the recipient of the Notice of Inspection must report to the FDA of any trial-related inspection by other national or drug regulatory authorities.

3.6.3. If the Importer on Record (IOR) is a different company (e.g., sponsor) and not the CRO applicant, is the IL provided to the applicant along with the CT approval?

Yes. Since the applications for CT and initial IL are simultaneously submitted by a single applicant, the decision on both of these applications shall be released at the same time to the same applicant.

3.6.4. Do all protocol amendments (i.e., notification, prior approval) require payment?

Yes. All protocol amendments (i.e., notification/prior approval) require payments. Total fee + LRF for each amendment is ₱ 1,010.00.

3.6.5. Is Notification Amendment needed to be implemented before or after the submission of notification to the FDA?

The implementation of the Notification Amendment is not strict whether done before or after the submission of notification to the FDA. However, the more important thing is that the sponsor or CRO must ensure to submit Notification Amendment to the FDA.

3.6.6. What is the schedule for the submission of the Annual Progress Report?

The Annual Progress Report for 2020 (i.e., January to December 2020) must be submitted within the second (2nd) quarter (i.e., 01 April to 30 June) of the following year. Succeeding Annual Progress Reports, e.g., for 2021, shall be submitted within the 2nd quarter of 2022.

3.6.7. What is the basis for the submission of End of Trial (EoT) notification?

The EoT notification must be submitted both on the following occasions, but may be provided separately:

- Last visit/close out in the Philippines as per Section VI, 8.1.1 of the A.O. No. 2020-0010; and
- Last visit/close out globally as per Section VI, 8.1.2. of the stated A.O.

The issuance can be accessed through this link: https://www.fda.gov.ph/wp-content/uploads/2020/05/Administrative-Order-2020-0010.pdf.

3.6.8. If there were violations noted on the conduct of a CT, who (e.g., sponsor, applicant, other clinical stakeholders) will receive the penalties or sanctions?

The recipient/s of the penalties or sanctions shall be determined through the appropriate investigation of the violation/s.

3.6.9. Is it mandatory to comply with the Letter of Authorization template (Appendix C6) of this A.O.?

Yes. It is mandatory to comply with Appendix C6 of the A.O. No. 2020-0010. However, if the Sponsor intends to expound on the authorization, an attachment to the this template may be provided.

3.6.10. Are all amendments, including Notification Amendment and For Approval Amendments needed to be uploaded to the Philippine Clinical Trial Registry?

Yes. The Philippine Health Research Registry (PHRR) will undergo necessary revisions to comply with the A.O. No. 2020-0010.

3.6.11. If a type of amendment is not specified in the A.O. No. 2020-0010, what must be done?

When a type of amendment is not stated in Appendix D1, do not tick any of the box, but write under "*Please Specify"* the type or brief description of the amendment and if the submission is a "Notification Amendment" or "For Approval Amendment".

3.6.12. Does the change of Principal Investigator (PI) and Site or additional PI and Site be issued with an approval letter?

No. The issued Acknowledgement of Receipt (AoR) during the submission will serve as the acknowledgement for the change of PI and site or addition of PI and site.

3.6.13. Does shelf life extension fall under the Prior Approval Amendment?

Yes. It is considered as Prior Approval Amendment.

3.6.14. Does the sponsor or CRO need to submit an amendment when a change in formulation or labelling of an IP is intended?

Yes. The sponsor or CRO needs to submit in these cases.

3.6.15. Are revised labels needed to be submitted to the FDA for approval?

Yes. Revised labels (i.e., primary or secondary packaging) must be submitted to the FDA for approval and re-labelling can only commence once said approval is given.

3.7. FDA Circular No. 2012-007-A

3.7.1. How long is the validity of an IL?

The validity of an IL is three (3) years and shall be issued with the approval of a CT (Roman IV.B.1. 1.4 of the F.C. No 2012-007-A; link: https://www.fda.gov.ph/wp-content/uploads/2019/05/FDA-Circular-No.2012-007-A.pdf)

3.7.2. Is extension of validity and addition of quantity in an IL allowed?

Yes. It is subject to the approval of the FDA. The extension of validity is effective for two (2) years. (Roman IV.B.1. 1.5 of F.C. No 2012-007-A; link: https://www.fda.gov.ph/wp-content/uploads/2019/05/FDA-Circular-No.2012-007-A.pdf)

3.7.3. Is this FDA Circular applicable for all studies?

This Circular is only applicable to all clinical trials that require registration to the FDA under the existing regulations.

