ADMINISTRATIVE ORDER
No. 2023-_____

SUBJECT : Rules and Regulations on the Issuance of Authorization for Registration Applications of Drug Products and Drug Substances by the Food and Drug Administration

I. BACKGROUND

Article II, Section 15, of the 1987 Constitution provides as a policy of the State to "protect and promote the right to health of the people and instill health consciousness among them". Towards this end, Republic Act (RA) No. 3720 entitled "Food, Drug, and Cosmetics Act", as amended by Executive Order No. 175 series of 1987, and further amended by RA No. 9711 or the "Food and Drug Administration (FDA) Act of 2009" were enacted, mandating the FDA to regulate health products through the issuance of appropriate authorizations prior to the manufacture, importation, exportation, sale, offering for sale, distribution, transfer, non-consumer use, testing, promotion, advertisement, or sponsorship of any health products.

Administrative Order (AO) No. 67 s. 1989, entitled "Revised Rules and Regulations on Registration of Pharmaceutical Products", was issued to provide comprehensive guidelines on the registration of pharmaceutical products with the FDA, consistent with RA No. 6675, otherwise known as the "Generics Act of 1988". However, with the fast-changing technologies and regulatory landscape in pharmaceutical regulations, there is a need to develop responsive policy guidelines for the authorization of drugs by providing scientific evidence on the quality, safety, and efficacy of the products being applied. Also, institutionalizing regulatory reliance is necessary to avoid redundancy in regulation particularly products that are already authorized in other countries that passed the stringent regulatory review process. Other health legislations also incorporate timely access to medicinal products and technologies.

Additionally, laws were issued to improve efficiency and adopt digitalization in government regulatory services, such as RA No. 8792 or the "Electronic Commerce Act of 2000" and RA No. 11032 or the *"Ease of Doing Business and Efficient Government Service Delivery Act of 2018"*.

Consistent with these laws, coupled with the regional and global developments on regulatory harmonization, this Order is being issued to provide the revised rules and regulations on registration applications of drugs which include drug products and drug substances applied for the FDA authorization.

II. OBJECTIVES

A. This Administrative Order is issued to provide the guidelines including the rules and regulations on registration applications for the issuance of FDA authorizations and other certifications for drug products and drug substances.

B. Specifically, this AO shall provide the regulatory guidelines for the following:

1. Identification of registrable drug products and drug substances;
2. Types of registration applications for drug authorization;
3. Regulatory review implemented by the FDA on the applications and the applicable evaluation routes; and
4. Regulatory decisions on the applications.

III. SCOPE

This Administrative Order shall apply to all drug products and drug substances for human use and for which registration applications are submitted to the FDA for the following authorizations:

A. Marketing Authorization;
B. Export Authorization;
C. DOH-Use Authorization;
D. Clearance for Foreign Donations

IV. DEFINITION OF TERMS

As used in this Administrative Order:

A. **Advanced therapy medicinal products (ATMPs)** refer to drug products for human use that are based on genes, tissues, or cells and offer groundbreaking new opportunities for the treatment of disease and injury. ATMPs include human cells, tissues, and cellular and tissue-based products (HCTPs) which are articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion or transfer into human recipients.

B. **Applicant** refers to any private company or government institution who submits a registration application for (a) a drug product or drug substance authorization, (b) an update to an existing authorization, or (c) a variation to an existing authorization.

C. **Authorization** refers to a permission embodied in a document granted by the FDA to a natural or juridical person who has submitted an application to implement the manufacture, importation, exportation, sale, offer for sale, distribution, transfer, and/or, where appropriate, the use, testing, promotion, advertising, or sponsorship of health products. The authorization can take the form of a permit, a license, a certificate of registration, of accreditation, of compliance, or of exemption, or any similar document. An FDA-authorized product refers to an FDA-registered product that has a valid or active FDA authorization.

D. **Authorization holder** refers to the local company, government institution, or legal entity duly licensed by the FDA in whose name the authorization for a drug product or drug substance has been granted. Such holder is responsible for all aspects of the product, including safety, efficacy, quality and compliance with the conditions of the authorization.

E. **Biological drug product** or **biological product** or **biologic** or **biotherapeutic product** refers to any product of biological origin, prepared with biological processes, derived from blood and plasma, or manufactured by biotechnology, consisting of substances of higher molecular weight whose purity, potency, and composition cannot readily and reliably be determined by chemical or physicochemical analysis. Examples of this group include vaccines, blood products, modified animal tissues, high molecular weight hormones, allergens, and the products of genetic engineering or other newer biotechnological techniques. This definition does not include antibiotics and substances that, although of biological origin, are of low molecular weight and can be isolated as pure substances, such as purified steroids and alkaloids.

F. **Blood product** refers to any therapeutic substance derived from human blood, including whole blood and other blood components for transfusion, and plasma-derived medicinal products.

G. **Brand name** refers to the proprietary name given by the manufacturer to distinguish its product from those of competitors.

H. **Certificate of Pharmaceutical Product (CoPP)** refers to a document issued in the format recommended by the World Health Organization (WHO) for the purpose of establishing the status of the pharmaceutical product in the Philippines under FDA regulations, to be internationally recognized by national drug regulatory authorities. The pharmaceutical product must be produced under a comprehensive system of quality assurance, conforming to Good Manufacturing Practice (GMP) standards as set by FDA.

I. **Certificate of Product Registration (CPR)** of a drug product or drug substance refers to the certificate issued by FDA for a product that has been applied and has successfully complied with the requirements for FDA authorization to ensure its safety, efficacy and quality. The type of authorization granted through an issued CPR include authorizations for marketing, for export, for DOH-use, and clearance for foreign donations, among others, and shall be indicated in the CPR.

J. **Collaborative Review Procedure (CRP)** refers to an assessment process recognized by FDA through reliance, work-sharing, or joint reviews with other international organizations, like the World Health Organization (WHO) Prequalification Team (WHO/PQT), or other drug regulatory agencies as may be identified by the FDA.

