

INFORMATION on completing the preclinical study (PS) report

The PS reports shall be completed by the applicant (registration certificate holder) in Ukrainian based on the data provided in registration dossier.

Item 1 of the PS report shall indicate the name of medicinal product (registration certificate №, if any), for which the preclinical study reports has been submitted. For registered medicinal products the name shall correspond to the name in registration certificate, as well as the type of medicinal product according to which the registration has been conducted or is planned. Subitem 2, item 1 shall indicate whether the pre-clinical studies have been conducted. If no, please specify why PS has not been conducted.

Item 2 shall specify the results of preclinical study of pharmacological properties of medicinal product, which prove its effectiveness in view of intended use in humans. Pharmacological studies include primary pharmacodynamics, secondary pharmacodynamics, safety pharmacology, and pharmacodynamic interactions studies. This item shall specify the conditions of study (in vitro, in vivo), species of animals, experimental model of disease, studied doses, routes of administration, and results of studies expressed in quantitative terms (e.g. dose-effect and/or time-effect curves, etc.). The results of experiment shall be clearly stated and their statistical validity proven.

Subitems 1, 2 shall indicate the results of primary and secondary pharmacodynamics study of medicinal product, describing its general pharmacological action and the adverse reactions occurred.

Subitem 3 shall specify the results of safety pharmacology study which demonstrate the effect of medicinal product under investigation on vital functions of laboratory animals: cardiovascular, respiratory and central nervous system. The potential effect of medicinal product on urinary system, autonomic nervous system, gastrointestinal tract and other systems (musculoskeletal, endocrine, immune) shall be further specified.

Subitem 4 shall indicate the results of pharmacodynamic interactions study showing the effect of one medicinal product on pharmacological activity of another one at the level of receptors or mediators, if there is a constant concentration of medicinal product in plasma.

Item 3 shall specify the results of pharmacokinetic studies, which include the analysis of all processes occurring with active substance and its metabolites within the organism, and cover study of absorption, distribution, biotransformation (metabolism) and excretion of these active substances. Also species of animal models, doses studied, route and frequency of administration (single or repeated) of medicinal product shall be indicated. The results of experiment shall be clearly stated and their statistical validity proven.

Item 4 shall specify the results of toxicity studies regarding the potential toxicity of medicinal product, risk to health or undesirable toxicity that may occur during its use in human in compliance with the recommended conditions of use.

Subitem 1 shall specify the results of single dose toxicity studies, including qualitative and quantitative analyses of toxic manifestations, which may result from a single administration of active substance, contained in medicinal product in such proportions and physico-chemical state as in the finished medicinal product. In addition, information shall be provided on the species of animals studied, doses, routes of administration, etc.

Subitem 2 shall specify the results of repeated (multidose) toxicity studies that reveal any physiological and/or anatomo-pathological changes induced by repeated administration of active substance or combination of active substances, and determine how these changes are related to dosage. This subitem shall also specify species of the animals studied, doses, routes of administration, duration of studies, etc.

Depending on the indications for use of medicinal product, it may be necessary to indicate the results of additional studies - studies in immature (juvenile) animals.

Subitem 3 shall indicate the results of genotoxicity study, namely reveal damages that active substance may cause in the genetic material of individuals (in vivo) or cells (in vitro). The standard test battery for genotoxicity includes a test for gene mutation in bacteria, in vitro test with cytogenetic evaluation of chromosomal damage with mammalian cells, or in vitro gene mutation test in mouse lymphoma cells, in vivo test for chromosomal damage in rodent hematopoietic cells.

Subitem 4 shall indicate the results of carcinogenicity study of medicinal product, as well as species of the animals studied, doses, routes of administration and duration of such studies (long-term, short-term).

Subitem 5 shall state the results of study of the medicinal product effect on reproductive function of adult males and females, its toxic and teratogenic effect on offspring at all stages of development from conception to sexual maturity, as well as latent effects when the medicinal product under investigation has been administered to treat female during pregnancy. Information shall also be provided on species of the animals studied, doses, routes of administration, duration of studies, etc.

Subitem 6 shall specify the results of local tolerance test demonstrating the local action of medicinal product (active substance and excipients) at sites in the body, which may come into contact with the medicinal product as a result

of its administration in clinical use. Local tolerance tests shall be conducted with the medicinal product being developed for human use.

In the case of chemicals applied to skin (e.g. dermal/cutaneous, rectal, vaginal), this subitem shall indicate the results of study of their sensitizing potential.

Subitem 7 shall indicate the results of study of antigenic properties of medicinal product (antibody production), its immunotoxicity, mechanism of action, drug dependence, toxicity of metabolites and impurities. Information shall also be provided on species of the animals studied, doses, routes of administration, duration of studies, etc.

Item 5 shall provide a general conclusion on preclinical study of medicinal product, including the results of all preclinical studies carried out at the stage of development of this product.

{Procedure amended by new annex 31 according to MoH Ukraine Order [№ 1528 of 27.06.2019](#) }