# MINISTRY OF HEALTH

## REGULATION No. 17
## of 19 April 2001
## on the requirements to the documentation for marketing authorization of medicinal products

## Chapter I
GENERAL PROVISIONS

**Article 1.** This Regulation specifies the requirements to the documentation, which shall be submitted for marketing authorization of proprietary and pharmaceutically equivalent medicinal products, manufactured in the country or abroad.

**Article 2.** Documentation for marketing authorization of medicinal products, variation and renewal of marketing authorization shall be presented in Bulgarian, English or Russian language.

## Chapter II
MANDATORY DATA IN THE DOCUMENTATION FOR MARKETING AUTHORIZATION OF MEDICINAL PRODUCTS

**Article 3.** (**1**) In order to obtain marketing authorization of proprietary medicinal products the manufacturer or an authorized representative of the manufacturer shall submit to the Bulgarian Drug Agency (BDA) an application (three copies required) for marketing authorization in the form presented in Annex 1.

(**2**) Together with the application pursuant to paragraph 1 a dossier copy of the medicinal product shall be submitted, including:

1. Administrative data, according to Annex 2;
2. Chemical and pharmaceutical data, according to Annex 3 or 3.1;
3. Toxico-pharmacological data, according to Annex 4;
4. Clinical data, according to Annex 5.

(**3**) When the application for marketing authorization is submitted by virtue of point 3 of Article 33 (1) of the Act on Drugs and Pharmacies in Human Medicine (ADPHM), chemical and pharmaceutical data are not required.

(**4**) When the application for marketing authorization is submitted by virtue of point 1 or 2 of Article 33 (1) of the ADPHM, data demonstrating the relevant variation should be presented in the toxico-pharmacological or clinical part of the dossier.

**Article 4.** In order to obtain marketing authorization of medicinal products, authorized in the European Community through Centralized procedure, the persons specified

in Article 3 (1) shall submit to the BDA an application (three copies required) for marketing authorization in the form presented in Annex 1.

(**2**) Together with the application pursuant to paragraph 1 a dossier copy of the medicinal product shall be submitted, including:

1. Administrative data, according to Annex 2.1;
2. Chemical and pharmaceutical data, according to Annex 3 or 3.1;
3. Contents of the toxico-pharmacological and clinical parts of the documentation.

**Article 5.** (**1**) In order to obtain marketing authorization of pharmaceutically equivalent medicinal products, the persons specified in Article 3 (1) shall submit to the BDA an application (three copies required) for marketing authorization in the form presented in Annex 1.

(**2**) Together with the application pursuant to paragraph 1 a dossier copy of the medicinal product shall be submitted, including:

1. Administrative data, according to Annex 2;
2. Chemical and pharmaceutical data, according to Annex 3 or 3.1;
3. Data for equivalence, according to Annex 6.

**Article 6.** In order to obtain marketing authorization of medicinal products based on an established prescription, documents specified in Article 5 (1) and point 1 and 2 of Article 5 (2) shall be submitted.

**Article 7.** In order to obtain marketing authorization of herbal medicinal products the persons specified in Article3 (1) shall submit to the BDA an application (three copies required) for marketing authorization in the form presented in Annex 1.

(**2**) Together with the application specified in paragraph 1 a dossier copy of the medicinal product shall be submitted, including

1. Administrative data, according to Annex 2;
2. Chemical and pharmaceutical data, according to Annex 3 or 3.2;
3. Toxico-pharmacological data, according to Annex 4 – for active substances, for which there are no scientific publications concerning their toxico-pharmacological data;
4. Summarised and updated bibliographic data about the clinical use of the active substance;
5. For a new combination of known active substances, assessment of the advantages of the proposed combination in relation to risk/benefit ratio shall be submitted.

(**3**) For herbal medicinal products with indications in different therapeutical area, as well as for new substance, clinical data according to Annex 5 shall be submitted.

**Article 8.** (**1**) In order to obtain marketing authorization of homeopathic medicinal products the persons specified in Article 3 (1) shall submit to the BDA an application (three copies required) for marketing authorization in the form presented in Annex 1.1.

(**2**) Together with the application specified in paragraph 1 a dossier copy of the medicinal product shall be submitted, including:

1. Administrative data, according to Annex 2.2;
2. Chemical and pharmaceutical data, according to Annex 3.3;

(**3**) For homeopatic medicinal products, designed for routes of administration other than oral and external, which have certain therapeutic indications or contain dilution less than 1/10 000 of the mother tincture (more than $1/100^{th}$ of the smallest dose used in allopathic therapy), a documentation for marketing authorization of medicinal products shall be submitted.