3.7.4. Can the new IL be used for both Investigational Products (IP) and ancillary supplies?

Yes. The IL will include a list of IPs, ancillary supplies, and quantity of such allowed for import.

3.7.5. What items are considered as ancillary supplies?

i. Ancillary supplies are products other than the test product, placebo or comparator that may be used in a trial. These include laboratory kits, reagents, and other materials used by participants in a trial.
ii. On the tracking of ancillary supplies, a system of traceability must be in place to ensure that all supplies are identified and accounted.
iii. For laboratory kits, reporting may be done up to the kit type only. However, a packing list per kit must be provided.

3.7.6. Will the requirement of one IL per shipment remain?

No. A single IL will be issued to a particular study stating the quantity of each investigational product and the ancillary supply allowed for import. This IL may be used for multiple shipments within its three (3) year validity period.

3.7.7. Can ongoing studies apply for an IL using the amended guidelines?

Yes. All on-going clinical trials shall be issued with an IL which is valid for three (3) years upon submission of the documentary requirements listed under Section IV.B.1.2 of the Circular.

3.7.8. Can ongoing studies choose to not to apply for an IL?

Yes. For cases if there are existing and valid ILs for ongoing trials and the Sponsor/CRO has determined that these will cover the remaining shipments for IPs and ancillary supplies, then, there is no need to apply for a new IL as per this Circular.

3.7.9. What does 'IP Sequential Number' mean in an IL application form?

If there are two (2) or more investigational products used in the clinical trial, IP Sequential Numbers are assigned for proper identification of each IP. This can be IP1, IP2, IP3, and so on.

3.7.10. How much overage of the IP quantity is acceptable?

The requested quantity for the overage of an IP should be sufficient and justifiable.

3.7.11. In cases of a disapproval, will the applicant be notified through email?

No. Any disapproval shall be issued through an official letter.

3.7.12. Is there a limit on the number of application for the extension of validity of an IL?

No. The application for the extension of validity of an IL may be applied multiple times for on-going clinical trials and must be with acceptable rationale.

3.7.13. Is there an application for amendment of an IL?

Yes. Application for amendment of an IL may be submitted if there are additional materials or quantities needed. The documentary requirements are the same with an initial IL application. However, if changes are related to the study sites or investigators (e.g., addition or change in study sites or investigators) and/or investigational product (e.g., shelf-life extension, additional manufacturer, etc.), a protocol amendment application must be submitted.

3.7.14. What does 'Investigational Product Code' mean in the Cover Letter for IP Notification?

Investigational Product Code refers to the name of the investigational product.

3.7.15. Is payment done for every shipment?

Yes. Every shipment made within the quarter requires a total payment + LRF of ₱ 510.00.

3.7.16. If there are no shipments within the quarter, should a notification be submitted to the FDA?

No. There is no need.

3.7.17. For on-going clinical trials with valid* ILs*, should actual shipments which utilize current* ILs *still need to be included in the notification?

No. Requirements of the Circular will only apply to the issued ILs after its implementation.

3.8. Import or Export Permit

3.8.1. What are the requirements of an Import Permit for Registration Sample?

a. Letter of Application must include the following:
   - Name of requesting party [personal or position]
   - Itemized, detailed description of product [generic name and brand name (if applicable) with dosage form and strength]
   - An estimated quantity or volume needed
   - Country of Origin
   - Purpose of the request letter
   - A waiver for the FDA Philippines' responsibility from any damage or injury arising from the use of the unregistered drug or device to be signed by the responsible official of the Institution

b. Proof of payment + LRF (₱ 510.00)
c. Proforma invoice which includes the batch no. & expiry date
d. Certificate of Analysis
e. Copy of the LTO

3.8.2. How much is the processing of an Import Permit for Registration Sample?

The processing fee + LRF is ₱ 510.00 per product.

3.8.3. What is the turnaround time on the processing of an Import Permit for Registration Sample?

The processing time is seventy-two (72) hours upon receipt of the application by the CRS.

