PHV-3 Non-interventional post-authorisation safety studies of human medicinal products

This guideline supersedes guideline PHV-3, version 1 as of September 16 2008

The guideline provides a more detailed definitions of terms, specifies the conditions governing the implementation, provision of information, and documents to the State Institute for Drug Control (SÚKL) in the sphere of non-interventional post-authorisation safety studies (NPSB) of human medicinal products which are fully or partially sponsored by the pharmaceutical industry or organisations and individuals supported by the pharmaceutical industry.

The purpose of this guideline is to facilitate the distinction of NPSB from clinical trials, other types of studies and marketing activities of Marketing Authorisation Holders. It, moreover, establishes the procedure of provision of information on active NPSB to SÚKL with the aim to facilitate and increase the effectiveness of pharmacovigilance procedures.

NPSB represent an active pharmacovigilance tool for the collection of valid data and their conduct substantially contributes to the evaluation of the safety profile of medicinal products under the conditions of common practice.

Related regulations:

- Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (Act on Pharmaceuticals), as amended;
- Decree No 228 /2008 Coll., on the marketing authorisation of medicinal products (hereinafter referred to as the "Decree");
- Volume 9A of The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Human Use

Powers by:
Section 92, paragraph 12 of the Act
Section 17 of the Decree

Abbreviations:

SPC	Summary of the Product Characteristics, as defined by the Act on Pharmaceuticals
NPSB Registry	The registry of non-interventional post-authorisation safety studies as referred to in this guideline

1. Definition of terms

Post-authorisation safety study (Section 3, paragraph 7 of the Act)
For the purposes of this Act, a post-authorisation safety study shall mean a pharmacoepidemiological study or a clinical trial carried out in compliance with the terms of the marketing authorisation, conducted with the aim of identifying or quantifying a safety hazard relating to an authorised medicinal product.

Research plan
Each study has to have its research plan. The mandatory particulars of the research plan have not been defined, yet its contents and form must clearly specify the method of conduct of the study. The compilation of the plan should be consistent with international rules and standards, examples of which are provided under chapter 4 of this guideline.

Non-interventional post-authorisation safety studies
These represent a sub-group of post-authorisation safety studies, and are covered by this guideline. A "Non-intervention post-authorisation safety study" is a term reserved solely for such studies, which meet **all of the following** conditions:

1. The purpose of the study is to identify or quantify a safety risk in respect of an authorised medicinal product.
2. The study uses only authorised medicinal products.
3. The conditions of use of the medicinal products in the study are fully consistent with the concerned, currently effective SPCs. Any amendments to the SPCs or other regulatory measures relevant to the safe use of products must be forthwith reflected also in the conducted studies.
4. All of the medicinal products used in the study must be already marketed in the Czech Republic and be available in the usual distribution network.
5. Medicinal products are prescribed and dispensed in a normal way, i.e. prescribed by the doctor and dispensed on medical prescription by the pharmacist. Promotional samples may never be used.
6. Medicinal products must not be provided free of charge or with a discount compared to their usual availability on the market. This applies also to the amounts of supplementary payments made by patients in pharmacies.
7. The selection of patients must not be in any way influenced in advance and must remain the sole discretion of the doctor within the scope of common practice. In the course of the study, the doctor must observe the research plan and the approved SPCs.

8. The remuneration for the doctor or the healthcare facility must not be an incentive for the inclusion of patients in the study, i.e. it may cover, at the maximum, the administrative costs and overhead (incl. compensation of the working hours of the involved personnel) associated with the collection of data and reporting of adverse reactions. This applies to all forms of compensations, financial as well as others.
9. The patient will not undergo any diagnostic or therapeutic procedures which would be motivated solely by the patient's inclusion in the study and would be hence carried out as an "extra", exceeding the scope of usual medical and health care.
10. Any diagnostic and therapeutic procedures conducted in the patients included by the doctor in the study must be covered only in the usual manner, i.e. without any support of the organiser of the study. Diagnostic procedures recommended by the SPC which are not sufficiently conducted in practice and are of relevance for the monitoring of safety of the therapy shall form an exception.

Studies which do not meet all of the 10 above-mentioned conditions cannot be labelled as "non-interventional post-authorisation safety studies".

A study which is labelled as "retrospective" may only use data which have already been recorded on data media (incl. paper), before the first contact of the organiser of the concerned study or as representative thereof and the doctor.