**Article 9.** (**1**) Variations to the terms of marketing authorization of medicinal products shall be type I variations or type II variations. Type II variations shall be considered all substantial changes in the data specified in Article 3 (2).

(**2**) Type I variations shall be all changes other than those referred to in paragraph 1, which are specified in Annex 1.2.

(**3**) For type I and II variations to marketing authorization of medicinal products the persons, specified in Article 3 (1) shall submit to the BDA an application (three copies required) in the form presented in Annex 1.2, administrative data, according to Annex 2.3 and relevant to the respective type of variation documentation.

(**4**) Urgent safety restrictions, undertaken by the marketing authorization holder or required by the BDA are followed by type II variation procedure to the marketing authorization.

(**5**) For variation to marketing authorization of medicinal products, authorized in the European Community through the Centralized procedure, besides the documents according to paragraph 3 or 4, the persons specified in Article 3 (1) shall submit to the BDA the Decision of the EU Commission and the CPMP Assessment report for the relevant variation or notification for changes in the marketing authorization.

**Article 10.** (**1**) For renewal of marketing authorization according to Article 31 (1) of the ADPHM the persons, specified in Article 3 (1) shall submit to the BDA an application (three copies required) in the form presented in Annex 1.3, administrative data, according to Annex 2.4, periodic safety update report in the form according to Annex 7 and supplementary information, if necessary.

(**2**) For renewal of marketing authorization of medicinal products according to Article 6, Article 7 and Article 8, except these specified in Article 7 (3) and Article 8 (3), the persons specified in Article 3 (1) shall submit to the BDA a three copy application in the form, presented in Annex 1.3 and administrative data, according to Annex 2.4, point I A, I B I and I B II.

**Article 11.** (**1**) After granting marketing authorization the persons, specified in Article 3 (1) shall be obliged to commission medical specialists to gather and assess data for observed adverse reactions, which shall be submitted to the BDA, as follows:

1. serious adverse reactions, occurring in the country - within 15 calendar days;

2. serious and unexpected adverse reactions, occurring out of the country - within 15 calendar days;

3. all other adverse reactions - within the frames of periodic safety update reports pursuant to in point 2 of Article 30a (1) of the ADPHM in the form, according to Annex 7.

(**2**) When requested by the BDA the persons, specified in Article 3 (1) shall submit additional information, including sales information, necessary for evaluation of the risk and the benefit associated with the medicinal product use.

## TRANSITIONAL PROVISIONS

§ 1. For the purpose of this Regulation:

1. *Centralized procedure* is a procedure for granting an authorization to place a medicinal product on the Common market of the European Community based on an application submitted to the European Agency for the Evaluation of Medicinal Products (EMEA) and expert assessment, approved by the Committee for Proprietary Medicinal Products (CPMP).

2. *Medicinal products based on an established prescription* are medicinal products, manufactured on the base of established and commonly used in the medicinal practice prescriptions, with historically proven safety and efficacy. They shall not be prepared in pharmacies, but by a manufacturer of medicinal products with manufacturing authorization in accordance with Chapter II of the ADPHM.

3. *Herbal medicinal products* are medicinal products, which consist of herbal drugs and/or herbal drug preparations as active substances.

4. *Herbal drugs* are plants or parts of plants in unprocessed state, used for medicinal or pharmaceutical purposes.

5. *Herbal preparation* are comminuted or powdered herbal drugs, extracts, tinctures, fatty or essential oils, expressed juices, processed resins or gums, manufactured by herbal drugs and preparations by fractionation, purification or concentration.

6. *New substance* is a substance, which is not contained in any medicinal product authorized in Bulgaria.

7. *Urgent safety restrictions* are interim changes to product information by the marketing authorization holder restricting the indication(s), and/or dosage of the medicinal product, or adding contra-indications, and/or warnings due to new information bearing on the safe use of the product.

8. *Unexpected adverse reaction* means an adverse reaction, the nature, severity or outcome of which is not consistent with the summary of product characteristics.

9. *Therapeutic equivalence* is available when the medicinal products contain the same active substance(s) and have the same clinical efficacy and safety.

*10. Biological equivalence (bioequivalence)* is available when the medicinal products are in the same dosage form, in which there is no substantial differences in the degree and rate of absorption after administration of the active substance in the same molar dose and under equal conditions.

## FINAL PROVISION

§ **2**. This Regulation is issued in pursuance of Article 18 (2) of the Act on Drugs and Pharmacies in Human Medicine.

Minister: I. Semerdjiev