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THE TANZANIA FOOD, DRUGS AND COSMETICS ACT
(CAP.219)

# REGULATIONS

*(Made under section 122 (1)(b)*

THE TANZANIA FOOD, DRUGS AND COSMETICS (ORPHAN MEDICINES) REGULATIONS, 2018

## PART I
## PRELIMINARY PROVISIONS

Short title and commencement

1. These Regulations may be cited as the Tanzania Food, Drugs and Cosmetics (Orphan Medicines) Regulations, 2018 and shall come into operation on the date of its publication in the government *gazette*.

Application

2. These Regulations shall apply to all regulatory controls related to registration, importation and monitoring of quality and safety of human and veterinary medicines designated as orphan medicines in Tanzania Mainland.

Interpretation

3. In these Regulations, unless the context otherwise requires:

Cap.219

"Act" means The Tanzania Food, Drugs and Cosmetics Act;

"Applicant" means any legal or natural person, established within or outside Tanzania, seeking to obtain or having obtained the designation of a medicinal product as an orphan medicinal product;

"Authority" means the Tanzania Food and Drugs Authority or its acronym 'TFDA' established under section 4(1) of the Act;

"Clinically superior" means that a medicine is shown to provide a significant therapeutic advantage over and above that provided by an approved medicine, in one or more of the following ways:

(a) greater effectiveness than an approved medicine (as

assessed by effect on a clinically meaningful endpoint in adequate and well controlled clinical trials);

(b) greater safety in a substantial portion of the target populations, for example, by the elimination of an ingredient or contaminant that is associated with relatively frequent adverse effects;

"Director General" means the Chief Executive of the Tanzania Food and Drugs Authority appointed under section 8(l) of the Act;

"Medicinal product" means a medicinal product for human or veterinary use as defined under the Act;

"Medicines" means a mixture of substances manufactured, sold or presented for use in:

(a) the diagnosis, treatment, mitigation or prevention of a disease, disorder, abnormal physical or mental state, or the symptoms thereof, in man or animal;

(b) restoring, correcting or beneficial modification of organic or mental functions in man or animal or;

(c) disinfection in premises in which food and drugs are manufactured, prepared or kept, hospitals, equipment and farm houses;

(d) articles intended for use as a component of any articles specified in clause (a), (b) or (c); but does not include medical devices or their components, parts or accessories;

"Manufacturer" means a person or firm that is engaged in the manufacture of products regulated under the Act;

"Orphan medicinal product" means a medicinal product designated as such under the terms and conditions set out under regulation 9 of these Regulations;

"Orphan medicine designation" means TFDA's act of granting a request for designation under regulation 9 of these Regulations;

"Same medicine" means:-

(a) if it is a medicine composed of small molecules, a medicine that contains the same active moiety as a previously approved medicine and is intended for the same use as the previously approved medicine;

(b) if it is a medicine composed of large molecules (macromolecules), a medicine that contains the same principal molecular structural features (but not necessarily all of the same structural features) and is

intended for the same use as a previously approved medicine.

## PART II
## GENERAL PROVISIONS

Rationale

4. An orphan medicine shall be approved where a medical condition occurs in small number of patients and less frequently to an extent that manufacturers see no commercial incentive in developing and bringing to the market such medicinal product for disease conditions in which the anticipated sales would not be sufficient to cover the costs of development, production and application for marketing authorization.

Need for orphan medicines

5. Any patient suffering from diseases, conditions or disorders that occur rarely in the population shall be entitled to the same quality of health care as other patients and allowed to access orphan medicines.

Applications for designation

6.-(1) Applicants wishing to register their medicinal products as orphan medicines shall apply to the Authority to request for such designation.

(2) The designation of an orphan medicine specified in sub regulation (1) shall be made by the Director General in consultation with the Technical Committee established under section 13 of the Act.

Marketing authorisation

7. Applicants of orphan medicines shall obtain marketing authorization in Tanzania after approval granted by the Director General.

Incentives to Applicants

8. Applicants of orphan medicines shall be eligible to incentives which shall include, but not limited to:

(a) fast track review of applications for marketing authorization;

(b) flexibilities in amounts of fees payable to the Authority and;

(c) technical assistance in complying with regulatory requirements in form of pre-submission meetings and consultations before and during the assessment process.

PART III
ORPHAN DESIGNATION

Conditions for designation

9. A medicinal product shall be designated as an orphan medicinal product if the applicant has submitted information to establish the following:

(a) that the medicine is intended for use in a life-threatening or chronically debilitating condition affecting not more than twenty five thousand (25,000) persons in Tanzania at the time of designation and or application of marketing authorization;

(b) that it is intended for use in a life-threatening, seriously debilitating or serious and chronic condition in Tanzania and that without incentives it is unlikely that the marketing of the medicinal product in the country would generate sufficient return to justify the necessary investment and;

(c) that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been registered in Tanzania or, if such method exists, that the medicinal product will be of significant benefit to those affected by that condition.

