Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Go to: http://www.quest-ce.com/CEP/SecundumArtem/misviewer.do?docId=116221057

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Sterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

Sterility assay

YES

NO

BUD of 30 days, or

months, whichever is

9

30 days

Sterility and microbiological assay

YES

NO

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Nonsterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

BUD of 60 days, or

months, whichever is

9

6 months

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Sterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

Sterility assay

YES

NO

BUD of 30 days, or

months, whichever is

9

30 days

Sterility and microbiological assay

YES

NO

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Nonsterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

BUD of 60 days, or

months, whichever is

9

6 months

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Sterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

Sterility assay

YES

NO

BUD of 30 days, or

months, whichever is

9

30 days

Sterility and microbiological assay

YES

NO

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Nonsterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

BUD of 60 days, or

months, whichever is

9

6 months

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Sterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

Sterility assay

YES

NO

BUD of 30 days, or

months, whichever is

9

30 days

Sterility and microbiological assay

YES

NO

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Nonsterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

BUD of 60 days, or

months, whichever is

9

6 months

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Sterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

Sterility assay

YES

NO

BUD of 30 days, or

months, whichever is

9

30 days

Sterility and microbiological assay

YES

NO

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Nonsterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

BUD of 60 days, or

months, whichever is

9

6 months

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Sterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

Sterility assay

YES

NO

BUD of 30 days, or

months, whichever is

9

30 days

Sterility and microbiological assay

YES

NO

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

Figure 1: Flow chart that can be used for assigning beyond-use dates of nonsterile and sterile compounded preparations.

Nonsterile BUDS

Self

YES

NO

BUD of 25% of time zero expiration date, or

stability testing

YES

NO

BUD of 60 days, or

months, whichever is

9

6 months

BUD of 30 days, or

months, whichever is

24 Hours

45 Days

91.4 +/- 1.9

160 Days

91.4 +/- 1.9

Send this completed form in for CE credit Today!

Please circle the most appropriate answer for each of the following questions. There is only one correct answer per question.

Inquire about commercial CE enrollment opportunities or call Quest Educational Services at 800-331-2004 for more information.

The pharmaceutical compounding by the FDA of drug stability for commercially manufactured dosage forms is different for each drug. Stability studies are intended to help determine if the drug has the same quality and strength as when it was manufactured. Firms must determine the stability of the drug in order to establish a beyond-use date for each weight or amount of drug compound. Stability studies are intended to help determine if the drug has the same quality and strength as when it was manufactured. Firms must determine the stability of the drug in order to establish a beyond-use date for each weight or amount of drug compound.

Criteria for experiment include the following:

1. There is little or no degradation of the active ingredient(s).
2. There is no degradation of the inactive ingredients or the container closure.
3. There is no evidence of microbiological growth.
4. There is no evidence of impurities or degradation products.
5. There is no evidence of any change in the physical properties of the drug product.

Objectives of the study include the following:

1. To determine the stability of the drug product, including its chemical and physical properties, over a specified period of time.
2. To determine the effect of environmental conditions on the stability of the drug product.
3. To establish suitable storage conditions for the drug product.
4. To establish suitable shelf life for the drug product.
5. To determine the stability of the drug product under normal conditions of storage and transport.

In addition to the above objectives, the study should also include the following:

3. The effect of transport and handling conditions on the stability of the drug product.
4. The effect of storage conditions on the stability of the drug product.

The above objectives should be achieved through the following methods:

1. Designing a stability study that is appropriate for the drug product.
2. Selecting an appropriate protocol for the stability study.
3. Conducting a stability study that is appropriate for the drug product.
4. Analyzing the results of the stability study.

The stability study should be conducted in accordance with the following guidelines:

1. The study should be conducted in a manner that is consistent with the requirements of the United States Pharmacopeia (USP).
2. The study should be conducted in a manner that is consistent with the requirements of the National Formulary (NF).
3. The study should be conducted in a manner that is consistent with the requirements of the American Society for Testing and Materials (ASTM).

The above guidelines should be followed in order to ensure that the stability study is conducted in a manner that is consistent with the requirements of the USP, NF, and ASTM.

The stability study should be conducted in a manner that is consistent with the requirements of the USP, NF, and ASTM. The above guidelines should be followed in order to ensure that the stability study is conducted in a manner that is consistent with the requirements of the USP, NF, and ASTM.

The stability study should be conducted in a manner that is consistent with the requirements of the USP, NF, and ASTM. The above guidelines should be followed in order to ensure that the stability study is conducted in a manner that is consistent with the requirements of the USP, NF, and ASTM.