K. **Drug** refers to chemical compound(s) or biological substance(s), other than food, intended for use in the treatment, prevention, or diagnosis of disease in humans or animals, including the following:
   1. any article recognized in official pharmacopoeias and formularies, including official homeopathic pharmacopoeias, or any documentary supplement to any of them, which are recognized and adopted by the FDA;
   2. any articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;
   3. any article, other than food, intended to affect the structure or any function of the body of human beings or animals; or
   4. any articles intended for use as a component of articles, specified in clauses (1), (2), or (3) not including devices or their components, parts or accessories.

L. **Drug combination pack** refers to a drug product, packaged in combination with another drug product, that may or may not have corresponding individual CPRs intended to be authorized together under a single CPR. The combination pack shall be differentiated from a fixed-dose combination such that the former exists in separate dosage forms while the latter is in a single pharmaceutical dosage form.

M. **Drug kit** refers to a packaged set of a drug product and its drug delivery system(s) or device(s) used for a particular medical activity or procedure involving the drug product including required documentation for the kit components and the entire kit. This does not include a packaged set of a drug product and other items not related to the use of the drug product but for other purposes such as promotional materials or emergency kits.

N. **Drug product**, **pharmaceutical product**, or **medicinal product** refers to drugs, medicines, biologicals, and pharmaceutical / biopharmaceutical products/specialties. It is the finished dosage form that contains a drug substance, generally, but not necessarily in association with other active or inactive ingredients.

O. **Drug substance**, also referred to as active ingredient, refers to any substance or combination of substances intended to be used in the manufacture of a drug product. The drug substance in a finished product dosage form is the **active pharmaceutical ingredient (API)** of that drug product. Such substances are intended to furnish pharmacological activity or to otherwise have a direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to have direct effect in restoring, correcting, or modifying physiological functions of the body.

P. **Facilitated Review Pathway (FRP)** refers to an alternative registration process whereby the FDA takes into account and gives significant weight to assessments performed by a reference drug regulatory agency in reaching its own decision. The FDA remains independent, responsible, and accountable for the decisions taken, even when it relies on the decisions, assessments, and information of others.

Q. **Fixed-dose combination** refers to a pharmaceutical preparation containing two or more pharmacologically active ingredients in a single formulation or dosage form.

R. **General sales list drugs** also referred to as **household remedy (HR)** refers to any non-prescription drug for human use that is not classified as for pharmacist-only, containing pharmaceutical substances of common ordinary use to relieve common physical ailments and which may be dispensed in original packages, bottles or containers, of which the nomenclature has been duly approved by the FDA.

S. **Generic drug** refers to a drug product created to be the same as the reference drug product in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use. These similarities help to demonstrate bioequivalence, which means that a generic drug works in the same way and provides the same clinical benefit as its reference drug product.

T. **Generic drug application (GDA)** refers to a registration application for a generic drug product that contains one or more chemical entities and is essentially the same as a reference drug product in terms of its qualitative and quantitative composition of active ingredients.

U. **Herbal medicines** refer to finished, labeled, medicinal products that contain as active ingredient(s) aerial or underground part(s) of plant or other materials or combination thereof, whether in the crude state or as plant preparations. Plant material includes juices, gums, fatty oils, essential oils, and other substances of this nature.

V. **Homeopathic drug** refers to a drug product that is formulated for use on the principle of "like cures like" wherein a disease is treated by the use of minute amounts of one or more substances which, in their undiluted forms, are capable of producing in a healthy human being, symptoms similar to those of the disease being treated. It is prepared following a homeopathic manufacturing procedure described by a homeopathic pharmacopeia.

W. **Human cells, tissues, and cellular and tissue-based products (HCT/Ps)** refer to articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into human recipients.

X. **Joint assessment** refers to the formal procedure in which the same application is simultaneously submitted to all participating [ASEAN] National Regulatory Authorities (NRAs).

Y. **Labeling materials** refers to the label on the immediate container, and the other printed or electronic materials that are made available with the drug at the time of purchase and/or when the product is used, such as the outer wrapper cartons, package insert/leaflet accompanying the product, which provide the accurate and necessary detailed information for the identification and proper use of the product.

Z. **Manufacturer** refers to an establishment engaged in any and all operations involved in the production of drug products including preparation, processing, compounding, formulating, filling, packaging, repackaging, altering, ornamenting, finishing and labeling with the end in view of its storage, sale or distribution: provided, that the term shall not apply to the compounding and filling of prescriptions in drugstores and hospital pharmacies.

AA. **Marketing authorization (MA)** refers to the approval granted by FDA to a marketing authorization holder allowing a drug to be legally marketed in the Philippines after having undergone a process of evaluation to determine the safety, efficacy and quality of the product and the appropriateness of the product information.

CC. **Medical gas** refers to any gas or mixture of gases intended for administration to patients for anesthetic, therapeutic, diagnostic, or prophylactic purposes, which may be manufactured in a liquefied, non-liquefied, or cryogenic state and administered as a gas.

DD. **New drug** refers to any drug product the composition of which is such that said drug product is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety of drugs, as safe for use and efficacious under the conditions prescribed, recommended, or suggested in the labeling thereof.

EE. **New drug application (NDA)** refers to a registration application for a drug product that contains (a) new chemical and/or biological entities **(new biological drug application [NBDA])** proposed to be used in the diagnosis, cure, mitigation,

treatment, or prevention of disease, (b) new dosage forms, (c) new dosage strengths, (d) new routes of administration, and (e) new indications.

FF. **Non-prescription drug** or **non-Rx drug**, also referred to as **over-the-counter (OTC) drug** refers to a drug product that can be dispensed even without a prescription of a licensed physician, dentist, or veterinarian, for the symptomatic relief of minor or self-limiting ailments.