Stage of application

10. An Applicant may submit an application to TFDA at any stage of development of a medicinal product, during review of the application or after marketing authorization has been granted for a different indication to obtain the designation status.

Application requirements

11. The application shall be accompanied by the following:

(a) covering letter containing a statement that the Applicant requests orphan medicine designation for a rare condition, which shall be identified with specificity;

(b) filled in and signed application form as provided in the First Schedule of these Regulations;

(c) medicinal product dossier compiled in line with the requirements provided in the Regulations for registration of medicines in force. The dossier shall also include discussion on the scientific

rationale to establish a medically plausible basis for the use of the medicine for the rare disease or condition, including all relevant data from in vitro laboratory studies, preclinical efficacy studies conducted in an animal model for the human disease or condition, and clinical experience with the medicine in the rare disease or condition that are available to the Applicant, whether positive, negative, or inconclusive. Copies of pertinent unpublished and published papers shall also be submitted;

(d) samples of the product in commercial packs intended for marketing in Tanzania;

(e) detailed information on the proposed therapeutic indication(s) as well as a detailed description of the rare disease(s) or condition(s) for which the medicine is being proposed for designation and marketing authorization;

(f) detailed justification that the criteria provided under regulation 9 have been fulfilled and a description submitted to the Authority where applicable;

(g) where the Applicant of a medicine that is otherwise the same as an already approved medicine seeks orphan medicine designation for the subsequent medicine for the same rare disease or condition, an explanation of why the proposed variation may be clinically superior to the first medicinal product must be submitted;

(h) where an applicant requests orphan medicine designation for a medicine for only a subset of persons with a disease or condition that otherwise affects 25,000 or more people ("orphan subset"), a demonstration that, due to one or more properties of the medicine, the remaining persons with such disease or condition would not be appropriate candidates for use of the medicine;

(i) a summary of the regulatory status and marketing history of the medicinal product in foreign countries, for what indication is the medicine approved in foreign countries and information on any adverse regulatory actions that have been taken against the medicinal product.

Processing of the application by the Authority

12. Upon receipt of the application the Authority shall:
(a) review the application against the criteria and documentation requirements specified in regulation 9 and 11 of these Regulations;
(b) where appropriate, request the applicant to supplement particulars and documents accompanying the application.

13.-(1) The Director General shall upon consideration of the recommendations of the Committee, where applicable, and having been satisfied that the criteria mentioned under these Regulations complied or for public interest, approve the request for designation of an orphan medicine within thirty (30) days from the date of receipt of the application.

(2) Unless otherwise established, the date of such approval shall be regarded as the date of designation as an orphan medicinal product in Tanzania.

14.-(1) The Authority shall inform the Applicant on the outcome of the application in writing within seven (7) days after the decision has been made.

(2) The written notice shall inform the Applicant of the requirements for maintaining orphan designation and measures to be taken to facilitate attainment of marketing authorization for the respective medicinal product.

(3) The date of notification shall mark the beginning of the scientific assessment of the application to establish the quality, safety and efficacy of the respective medicinal product.

Refusal to grant orphan designation

15. The Authority shall refuse to grant a request for orphan medicine designation in case of any of the following conditions:
(a) the medicinal product is not intended for a rare disease or condition because:
(i) there is insufficient evidence to support the estimate that the medicinal product is intended for treatment of a disease or condition in fewer than 25,000 people in Tanzania mainland;
(ii) where the medicinal product is intended for prevention, diagnosis or treatment of a disease or condition affecting 25,000 or more

people in Tanzania, the Applicant has failed to demonstrate that there is no reasonable expectation that cost of bringing the product into the market will be recovered from sales of the medicine for such disease or condition in Tanzania;

(b) there is insufficient information about the medicine, or the disease or condition for which it is intended, to establish a medically plausible basis for expecting the medicine to be effective in the prevention, diagnosis, or treatment of that disease or condition;

(c) the medicine is otherwise the same as an already approved medicine for the same rare disease or condition and the Applicant has not submitted a medically plausible hypothesis for the possible clinical superiority of the subsequent medicinal product; and

(d) if the request for designation contains an untrue statement of material fact or omits material information or if the request is otherwise ineligible under this part.

Publication of orphan medicine designations

16. The Authority shall update a publicly available cumulative register of all medicines designated as orphan medicines as provided for in the Second Schedule of these Regulations. The register shall contain the following information:

(a) the name and address of the Applicant;

(b) the generic name and trade name, if any, or, if neither is available, the chemical name or a meaningful descriptive name of the medicine;

(c) the date of the granting of an orphan designation;

(d) the designated use in the rare disease or condition; and

(e) the date that the medicine will no longer maintain the designation.