2. Method of informing SÚKL

The scope of information and method of informing SÚKL is in the case of NPSB similar to any other non-interventional post-authorisation study and is governed by guideline UST–35. Like in any other non-interventional post-authorisation studies NPSB are governed by the Decree which imposes upon the Marketing Authorisation Holder the obligation to inform the Institute in electronic format about the intention to carry out a non-intervention al post-authorisation safety study and to provide the following data:

- Name(s), surname and place of business of the Marketing Authorisation Holder where a natural person is concerned, or the business name and registered office of the Marketing Authorisation Holder where a legal person is concerned;
- Identification of the product to be the subject of the study, by means of the code allocated to the product by the Institute (Section 32, paragraph 5 of the Act refers);
- Title of the study;
- Study identification number, under which all documents of the Marketing Authorisation Holder are maintained;
- The purpose, design, blinding, scope, and endpoints of the study;
- Study start date, expected end dates of data collection, completion of analyses and submission of the final report.

All relevant NPSB outcomes *(i.e. including negative findings)* must be stated in the Periodic Safety Update Report for the product (PSUR – section "Studies"). Where a quantitatively or qualitatively new risk is identified, the Marketing Authorisation Holder shall be obliged to forthwith notify SÚKL to this effect and to adopt adequate measures to minimise the risk. Suspected adverse reactions to the medicinal product monitored by NPSB shall be, for the purposes of the pharmacovigilance system, considered as spontaneous reports.

Relevant forms for the notification of non-interventional post-authorisation studies and their completion are available from www.sukl.cz, Reports for SÚKL section. Upon form completion, the person notifying the study, i.e. the competent person of the Marketing Authorisation Holder or an agent thereof, shall send the notification with their certified electronic signature.

The form for notification of non-interventional post-authorisation studies and its completion (start-form)

Information on the medicinal product

SÚKL code
Complete the SÚKL code in the format 702 or 0000702.
Once the code is entered, the form will be automatically loaded with other identification data of the medicinal product and of the Marketing Authorisation Holder.
If the study is conducted for more than one medicinal product, the form enables the entry of other codes by repeating the entry procedure.

Information on the study

Type of study – please select one of the options provided

Then complete the **study title, Study ID under which the holder's study-related documents are maintained, purpose of the study, and description of the study** (e.g. quantitative research, questionnaire method - (Face to Face or other), telephone research)**.**

Dates

Complete the **Study start date, Expected data collection closing date, Expected analyses completion date, and Expected final report submission date** in the dd.mm.yyyy format.

Once the form is fully completed, the electronic signature of the notifying person inserted, and the form is posted, the information you have entered will be loaded to the SÚKL database and a new page will come up - "Confirmation of receipt of data regarding a non-interventional post-authorisation study". The confirmation will give the essential data of your notification and a **SÚKL ID** (identifier) will be generated to be used for the Study completion notification form later on. Your study will be also maintained under this ID in the SÚKL Registry.

Non-interventional post-authorisation study completion notification form (end-form)

This form is intended for study completion notification which has to be made within 150 days of the study completion date.

SÚKL identifier

Enter the **SÚKL identifier** (ID) generated upon study start notification.
Once the identifier is inserted, data entered into the system upon study start notification will be generated.

Date

Complete the **study completion date** and attach the **final report** in pdf, doc, xml format.

Study site and reimbursement of costs

- Enter the **Identification number of the site representative** (IČPP) or **Identification number of the site** (IČP);
- Enter the **name and surname of the doctor responsible for the study conduct** in the healthcare facility;
- Enter the **method of reimbursement** of investigator's costs;
- Enter the reimbursement count of investigator's costs.

Complete these fields for individual healthcare facilities or for the investigator. To repeat, press the "Repeat this section" button.

3. Source materials for inspection

The Marketing Authorisation Holder should, for the duration of the study and for at least the period stipulated by legal regulations, keep the following, explicitly identifiable documents:

a) Documents which in detail describe the study design and method of conduct, including the organisation of data collection and evaluation thereof (research plan, project documentation, etc.);
b) Documents containing data obtained from the study (e.g. questionnaires, adverse drug reaction reports, etc.);
c) Documentation of the performed data analysis, study results;
d) Study progress and final reports;
e) Publications and promotional materials used during the study and those reflecting study conclusions.

Where there is a reasonable suspicion that the conditions of conduct of NPSB described in this guideline have been breached, the following source materials may be also requested:

f) Study budget with a detailed break-down of costs of individual parts of the study, in particular compensations, gifts and remunerations of persons involved.
g) Contracts concluded by individual entities involved in the conduct of the study thereamongst. If oral contracts only have been concluded, the description of their content signed by the responsible person.

4. Recommended sources of other information

In the preparation and conduct of NPSB, it is advisable to observe the principles of good epidemiological practice published by international epidemiological and pharmacoepidemiological associations. These principles are available from the internet, for example:

- http://www.dundee.ac.uk/iea/GoodPract.htm

- http://www.pharmacoepi.org
- http://www.cioms.ch
- http://www.epiresearch.org