3.8.4. What are the requirements of an Import/Export Permit for Bioequivalence (BE) testing?

a. Letter of Application must include the following:
   - Name of requesting party [personal or position]
   - Itemized, detailed description of product [generic name and brand name (if applicable) with dosage form and strength]
   - An estimated quantity or volume needed to be exported
   - Name of the Company with address of destination
   - Purpose of the request letter
   - A waiver for the FDA Philippines' responsibility from any damage or injury arising from the use of the unregistered drug or device to be signed by the responsible official of the Institution

b. Proof of payment + LRF (₱ 510.00)
c. Picture of the packaging which includes the manufacturer, batch or lot number, and expiry date

3.8.5. How much is the processing of an Import/Export Permit for BE testing?

The processing fee + LRF is ₱ 510.00 per product.

3.8.6. What is the turnaround time on the processing of an Import/Export Permit for BE testing?

The processing time is thirty (30) calendar days upon receipt of the application by the CRS.

3.8.7. What are the requirements of an Export Permit for Clinical Trial Use?

a. Letter of Application – itemized, detailed description of the clinical trial materials with corresponding quantity for each approved investigator per site
b. Proof of payment + LRF per product (₱ 510.00)
c. Waiver statement which states that the FDA will not be held liable from any damage or injury arising from the use of the investigational drug product
d. Copy of the approval of the CT Protocol which includes the lists of approved investigators with corresponding site or hospital
e. Copy of the proforma invoice which includes proforma invoice per approved investigators with corresponding site or hospital

3.8.8. Who processes the importation and exportation permit of products for personal use?

The Office responsible for this application is the Customs Liaison Unit of the FROO.

4. ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
AIDS	Acquired Immune Deficiency Syndrome
AO	Administrative Order
AoR	Acknowledgement of Receipt
BC	Bureau Circular
BOC	Bureau of Customs
BE	Bioequivalence
CCRR	Center for Cosmetic Regulation and Research
CDRR	Center for Drug Regulation and Research
CDRRHR	Center for Device Regulation, Radiation Health, and Research
CFRR	Center for Food Regulation and Research
CIOMS	Council for International Organizations of Medical Sciences
CLIDP	Certificate of Listing of Identical Drug Product
CPR	Certificate of Product Registration
CRO	Contract Research Organization
CRS	Clinical Research Section
CSP	Compassionate Special Permit
CT	Clinical Trial
DENR	Department of Environment and Natural Resources
DHPC	Direct Healthcare Professional Communication
DLP	Data Lock Point
DRA	Drug Regulatory Authority
DSUR	Development Safety Update Report
DTN	Document Tracking Number
EMA	European Medicines Agency
EoT	End of Trial
FC	FDA Circular
FDA	Food and Drug Administration
FDAC	Food and Drug Action Center
FROO	Field Regulatory Operations Office
GVP	Good Pharmacovigilance Practices
HIV	Human Immunodeficiency Virus
IBD	International Birth Date
ICH	International Conference on Harmonisation
ICSR	Individual Case Safety Report
IL	Import License
IOR	Importer on Record
IP	Investigational Product
IRR	Implementing Rules and Regulations
LRF	Legal Research Fund
LSSC	Legal Services Support Center
LTO	License to Operate
MA	Marketing Authorization
MAH	Marketing Authorization Holder

mL	Milliliter
MR	Monitored Release
NDP	New Drug Product
OTC	Over-the-Counter
PASS	Post-Authorisation Safety Study
PBRER	Periodic Benefit Risk Evaluation Report
PCPR	Principal Certificate of Product Registration
PHRR	Philippine Health Research Registry
PMS	Post-Marketing Surveillance
PRO	Product Recall Order
PSMF	Pharmacovigilance Site Master File
PSUR	Periodic Safety Update Reports
PV	Pharmacovigilance
RA	Republic Act
REU	Regulatory Enforcement Unit
SKU	Stock Keeping Unit

REVISION HISTORY

Date	Version	Changes
13 February 2020	1.0	N/A
19 February 2020	2.0	Title page: changed to Version 2.0, added "Date of Revision"; Section 1.1.2: revised ereport scheme from online reporting facility to reporting through e-mail; Section 1.1.7: changed contact details from PMS to PRSDD; Section 1.1.13: added needed submission of contact details; Section 1.4.3: revised scheme on releasing of stocks with request for cancellation of MA; Section 1.5.4: added Certificate of Treatment & FDA Report; Section 2.1.6: added "calendar" to days; Section 3.6.5: changed numbering from a…b… to i…ii…; Section 3.16.13: changed meaning of ICSR abbreviation; Changed symbol of currency from "Php" to "₱"; Changed color to hyperlinks and e-mail addresses to blue
09 October 2020	3.0	All sections revised for updating of processes and/or requirements.