GG. **Orphan drug** refers to any drug or medicine used to treat or alleviate the symptoms of persons afflicted with a rare disease and declared as such by the DOH upon recommendation of the National Institutes of Health (NIH).

HH. **Pharmacist-only non-prescription drug** refers to a non-prescription drug classified by FDA to be obtained only from a licensed pharmacist, with mandatory pharmacist's advice on their selection and proper use. These drug products shall be sold only in FDA-licensed drug outlets under the direct supervision of a registered and licensed pharmacist.

II. **Precursor** refers to any substance that is intended to be used in the manufacture of a drug substance or API and that can be converted into such through chemical, biochemical, or other means. Precursors may include, but are not limited to, starting materials, intermediates, reagents, catalysts, solvents, and any other substance that contributes to the production of a drug substance or API.

JJ. **Prescription drug** or **Rx drug**, also referred to as **ethical medicines,** refers to a drug product that can only be dispensed by a pharmacist to a patient, upon the presentation of a valid prescription from a physician, dentist, or veterinarian and for which a pharmacist's advice is necessary

KK. **Radiopharmaceutical product** or **radiopharmaceutical preparation** or **radioactive drug** refers to a finished dosage form that contains a radioactive substance in association with one or more ingredients and that is intended to diagnose, stage a disease, monitor treatment, or provide therapy. A radiopharmaceutical includes any non-radioactive reagent kit or radionuclide generator that is intended to be used in the preparation of any such substance. Since radiopharmaceuticals contain radioactive materials, these products are regulated by the Philippine Nuclear Research Institute (PNRI) which is mandated to undertake the licensing and regulation of the peaceful applications of nuclear and radioactive materials and nuclear facilities for its radioactivity, and also by FDA for its quality, safety, and efficacy as a drug preparation.

LL. **Reference biotherapeutic product (RBP)** refers to a product used as the comparator for head-to-head comparability studies with a similar biotherapeutic product in order to show similarity in terms of quality, safety, and efficacy. Only an originator product that was licensed on the basis of a full registration dossier can serve as an RBP. The term does not refer to measurement standards such as international, pharmacopeial, or national standards or reference standards.

MM. **Reference drug regulatory authority (RDRA)** refers to a national or regional regulatory authority for drugs, vaccines, and biologicals being relied upon by the FDA for a more efficient approach to arriving at a decision thereby improving and expediting quality assured, effective, and safe products.

NN. **Reference drug product** refers to a pharmaceutical product that has been granted marketing authorization by FDA or by a reference drug regulatory authority recognized by FDA. The authorized pharmaceutical product may be the innovator or a generic equivalent.

OO. **Registration** refers to the process of approval of an application to register health products prior to engaging in the manufacture, importation, exportation, sale, offer for sale, distribution, transfer, and where applicable, the use, testing, promotion, advertisement, and/or sponsorship of health products. An FDA-registered product refers to a product that has been applied and has successfully complied with the necessary requirements for FDA authorization.

PP. **Similar biotherapeutic product (SBP)** or **biosimilar** refers to a biotherapeutic product that is similar in terms of quality, safety, and efficacy to an already licensed reference biotherapeutic product.

QQ. **Stop-clock** refers to a period of time provided for processes outside of FDA's control (e.g., awaiting response, compliance and/or requested documents from the applicant, the World Health Organization (WHO) Prequalification Team (PQT), and other external stakeholders) during which the regulatory time is officially stopped and is not counted in the provided regulatory turn-around-time for FDA.

RR. **Traditional Medicine** refers to any medicinal product consisting of active ingredients derived from natural sources (plants, animals, and/or minerals) used in the system of traditional practice.

SS. **Vaccine** refers to a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins.

V. GENERAL GUIDELINES

A. Drug Registration Overview

1. Filing of Application

a. Only a duly licensed drug manufacturer, trader, or distributor-importer/exporter may file an application for registration of a drug product or drug substance. The applicant shall authorize officers or employees to submit the application.

b. The applicant shall be responsible for the submission of complete and correct application documents to this Office and ensure unrestricted access to the e-mail address and other contact information declared in the submission.

c. FDA shall require a statutory declaration by the applicant verifying any information contained in or relating to the application to be true and correct and will be held responsible for any misdeclaration pertaining to the drug product or drug substance being applied.

d. For drug product registration, separate applications shall be required for the following conditions:

i. Different API(s)

(1) different salt or isomer form of the API

(2) additional API to a single component or multicomponent product

(3) removal of API from a multicomponent product

(4) different strength of one or more APIs

(5) higher overage than previously applied

ii. Different pharmaceutical form/dosage form

iii. Different route of administration (exception for parenteral route)

iv. Different drug product formulation (added and/or removed excipients)

v. Different primary packaging material for a registered drug product, including its attached device, delivery system

vi. Different cell substrate/viral or bacterial seeds that are unrelated to the licensed master cell bank (MCB)/master seed lot (MSL) or pre-MCB/MSL material (for biological drug products)

vii. Different component(s) (for drug kits)

e. Products which are identical to an authorized product (Principal CPR) in terms of the manufacturer and of the pharmaceutical formulation may be applied for a Certificate of Listing of Identical Drug Product (CLIDP).

f. It shall be the responsibility of the applicant to scrutinize the drug they are applying, determine the application type and evaluation pathway, and to understand the requirements and procedures prior to submission of application.

g. For branded products, the brand name(s) proposal shall be submitted with the registration application and shall be processed simultaneously following the guidelines in AO No. 2005-0016: General Policies and Guidelines Governing Brand Names of Products for Registration with the Bureau of Food and Drug or its amendments.