Cancellation of orphan medicine designation

17. The Authority may revoke orphan-medicine designation for any medicinal product if it is satisfied that:

(a) the request for designation contained an untrue statement of material fact or;

(b) the request for designation omitted material

information required to facilitate informed decision for designation; or

(c) it is found out that the medicine had not been eligible for orphan medicine designation at the time of submission of the request.

## PART IV
## MARKETING AUTHORIZATION

Procedure for Marketing Authorization

18. The application for registration of a designated orphan medicinal product shall be granted marketing authorization after completion of the scientific review and fulfillment of the conditions of registration of medicinal products in Tanzania as specified under the Act.

Role of the Authority

19.-(1) The Authority shall expedite the review of the application in collaborative and interactive manner with the Applicant to ensure that approval is granted within a period of not more than two (2) months from the date of orphan medicinal product designation.

(2) In case the application is not approved within prescribed time, consideration for extension of time for review shall be agreed by the Applicant and the Authority.

Inclusion in the list of registered medicines

20. Upon approval, the product shall be included in the list of registered medicinal products in the format prescribed in section 53 of the Act. Special identification shall be used to differentiate orphan medicines from the products approved through normal procedures.

Scheduling of registered orphan medicines

21.-(1) The new chemical entities for orphan medicines in which the active moiety is a principal constituent, shall be included in the Schedule for Prescription Only Medicines in the Medicines Scheduling Regulations in force.

(2) Notwithstanding sub regulation (1) regardless of previous scheduling status, prior approved molecules that are approved as orphan medicines shall be designated as Prescription Only Medicines.

Scope of orphan medicines

22.-(1) The marketing authorization granted for an orphan medicinal product shall cover only those therapeutic indications which fulfill the criteria set out in these Regulations.

(2) Without prejudice to the provision under sub

regulation (1) of this regulation, the Applicant may apply for a separate marketing authorization for other indications outside the scope of these Regulations.

Maintenance of registration and designation

23. Medicinal products granted marketing authorization as orphan designation shall be valid for a maximum period of two (2) years from the date of registration and shall be renewable upon submission of an application for renewal.

Renewal of registration

24.-(1) All applications for renewal of orphan medicines shall be treated in the same manner as for any other medicinal product except for fees and charges as prescribed in these Regulations.

(3) Applicants for renewal of orphan medicines shall submit to the Authority information to demonstrate that the respective product(s) are still subject to the criteria for orphan designation.

## PART V
## INCENTIVES

Application fees

25. No application fees shall be charged by the Authority for designation and subsequent marketing authorization of orphan medicines.

Exemption of fees

26. Medicinal products approved as orphan medicines shall not be eligible for payment of annual retention fees as well as fees for renewal of registration until after the designation has ended.

Fast track assessment of applications

27. Applications for marketing authorization of orphan medicinal products shall be reviewed and concluded within two (2) months from the date of orphan designation.

Request for additional data

28.-(1) The Authority shall use any possible collaborative approach and real-time communications to Applicants on matters pertaining to pending applications in order to facilitate the timely approval of such applications.

(2) Any responses to questions arising from any stage of the assessment shall be reviewed by the Authority within five (5) days from the date of receipt and Applicants shall be notified on the outcome immediately.

Failure to provide additional data

29.-(1) Where an Applicant fails to provide adequate responses within specified time, the application may be ceased or rescinded from consideration for the designation and/or subsequent marketing authorization.

(2) Any ceased or rescinded application may, upon resubmission and fulfillment of conditions for designation and registration shall without prejudice to the generality of sub-regulation (1) be granted marketing authorization as an orphan medicinal product.

Assistance in compliance with regulatory requirements

30.-(1) Companies developing orphan medicinal substances or small innovative companies with no prior experience in regulatory submissions shall be eligible for technical assistance from the Authority with a view to facilitate compliance with regulatory requirements before and after registration of their medicinal products.

(2) Experienced and large scale companies, upon need shall be eligible to incentives as specified in these Regulations.

Other regulations

31. These Regulations shall be read together with other regulations in force in relation, but not limited to control of registration, fees and charges, importation and any other regulations as may be made under the Act.

Offences

32. Any person who contravenes the provisions of these Regulations shall be guilty of an offence and upon conviction shall be fined or sentenced as prescribed under the Act.

Appeals

33. Any person aggrieved by the decision of the Authority may appeal in accordance with the procedure as provided for under the Act.

