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

London, 28 January 1998
CPMP/QWP/159/96 corr

COMMITTEE FOR PROPRIETARY MEDICINAL PRODUCTS (CPMP)

NOTE FOR GUIDANCE ON MAXIMUM SHELF-LIFE FOR STERILE PRODUCTS FOR HUMAN USE AFTER FIRST OPENING OR FOLLOWING RECONSTITUTION

DISCUSSION IN THE QUALITY WORKING PARTY (QWP)	June 1995 October 1995 February 1996
TRANSMISSION TO THE CPMP	June 1996
RELEASE FOR CONSULTATION	June 1996
DEADLINE FOR COMMENTS	December 1996
TRANSMISSION TO CPMP	June 1997
RELEASE FOR SECOND PERIOD OF CONSULTATION	June 1997
DEADLINE FOR COMMENTS	September 1997
APPROVAL BY CPMP	January 1998
DATE FOR COMING INTO OPERATION	July 1998

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Switchboard: (+44-171) 418 8400 Fax: (+44-171) 418 8447
E_Mail: mail@emea.eudra.org http://www.eudra.org/emea.html

MAXIMUM SHELF-LIFE FOR STERILE PRODUCTS FOR HUMAN USE AFTER FIRST OPENING OR FOLLOWING RECONSTITUTION

GENERAL STATEMENT:

This guidance applies to all sterile products for human use, with the exception of Radiopharmaceuticals and extemporaneously prepared or modified preparations.

Because it is difficult to predict all the possible conditions under which the product will be opened, diluted, reconstituted and stored, etc., the user is responsible for maintaining the quality of the product that is administered to the patient. In order to help the user in this responsibility, the applicant should conduct appropriate studies and provide the relevant information in the User Information Texts, (e.g. SPC, Package insert, labels) following the examples given in italics below.

The applicant should also take note of the recommendations contained in the European Pharmacopoeia, with respect to storage times and conditions for specific categories of sterile products, once opened.

This guidance relates to the time between opening the product and time of administration to the patient; it takes no account of the duration of the administration process itself.

UNPRESERVED STERILE PRODUCTS

General

Chemical and physical in-use stability has been demonstrated for x hours/days at y ^{o}C.

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbial contamination, the product should be used immediately.

If not used immediately, in-use storage times and conditions are the responsibility of the user.

Specific text for Preparations for Infusion or Injection

Chemical and physical in-use stability has been demonstrated for x hours/days at y ^{o}C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 ^{o}C, unless reconstitution / dilution (etc) has taken place in controlled and validated aseptic conditions

AQUEOUS PRESERVED STERILE PRODUCTS (including antimicrobial preservatives or intrinsically self-preserving)
NON-AQUEOUS, E.G. OILY PREPARATIONS

Chemical and physical in use stability has been demonstrated for x hours/days at y ^{o}C.

From a microbiological point of view, once opened, the product may be stored for a maximum of z days at t ^{o}C. Other in-use storage times and conditions are the responsibility of the user.

The applicant should justify the values of z and t on a case by case basis; z should not normally be greater than 28 days.