2. Pre-Assessment

a. All registration applications shall undergo pre-assessment to ensure the completeness of submitted applications and documentary requirements. The pre-assessment of applications shall be done within the prescribed working days and office hours of the FDA. Schedule of submissions shall follow the latest guidelines on FDA submission platform.

b. Applications with incomplete documentary requirements and incorrect data entry and format shall not be accepted and will not proceed to the next step of the process.

c. If an application is identified to be more appropriately submitted under a different authorization type, application type, or review route, the application will not be accepted.

d. The FDA shall inform the applicant of the result of the pre-assessment through the provided e-mail address of the applicant. If the application passes the pre-assessment step, the applicant shall receive the Order of Payment with a reference number indicating the fees to be paid. If the application does not pass the pre-assessment step, the FDA shall notify the reason/s for non-acceptance (e.g., deficiency/ies) and prompt the applicant to submit a new application.

e. Payment shall be made within the time stipulated in the latest implementing guidelines. The application shall be considered withdrawn if payment has not been made within the stipulated time.

f. The pre-assessment process only checks for the completeness of the application documentary requirements for evaluation. Successfully passing the pre-assessment step does not denote the adequacy of the data for regulatory approval.

3. Evaluation

a. The complete document submission shall be reviewed and evaluated. The suitability of use under local conditions and regulatory requirements shall be assessed. The FDA shall consider the benefits and risks as they apply to the Philippine context based on the available data provided by the applicant.

b. The FDA may require clarifications, additional information, or the additional supporting documents as laid out in the list of requirements in the latest Citizen's Charter, as deemed necessary, to ensure the safety, efficacy, and quality of the drug intended for registration. In such cases, a Notice of Deficiency (NOD) shall be issued to the applicant who will be required to comply within a specified timeframe. A stop-clock shall start upon issuance of NOD and shall end upon the receipt of a complete and satisfactory response/compliance from the applicant. The application will be disapproved if the applicant fails to observe the specified response/compliance deadline. The submission of additional supporting data not requested by the FDA following the acceptance of the application will not be considered unless a prior arrangement with FDA is made for the submission concerned.

c. The FDA may consider engaging external evaluators, experts, and advisory committees in the evaluation process, when necessary. These experts include scientists and clinicians from both local and overseas institutions. All external evaluators and experts are bound by agreement to protect the information made available to them. The identity of the evaluators is kept confidential.

4. Regulatory decision

a. Upon evaluation, the FDA shall arrive at a final decision on the registration application based on compliance with existing standards set by FDA. An application can be considered either "approved" or "disapproved."

b. An approved application means that the drug product or drug substance has been evaluated as conforming to the standards required for the authorization being sought and has been successfully registered with the FDA. The registered drug shall be included in the FDA's Drug Registry. A Certificate of Product Registration (CPR) shall be issued to the applicant, reflecting the type of authorization granted by the FDA, as well as its validity, and restrictions, among others, as applicable.

c. A disapproved application means that the application submitted failed to provide sufficient evidence to ensure the quality, safety, and/or efficacy of the drug product or drug substance based on the standards required for the authorization being sought.

5. Post-approval changes (PAC) / variations

a. Upon the registration of a drug product or drug substance, the authorization holder is responsible for ensuring the product's quality, efficacy, and safety throughout its life cycle.

b. The FDA must be informed by the authorization holder of any changes or any amendment to the dossier which may affect the quality, efficacy, and/or safety of drug product or drug substance.

c. An application for PAC may be submitted at any time within the validity of the CPR. All applications for PAC shall be submitted following the procedures, requirements, and schedule prescribed in the latest implemented guidelines.

d. Acceptable notifications for minor variations such as change in product labeling, and applications for major variations such as addition of alternative drug manufacturing site (i.e., bulk manufacturer, primary packager, secondary packager and batch release site) for the same manufacturing activity, shall follow the latest implemented variation guidelines.

e. It should be noted, however, that actions on a registration application are based on the complete set of specifications of the drug proposed to appear in the label, i.e., formulation, dosage form, strength, therapeutic indication, and manufacturer, and include the classification of the drug according to market access to which type of marketing authorization application.

f. After a PAC affecting the labeling materials is approved, there shall be a one-year period during which the previous labeling materials can still be used by the manufacturer. Once the one-year period expires, the products manufactured must exclusively use the updated materials approved.

6. Renewal of authorization

a. In order for a drug product or drug substance authorization to remain valid and to retain its active status in the FDA Drug Registry, an application for renewal shall be submitted by the authorization holder.

b. All applications for renewal of authorization shall be submitted following the procedures, requirements, and schedule prescribed in the latest implemented guidelines.

c. Applications for the renewal of authorization shall be reviewed and evaluated on the basis of the product and the applicant meeting the current FDA implemented standards of identity, purity, strength, quality, safety, efficacy and therapeutic value.

7. Cancellation of authorization

a. The authorization of a corresponding drug product or drug substance may be cancelled by the authorization holder voluntarily at any time during its validity stating the reason for cancellation.

b. The FDA can execute its power to impose mandatory cancellation or revocation of authorization in instances mentioned in Book II, Article I, Sec.

4. Grounds for Disapproval of Application and Suspension or Cancellation of License, Registration, or Authorization of the IRR of R.A. 9711.

c. Once canceled, any requests for reinstatement of drug product or drug substance authorization shall not be accommodated by the FDA. New application shall be submitted for the product or substance to be authorized again. Accordingly, the drug product or drug substance registration status shall be updated in the FDA Drug Registry.

d. It shall be the responsibility of the authorization holder to discontinue the supply of the drug product or drug substance with canceled authorization. Any recall proceedings shall be the responsibility of the marketing authorization holder following the latest implemented guidelines.

B. General Conditions

1. Eligibility requirements

a. For the marketing authorization of locally manufactured drug products and drug substances, only applications from establishments with a valid LTO as drug manufacturer or trader and a GMP Clearance from FDA are acceptable. For the marketing authorization of imported drug products and drug substances, only applications from establishments with a valid LTO as drug importer and a GMP Clearance of the Foreign Drug Manufacturer issued by FDA are acceptable. For applications of Certificate of Listing of Identical Drug Product (CLIDP), only applications from establishments with a valid LTO as drug distributor are acceptable.

b. For authorization of drug products for DOH-use, only applications from the DOH are acceptable.

c. For authorization of export-only drug products and drug substances, only applications from local drug manufacturers intending to solely market their product outside of the country are acceptable.

d. For clearance of drug products donated by foreign entities, applications from individuals, organizations, institutions, both public and private, and all levels of government engaged in the importation, facilitation and management of all regular donations of foreign origin covering drug products during non-emergency situations are acceptable.

