The European Agency for the Evaluation of Medicinal Products
Evaluation of Medicines for Human Use

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COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

NOTE FOR GUIDANCE ON DECLARATION OF STORAGE CONDITIONS: A: IN THE PRODUCT INFORMATION OF MEDICINAL PRODUCTS B: FOR ACTIVE SUBSTANCES

ANNEX TO NOTE FOR GUIDANCE ON STABILITY TESTING OF NEW DRUG SUBSTANCES AND PRODUCTS

ANNEX TO NOTE FOR GUIDANCE ON STABILITY TESTING OF EXISTING ACTIVE SUBSTANCES AND RELATED FINISHED PRODUCTS

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NOTE FOR GUIDANCE ON A. DECLARATION OF STORAGE CONDITIONS IN THE PRODUCT INFORMATION OF MEDICINAL PRODUCTS

1. BACKGROUND

Suitable storage conditions, consistent with those defined in the SPC should be included in the package leaflet and on the product labelling, if appropriate, as stated in Directive 2001/83/EC. The storage conditions for medicinal products should be based on evaluation of the stability studies undertaken on the finished product. The storage conditions for active substances should be based on evaluation of the stability studies undertaken on the active substance. Details of the conditions recommended for these stability studies are included in the relevant CPMP/ICH Guidelines where storage conditions for real time studies were chosen as 25°C/60% RH supported by accelerated conditions and based on the mean kinetic temperature of the various climatic zones in the EU. The mean kinetic temperature includes the annual variations, i.e. lower and higher temperatures during winter and summer seasons. Thus, storage at a continuous temperature of 25°C during real time stability studies covers the actual temperature exposure likely to be encountered under ambient conditions throughout Europe, including real time excursions from 25°C.

2. OBJECTIVE

The purpose of this guidance note is to set out uniform statements on storage conditions for inclusion in the labelling of medicinal products and to define when they apply.

3. SCOPE

This guidance note is intended as an Annex to the stability guidelines and relates to marketing authorisations for all product categories.

4. CORE STORAGE STATEMENTS

The storage conditions must be possible for the user to follow and it is therefore necessary to restrict the statements to those achievable in practice. Results from stability studies, presented at the time of submission, should serve as guidance and there should be a direct linkage between the label statements and the demonstrated stability characteristics of the finished product. The use of terms such as ‘room temperature’ or ‘ambient conditions’ is unacceptable.

Testing conditions where stability has been shown	**Required labelling statement**	**Additional labelling statement*, where relevant**
25°C/60%RH (long term) 40°C/75%RH (accelerated) or 30°C/65%RH (long term) 40°C/75%RH (accelerated)	None***	Do not refrigerate or freeze
25°C/60%RH (long term) 30°C/60 or 65%RH (intermediate) or 30°C/65%RH (long term)	Do not store above 30°C or Store below 30°C	Do not refrigerate or freeze
25°C/60%RH (long term)	Do not store above 25°C or Store below 25°C	Do not refrigerate or freeze
5°C ± 3°C (long term)	Store in a refrigerator or Store and transport refrigerated **** **	Do not freeze
Below zero	Store in a freezer or Store and transport frozen ***** **	

* Depending on the pharmaceutical form and the properties of the product, there may be a risk of deterioration due to physical changes if subjected to low temperatures. Low temperatures may also have an effect on the packaging in certain cases. An additional statement may be necessary to take account of this possibility.

** The SPC and Package Leaflet (PL) should include a reference to the temperature range e.g. (2°C to 8°C)

*** The following SPC and PL statements are required:

This medicinal product does not require any special storage conditions.

**** The stability data generated at 25°C/60%RH (acc) should be taken into account when deciding whether or not transport under refrigeration is necessary. The statement should only be used in exceptional cases.

*****The statement should only be used when critical.

The exact wording of the statements given in the table above will be applied throughout the Community taking into consideration that because of national linguistic and cultural differences, two alternatives are presented for storage below 25°C and below 30°C, respectively, and it is the decision of the competent authority which of these should be used. Any other statements are only acceptable if unavoidable and, in particular, where the core storage statements are documented to be inappropriate. The alternative proposal is to be supported by relevant data and must be realistically achievable in practice.

5. OTHER SPECIFIC STORAGE STATEMENTS

In principle, medicinal products should be packaged in containers that ensure stability and protect the finished product from deterioration. A storage statement should not be used to compensate for inadequate or inferior packaging. Nevertheless, the following statements may be used to emphasise the need for precautions to the patient.

	Storage problem	**Additional labelling statements* depending on the packaging**
1.	Sensitivity to moisture	Keep the container*** tightly closed
2.	Sensitivity to moisture	Store in the original package
3.	Sensitivity to light**	Store in the original package
4.	Sensitivity to light**	Keep container*** in the outer carton

* An explanation for the labelling statement should be given in the package leaflet (e.g. ”in order to protect from light”) and on the outer packaging, where space permits.

** Details of evaluation are included in the CPMP/ICH Guideline on photostability testing.

*** The actual name of the container should be used, e.g. bottle, blister

The exact wording of the above texts will be uniformly applied throughout the Community.

NOTE FOR GUIDANCE ON B. DECLARATION OF STORAGE CONDITIONS FOR ACTIVE SUBSTANCES

The principles elaborated above in relation to standard storage declarations for finished medicinal products should also form the basis for storage declarations of active substances.

For substances to be stored/transported refrigerated or frozen, the temperature range should be included in the labelling.