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SCHEDULES

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FIRST SCHEDULE

*(Made under Regulation 11(b)*

APPLICATION FORM FOR DESIGNATION OF ORPHAN MEDICINAL PRODUCTS

| | |
|---|---|
| Application Number | Official use only |
| Date of submission of the application | Official use only |
| 1.0 PARTICULARS OF THE PRODUCT | |
| 1.1 | Type of the medicinal product application<br>New<br>Generic<br>Renewal*<br>* If variation has been made, information supporting the changes should be submitted. See variation guidelines for registered medicinal products. |
| 1.2 | Proprietary Name |
| 1.3 | International Non-proprietary Name (INN) of the Active Pharmaceutical Ingredient (API) |
| 1.4 | Strength of Active Pharmaceutical Ingredient (API) per unit dosage form: |
| 1.5 | Name and address (physical and postal) of Applicant and Local Technical Representative |
| 1.5.1 | Name and address (physical and postal) of Applicant |
| (Company) Name:<br>Address:<br>Country:<br>Telephone:<br>Telefax:<br>E-Mail: | |
| 1.5.2 | Name and address (physical and postal) of Local Technical Representative |
| (Company) Name:<br>Address:<br>Country:<br>Telephone:<br>Telefax:<br>E-Mail: | |
| 1.6 | Pharmaceutical Dosage form* and route of administration*<br>* List of standard terms for dosage forms and routes of administration is available on Guidelines on List of Standard Terms for Pharmaceutical Dosage Forms and Routes of Administration. |
| 1.6.1 | Dosage form: |
| 1.6.2 | Route(s) of administration (use current list of standard terms) |
| 1.7 | Packing/pack size: |
| 1.8 | Visual description<br>(Add as many rows as necessary) |
| 1.9 | Proposed shelf life (in months): |
| 1.9.1 | Proposed shelf life (after reconstitution or dilution): |

| | |
|---|---|
| 1.9.2 | Proposed shelf life (after first opening container): |
| 1.9.3 | Proposed storage conditions: |
| 1.9.4 | Proposed storage conditions after first opening: |
| 1.10 | Justification for Orphan medicinal product designation |
| 1.10.1 | *Provide detailed justification for your application for inclusion of the product into the list of Orphan medicinal products in Tanzania (attach separate sheets);* |
| 1.11 | Name(s) and complete physical address(es) of the manufacturer(s) |
| 1.11.1 | Name(s) and physical address (es) of the manufacturing site of the finished pharmaceutical product (FPP), including the final product release if different from the manufacturer. Alternative sites should also be declared here.<br>All manufacturing sites involved in the manufacturing process of each step of the finished product, stating the role of each including quality control / in-process testing sites should be listed.<br>(Add as many rows as necessary |
| Name:<br>Company name:<br>Address:<br>Country:<br>Telephone:<br>Telefax:<br>E-Mail: | |
| 1.11.2 | Name(s) and physical address(es) of the manufacturer(s) of the active pharmaceutical ingredient(s) (API)<br>(Add as many rows as necessary)<br>All manufacturing sites involved in the manufacturing process of each source of active substance, including quality control / in-process testing sites should be listed. |
| Name:<br>Company name:<br>Address:<br>Country:<br>Telephone:<br>Telefax:<br>E-Mail: | |
| 1.12 | Qualitative and Quantitative composition of the active substance(s) and excipient(s)<br>A note should be given as to which quantity the composition refers (e.g. 1 capsule). |

| Name of active ingredient(s)* | Quantity / dosage unit | Unit of measure | Reference/ monograph standard |
|---|---|---|---|
| 1. | | | |
| 2. | | | |
| e.t.c | | | |
| Name of excipient(s) | | | |
| 1. | | | |
| 2. | | | |
| e.t.c | | | |

Note: * Only one name for each substance should be given in the following order of priority: INN**, Pharmacopoeia, common name, scientific name

** The active substance should be declared by its recommended INN, accompanied by its salt or hydrate form if relevant.

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| Details of averages should not be included in the formulation columns but should be stated below:<br>- Active substance(s):<br>- Excipient(s): |
| 2.0 DECLARATION BY AN APPLICANT |
| I, the undersigned certify that all the information in this form and accompanying documentation is correct, complete and true to the best of my knowledge.<br><br>Name: ……..…….<br>Position in the company:……<br>Signature: ……..……<br>Date:……..<br>Official stamp:……..<br><br>* Note: If fees have been paid, attach proof of payment |

SECOND SCHEDULE

*(Made under Regulation 16)*

LIST OF PRODUCTS DESIGNATED AS ORPHAN MEDICINAL PRODUCTS

| Ref No. | Brand name | Active Ingredient | Dosage form and Strength | Indications | Applicants name and address | Manufacturer's name and address | Pack size | Designation date |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | |
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| | | | | | | | | |

Dodoma,
22 June, 2018

UMMY A. MWALIMU
*Minister for Health, Community Development, Gender, Elderly and Children*