2. For drug products, registration application shall be for FDA authorization to allow the use (for marketing, export, DOH-use, or as donation) a finished drug product to/by patients or healthcare providers. Through the approval of the application, it is ensured that the drug product is safe, efficacious, and of good quality when used according to its intended purpose.

3. For drug substances, the registration application shall be for FDA authorization to allow the production and marketing of the drug substance as a raw material to other pharmaceutical companies. Through the approval of the application, it is ensured that the drug substance is of good quality for use in the manufacture of drug products.

4. When applying for the registration of a drug product or drug substance, the applicant must ensure that all information contained in the application is true, correct and is not misleading. It shall be the responsibility of the applicant to

inform the FDA of any emerging information that may affect the risk-benefit assessment of the drug, as soon as the applicant becomes aware of such information. Failure to fully disclose material information about the drug is a ground for disapproval of registration application and a basis for cancellation of the establishment's LTO as provided in Book II, Article 1, Sec. 4-A of the IRR of RA 9711.

5. The standards for the drug product and drug substance authorizations, the application requirements and the evaluation procedures shall be established and updated to all covered drug products through appropriate FDA issuances.

C. Drug Categories

1. Market Access Classification

a. In general, all products are classified according to market access considering the safety of the API and the finished drug product. Drug products may be classified as prescription drug or non-prescription drug. Non-prescription drugs are further classified as pharmacist-only non-prescription drug or general sales non-prescription drug:

i. Prescription Drugs, also referred to as Rx drugs, prescription-only medicines (POM) and ethical medicines, refer to drug products that can only be dispensed by a pharmacist to a patient, upon presentation of a valid prescription from a physician, dentist, or veterinarian and for which a pharmacist's advice is necessary (Article 1, section 5 (l), in relation to Article 8, Section 52, of RA No. 10918 or the Philippine Pharmacy Act).

(1) A product shall be classified as a prescription drug if:

(a) it is likely to present a risk either directly or indirectly, even when used correctly if utilized without medical supervision; or

(b) it is frequently used incorrectly, likely to present a direct or indirect risk to human health; or

(c) it contains substances or preparations thereof, the activity and/or adverse reactions of which require further investigation or additional monitoring; or

(d) the product is prescribed for parenteral administration.

(2) Prescription drugs with special requirements:

(a) Dangerous drug preparation requiring an S-2 License and Dangerous Drugs Board (DDB) Prescription as listed in the latest version of the List of Scheduled Controlled Substances released by DDB.

(b) Advanced Therapy Drug Products (ATMPs) for implantation, transplantation, infusion, or transfer into human recipients (as a standard-of-care for a specific approved indication in accordance with DOH-approved national practice guidelines) to be performed only in hospitals and non-hospital-based stem cell facilities which are licensed by the DOH

(c) Radiopharmaceuticals refer to a chemical compound labeled with radioisotope(s) and administered to patients for diagnosis

and/or therapy. Only Authorized Nuclear Pharmacists are allowed to prepare and dispense radiopharmaceuticals.

ii. Pharmacist-Only Non-Prescription Drugs, also referred to as non-Rx drugs and over-the-counter drugs, refer to drug products that can be dispensed even without the prescription of a licensed physician, or dentist, for the symptomatic relief of minor or self-limiting ailments; and to be obtained only from a licensed pharmacist, with mandatory pharmacist's advice on its selection and proper use. These drug products shall be sold only in FDA-licensed drug outlets under the direct supervision of a registered and licensed pharmacist.

(1) A product shall be classified as pharmacist-only non-prescription drug if:

(a) Consultation with a pharmacist is necessary to confirm the appropriate choice of therapy;

(b) The contraindications, drug interactions, precautions or warnings need reinforcement by a pharmacist or are not easily recognized by the patient;

(c) Special precautions are needed in the storage and handling of the product; or

(d) It does not conform with any of the conditions for a prescription drug product [See Section V,C,1,a,i,(1)].

iii. General Sales List (GSL) Drugs – also referred to as household remedies, refer to non-prescription drugs products for human use classified by FDA which may be dispensed without a prescription and only be sold by retail, offered, or exposed for sale either at licensed drugstores or retail outlets for non-prescription drugs (RONPD)s.

(1) A product shall be classified as general sales non-prescription drug if:

(a) The product is reasonably safe and can be sold or supplied without the need for supervision by a registered physician, dentist, or pharmacist;

(b) The contraindications, drug interactions, precautions and warnings are easily recognized by the patient; and

(c) The hazard to health, the risk of misuse, the risk of misdiagnosis, the need to take special precautions in the storage and handling of the product is minimal.

(d) It does not conform with any of the conditions for a prescription drug product [See Section V,C,1,a,i,(1)] and pharmacist-only non-prescription drug product [See Section V,C,1,a,ii,(1)].

b. The FDA shall provide and publish an updated list of drug molecule with corresponding market access classifications.

c. Products with drug substance(s) not yet included in the list shall be assigned with market access classification prior to issuance of CPR. Assigning the classification shall be part of the registration process.

d. Products in fixed-dose combination should be classified with reference to the list of active pharmaceutical ingredients considering the API content. A product shall be classified conservatively on the following conditions: If the product contains any API listed as prescription drug, then the drug product should be classified as prescription drug. If the product contains an API not listed as prescription drug but has an API listed as pharmacist-only non-prescription drugs, then the product should be classified as pharmacist-only non-prescription drug. If the product contains an API neither listed as prescription drug nor pharmacist-only non-prescription drug and both are general sales non-prescription drug, then the product should be classified as general sales non-prescription drug.

e. The MAH may request for reclassification of a drug product from the prescription drugs list to the pharmacist-only non-prescription drugs list or from pharmacist-only non-prescription drugs list to general sales non-prescription drug by filing a corresponding application for PAC. No prescription drug is allowed to be directly switched to general sales non-prescription drug. The FDA has the right to reclassify a drug product without requests from the MAH whenever appropriate as supported by scientific evidence. Whenever an API is reclassified to another classification, the MAH may apply for Variation to reflect the new classification status of the product.

f. Only non-prescription drugs products and those under the general sales list are allowed for advertisements and promotions. Except through medical journals, publications, or literature exclusively meant for medical and associated professionals, no drug product categorized as Prescription drug shall be advertised or promoted in any form of mass media.

2. Product Types

a. The types of drug products and substances covered in this guideline can be classified as:

i. Chemical entity – considered as conventional drug, refers to any chemical element, naturally occurring chemical material or chemical product obtained by chemical change or synthesis (including macromolecules produced by chemical synthesis, such as peptides/oligo-nucleotides), or any metabolites from a micro-organism (such as antibiotics).

ii. Biological entity – refers to any macromolecule extracted from an organism (such as proteins, nucleic acids, proteoglycans, cytokines and growth factors), or any substance derived from a biological system, including any of the following:

(1) Whole cell or micro-organism, such as a whole virus or bacterium used as a vaccine;
(2) Part of a micro-organism, such as a sub-unit vaccine;
(3) Plasma-derived product;
(4) Biotechnology-derived substance, such as a protein or polypeptide; or
(5) ATMPs which include:
(a) Gene therapy drug product;
(b) Somatic cell therapy drug product; and
(c) Tissue-engineered product.

iii. Radiopharmaceutical – refers to pharmaceutical formulations consisting of radioactive substances (radioisotopes and molecules labelled with radioisotopes), which are intended for use either in diagnosis or therapy. The most striking feature versus conventional pharmaceuticals is the property of the radionuclide, which disintegrates or decays with time, often resulting in a limited shelf-life of the product. The physical half-life of the radionuclides used in radiopharmaceuticals is generally short, and hence the final preparation needs to be carried out before administration to the patient.

iv. Homeopathic drug – refers to a drug product that is formulated for use on the principle of "like cures like". It is prepared following a homeopathic manufacturing procedure described by a homeopathic pharmacopeia.

v. Medical gas – refers to any gas or mixture of gases intended for administration to patients for anesthetic, therapeutic, diagnostic, or prophylactic purposes, which may be manufactured in a liquefied, non-liquefied, or cryogenic state and administered as a gas. Medical gases include oxygen, nitrogen, nitrous oxide, carbon dioxide, helium, carbon monoxide, and medical air which meet the standards set forth in an official compendium.

vi. Herbal medicine – herbal medicine refers to finished, labeled, medicinal products that contain as active ingredient(s) aerial or underground part(s) of plant or other materials or combination thereof, whether in the crude state or as plant preparations. Herbal medicines, however, may contain excipients in addition to the active ingredient(s). Medicines containing plant material(s) combined with chemically-defined active substances, including chemically-defined, isolated constituents of plants, are not considered to be herbal medicines. It shall not include any sterile preparation, vaccines, any substance derived from human parts, any isolated and characterized chemical substances.

vii. Traditional Medicine – refers to any medicinal product consisting of active ingredients derived from natural sources (plants, animals, and/or minerals) used in the system of traditional practice. It shall not include any sterile preparation, vaccines, any substance derived from human parts, any isolated and characterized chemical substances.

vii. Orphan drug – refers to any drug or medicine used to treat or alleviate the symptoms of persons afflicted with a rare disease and declared as such by the DOH upon recommendation of the National Institutes of Health (NIH).

b. In view of the foregoing enumeration, the FDA is not precluded from determining the inclusion of all other types of drug products and substances as it may deem necessary.

3. Pharmacologic Category

Drug products and substances shall be classified according to the 2nd, 3rd, and 4th levels of the pharmacologic/therapeutic categories of the WHO Anatomical Therapeutic Chemical (ATC) Classification system.

D. Types of applications

1. Authorization applications

a. Marketing authorization

i. New drug application (NDA) / New biological drug application (NBDA)

(1) NDA/NBDA-1: For the first strength of a product containing a new chemical or biological entity. This means the entity is currently not a registered entity in the country.

(2) NDA/NBDA -2: For the first strength of a product containing:

(a) New fixed-dose combination of registered chemical or biological entities.

(b) Registered chemical or biological entities in either of the following:

(i) New dosage forms, such as tablets, capsules, and injectables.

(ii) New presentation, such as single-dose vials, multi-dose vials, and pre-filled syringes.

(iii) New formulation, such as preservative-free.

(c) Registered chemical or biological entities for use by a new route of administration.

(d) Registered chemical or biological entities for a new indication, dosage recommendation, or patient population.

(e) For products that do not fall under the requirements for NDA/NBDA-1, NDA/NBDA-3, or generic drug application (GDA).

(3) NDA/NBDA-3: For subsequent strengths of a product that has been registered or has been submitted as an NDA/NBDA-1 or NDA/NBDA-2. The product name, dosage form, presentation, indication, dosing regimen, and patient population should be the same as that for the NDA/NBDA-1 or NDA/NBDA-2 submission.

ii. Biosimilar product application: Biosimilar products are required to be submitted via NBDA-2 or NBDA-3.

(1) NBDA-2: For the first strength of a biosimilar product with the same dosage form and route of administration as the reference biological drug product.

(2) NBDA-3: For subsequent strengths of a biosimilar product that has been registered or has been submitted as an NBDA-2. The product name, dosage form, indication, dosing regimen, and patient population should be the same as that for the NBDA-2 submission.

iii. Generic drug application (GDA)

(1) A drug product shall undergo generic drug application provided that:

(a) it has the same dosage strength and form, route of administration, and conditions of use (e.g., indication, dosing regimen, and patient group) as the reference drug product, and

(b) it exhibits bioequivalence with a reference drug product.

iv. Drug Substance Application

(1) Drug substances applied for registration shall be issued the appropriate FDA authorization specific for use in the manufacture of drug products.

(2) It is important to note that this does not apply to precursors, which are intermediate chemical compounds used in the synthesis of drug substances or APIs.

b. Export-only Authorization

Only drug products manufactured in the Philippines by an FDA-licensed drug manufacturer intended to be solely marketed outside of the country may be applied for Export-only Authorization.

c. DOH-use Authorization

Only drug products to be procured locally or internationally and used by the DOH may be applied for DOH-use Authorization. All drug products applied for DOH-use Authorization shall undergo review process similar to Marketing Authorization (refer to Section V,D,1,a).

d. Clearance for Foreign Donation

i. All donations shall be based on the four core principles as stipulated in the WHO 2010 Guidelines on Foreign Donations and its amendments. These are namely:

(1) maximum benefit to the recipient

(2) have respect for the wishes and authority of the recipient,

(3) there shall be no double standards in quality, and

(4) there shall be effective communication between donor and recipients

ii. Foreign donations comprising drug products shall be accepted if these conform with the following acceptance criteria:

(1) Must have counterpart with marketing authorization

(2) Drug products must at least satisfy one (1) of the following conditions:

(a) Must contain the same active ingredients, dosage form, and strength as those products already approved by and registered at FDA;

(b) Orphan drugs and drugs for compassionate use; or

(c) Critically needed drugs (Note: Subject to approval by the Secretary of Health)

(3) Must NOT be classified under experimental/investigational drugs registration of FDA

(4) For foreign donated dangerous drugs, guidelines based on Dangerous Drugs Board (DDB) Board Regulation No. 1 s. 2014 or its amendments shall be followed.

(5) Must have a shelf-life of at least 12 months (or 1 year) at the expected date of arrival

(6) For drug products with a shelf-life below 12 months, these must satisfy at least one of the following conditions:

(a) The product has a total shelf life of less than 2 years AND has a remaining at least one-third (1/3) of its shelf-life at the expected date of arrival
(b) Must be recommended as suitable for distribution as per case assessment by the DOH/TWG and approved by the Secretary of Health despite the limited product shelf-life remaining

2. Post-Registration Applications

a. Post-Approval Change (PAC)

i. Changes to a drug product or drug substance throughout the validity of its authorization must be submitted to FDA through PAC application. These include administrative/editorial, quality, and clinical/non-clinical changes.

ii. No PAC application shall be filed together with the renewal registration of a drug product or drug substance. It should be either PAC applications that have been submitted and approved prior to submission of the application for renewal, or the PAC applications shall be submitted after approval of the application for renewal.

iii. In general, once the application has been approved/processed, the changes should be implemented.

iv. Applications shall follow the latest implementing guidelines for variation or PAC of drugs.

b. Renewal of Authorization

i. A registered drug product or drug substance with an active status applied for renewal of registration before the expiration of the CPR validity shall be eligible for automatic renewal.

ii. A registered drug product or drug substance with an inactive status may be applied for renewal of registration within one hundred twenty (120) calendar days from the expiration of the CPR validity with a surcharge or penalty equivalent to twice the renewal registration fee and an additional 10% per month or a fraction thereof of continuing non-submission of such application. Beyond this period, the product or substance shall be considered not eligible for the renewal registration application.

iii. No PAC application shall be filed together with the renewal registration of a drug. Separate application/s shall be submitted for all changes to the drug registration following the latest implemented guidelines.

c. Cancellation of Authorization

i. The authorization holder shall submit a notification for cancellation of a drug product or drug substance authorization voluntarily anytime during its validity stating the reason for cancellation and the latest distribution.

E. Registration Review Pathways

1. Full review

Full review route shall apply to a drug that has not been approved by any reference drug regulatory authority (RDRA) at the time of submission.

2. Abridged review

Abridged review shall be available for a drug that has been approved by at least one RDRA at the time of submission. Application, requirements, and recognized RDRAs shall follow the latest implemented guidelines.

3. Verification review

Verification review route shall be available for a drug with similar indication(s), dosing regimen(s), patient group(s), and/or direction(s) for use that has been approved by at least two of FDA's RDRAs. Application, requirements, and recognized RDRAs shall follow the latest implemented guidelines.

4. Collaborative review

Collaborative review route shall be available for a drug that is the same as the product prequalified by the WHO/PQT. All aspects of the drug's quality, including but not limited to the formulation, manufacturing site/s, release and shelf-life specifications, primary packaging, and commercial presentation must be the same as those currently approved by the WHO/PQT at the time of submission. The proposed indication/s, dosing regimen/s, patient group/s, and/or direction/s for use should be the same as those approved by the WHO/PQT. Application and requirements shall follow the latest implemented guidelines.

5. Joint Assessment

Formal Procedure in which the same application is simultaneously submitted to all participating ASEAN NRAs. Drugs outside priority areas can submit applications for consideration by ASEAN NRAs as long as the products have already been approved by reference NRA, prequalified by WHO, or assessed through special regulatory pathways (e.g. EU Article 58 or US FDA) approval. In addition, products should be manufactured in a PIC/S-GMP compliant site.

In view of the foregoing enumeration, the FDA is not precluded from determining the inclusion of any alternative review pathways as it may deem necessary.

F. Validity

For marketing, export-only, and DOH-use authorizations, the authorization issued by FDA shall have an initial validity of five (5) years for all types of applications, or as provided by the latest issuance of FDA. The CPR may be renewed for another 5 years, or 10 years upon the discretion of the applicant.

For foreign donations, the authorization for the product to be donated shall have a validity period of one (1) year. The product may be used by the recipient of the donation until the end of the product shelf-life.

G. Drug Registry

The FDA Drug Registry, which shall contain all registered drug products and drug substances issued with FDA authorization shall be made available and officially accessed through the FDA-available online platforms. This registry shall reflect the full information on the drug including its registration and authorization status (authorization type and validity [a valid authorization means active status, while an

invalid/lapsed authorization means inactive status]), approved physical and electronic labeling materials, as well as post-approval changes and updates.

H. Fees and Charges

The appropriate fees and charges as specified under existing regulations shall apply, including a Legal Research Fee (LRF), or any amendment or latest issuance thereafter.

I. Processing Time

The processing time or prescribed turn-around time per type of application shall follow the latest Citizen's Charter of the FDA Center for Drug Regulation and Research (CDRR).

J. Reconsideration and Re- application

Applications that are disapproved due to non-compliance with the requirements for registration can submit a one-time reconsideration or re-application.

Reconsideration application shall be submitted within three (3) months from the date of the Letter of Disapproval (LOD) and payment of the required fees. The applicant shall put the reconsideration in writing and shall point specifically the deficiencies or conclusions in the LOD which they think are supported by the evidence or required documents submitted. The applicant is not allowed to provide additional supporting documents for reconsideration.

Re-Applications shall be submitted within six (6) months from the date of the LOD and payment of the required fees. The applicant shall submit additional supporting documents, if necessary, in compliance with the deficiencies. Applications submitted 6 months after the date of notice of disapproval shall be considered as initial registration.

L. Implementation arrangements

For the purposes of the implementation of this Order, the FDA shall undertake the following:

1. Issue guidelines, including but not limited to the application procedure, forms, documentary requirements, and such other requirements as may be prescribed by regulations to ensure the safety, efficacy, and good quality of such drug through FDA issuances; and
2. Endeavour to incorporate digitization and digitalization initiatives such as transition to electronic labeling and other reengineering and streamlining activities to ensure the efficiency of the registration process.

VI. MANDATORY REVIEW

Within three (3) years of its implementation, this Order shall be reviewed and evaluated to determine whether the policy's objectives, impact, and effectiveness are achieved.

VII. SEPARABILITY CLAUSE

The provisions of this Order are hereby declared separable and in the event of any such provision/s is/are declared invalid or unenforceable, the validity or enforceability of the remaining portions or provisions which are not affected by such declaration shall remain in full force and in effect.

VII. PENALTY CLAUSE

Violation of any provision of this Administrative Order shall be sanctioned, such as, but not limited to, imposition of fines, suspension, cancellation, or revocation of any authorization issued by the FDA.

VIII. REPEALING CLAUSE

All Administrative Orders and other administrative issuances that are inconsistent with the provisions of this regulation are hereby repealed or modified accordingly, such as but not limited to the following:

A. Administrative Order No. 67 s. 1989: Revised Rules and Regulations on Registration of Pharmaceutical Products;
B. Administrative Order No. 96 s. 1990: Guidelines on the Registration of Fixed-Dose Combination Drug Products;
C. Administrative Order No. 117 s. 1992: Providing for the Classification of Household Remedies;
D. Administrative Order No. 23-c s. 2000: Policies and Guidelines on Over-the-Counter (OTC) Drug Products;
E. Administrative Order No. 142 s. 2004: Bureau of Food and Drugs (BFAD)'s issuance of Certificate of Product Registration for Foreign Assisted Projects Procurement and Laboratory Testing of Pharmaceutical and Biological products Procured by and/or delivered to the Department of Health;
F. Administrative Order No. 172 s. 2004: Guidelines on the Registration of Herbal Medicines;
G. Administrative Order No. 184 s. 2004: Guidelines on the Registration of Traditionally-Used Herbal Products;
H. Administrative Order No. 2005-0007: Amending Administrative Order No. 142, s. 2004 by providing exemption from the requirement of Certificate of Product Registration for all goods procured through UNICEF, UNDP, WHO, and GDF;
I. Administrative Order No. 2005-0030: Guidelines and Procedure for the Automatic Renewal of the Certificate of Product Registration issued by the Bureau of Food and Drugs;
J. Administrative Order No. 2005-0031: Guidelines and Procedure for the Issuance of the Principal Certificate of Product Registration and the Listing of Identical Drug Products based on the Identity of Manufacturer and Pharmaceutical Formulation;

K. Administrative Order No. 2006-0021: Supplemental Guidelines to Administrative Order (AO) 67 s. 1987, Revised Rules and Regulations on Registration of Pharmaceutical Products and Bureau Circular 05 s. 1997 in evaluating New Drug Applications;
L. Administrative Order No. 2016-0008: Revised Rules and Regulations Governing the Generic Labeling Requirements of Drug Products for Human Use;
M. Administrative Order No. 2020-0001: Guidelines in the Importation, Facilitation, and Management of Foreign Donations involving Health and Health-Related Products;
N. Bureau Circular No. 12 s. 1991: Clarification of New Registration when there is a Change of Manufacturer;
O. Bureau Circular No. 5 s. 1997: Revised Checklist of Requirements and the 1997 Guidelines for the Registration of Pharmaceutical Products; and
P. FDA Circular No. 2021-020: Revised Post-Marketing Surveillance Requirements for New Drugs under Monitored Release.

IX. TRANSITORY CLAUSE

All current and prospective Authorization Holders of drug products and drug substances must ensure compliance with the provisions of this Administrative Order through the implementing guidelines to be issued. Sufficient time will be provided until the implementation of the new guidelines to ensure seamless adherence. Pending the issuance of the implementing guidelines, the existing regulations shall continue to be followed.

X. EFFECTIVITY

This Order shall take effect fifteen (15) days after the publication in the Official Gazette or a newspaper of general circulation and filing with the University of the Philippines Office of the National Administrative Register.