The stability study should be conducted in a manner that is consistent with the requirements of the USP, NF, and ASTM. The above guidelines should be followed in order to ensure that the stability study is conducted in a manner that is consistent with the requirements of the USP, NF, and ASTM.
Drug Stability, Expiration Dates and Beyond-use Dates

The term "drug stability" used by the FDA for drug stability for commercially manufactured dosage forms is defined for each drug substance and its dosage form in the compendia of either the USP (United States Pharmacopeia) or the NF (National Formulary). A typical Stability Protocol includes three phases: study, test, and storage. It is used to design the stability study for each drug substance and its dosage form, and to establish storage requirements for the drug substance in its approved dosage form. From 2 to 3 years, a product's stability must be assured with regard to its chemical and physical properties. Therefore, it is important to determine the influence of each variable on the stability of the drug. The influence of the container and closure, the manufacturing method, and the time of analysis are evaluated throughout the study. The formulation is evaluated in terms of its physical and chemical properties and its compatibility with different materials and conditions of storage and handling.

For pharmaceutical compounding, the General Notice of the USP states: "The label on the container or package of an official preparation packed into a stainless steel or other column containing mobile phases and hydrophobic stationary phases. The method involves subjecting the samples containing the drug and its degradation products to stress testing. The process is completed, then the data is analyzed. A detector is monitored. As each individual "component" or drug is detected, the CSPs are properly stored and are exposed for not more than 90% of the sample interval. Each obtained sample is analyzed and placed into a table format such as Table 1 and Table 2.

Table 2: Stability of terbinafine hydrochloride 25 mg/mL in oral liquid refrigerated at -25°C and stored at room temperature

<table>
<thead>
<tr>
<th>Drug</th>
<th>Stability at -25°C</th>
<th>Stability at Room Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Terbinafine hydrochloride</td>
<td>97.0 (1.0)</td>
<td>92.0 (1.5)</td>
</tr>
<tr>
<td>HPLC peak area %</td>
<td>Similar to the standard curve</td>
<td>Similar to the standard curve</td>
</tr>
</tbody>
</table>

Table 3: Stability of valacyclovir hydrochloride 50 mg/mL in oral liquid refrigerated at -25°C and stored at room temperature

<table>
<thead>
<tr>
<th>Drug</th>
<th>Stability at -25°C</th>
<th>Stability at Room Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valacyclovir hydrochloride</td>
<td>96.8 (2.4)</td>
<td>96.0 (2.5)</td>
</tr>
<tr>
<td>HPLC peak area %</td>
<td>Similar to the standard curve</td>
<td>Similar to the standard curve</td>
</tr>
</tbody>
</table>

Conclusions

Pharmacy error, assay and stability-indicating assays would allow a simple and straightforward method for determining the stability of a drug substance. The tests that are capable of differentiating the intact drug from any degradation products would be most useful. The data presented in this study shows that the CSPs are properly stored and are exposed for not more than 90% of the sample interval. Each obtained sample is analyzed. The compounding processes are under control and that the drug substance is stable under stress testing conditions. The results of this study can be used to guide the stability testing protocols for the drug substance in its approved dosage form. It may be reasonable to consider the data presented for the terbinafine hydrochloride 25 mg/mL and the valacyclovir hydrochloride 50 mg/mL oral liquid products.
DISEASE STABILITY, EXPIRATION DATES AND BEYOND-USE-DATES

The required demonstration by the FDA of drug stability for commercially manufactured dosage forms is different for each type of compound and for each type of formulation. Generally, a compounded preparation shall bear a beyond-use date. The 'beyond-use date' or 'BUD' is the last date on which the product may be administered. The selection of the date is customarily set to 100% and each subsequent data value is interpolated between 14 days and 21 days if the order of magnitude is used. If a sterility testing program is in place, the BUDs listed in Table 2 can be used. The beyond-use date is not later than 6 months.

The stability study is summarized in Table 1. The following information is summarized in Figure 1, a flow chart showing the process of preparing a beyond-use date. A steady state is achieved by allowing the solution to come into equilibrium with the environment. When equilibrium is reached, the solution is sampled weekly for four weeks. The data is transferred to an amber glass bottle where the final vehicle is obtained.

**Example 1: Valacyclovir hydrochloride 50 mg/mL oral liquid**

The valacyclovir hydrochloride 50 mg/mL oral liquid was prepared using the copper and a copper vessel. The copper was used to make the sample in place. If a sterility testing program is in place, the BUDs listed in Table 2 can be used. The beyond-use date is not later than 6 months.

The beyond-use date is not later than the intended duration of therapy. The beyond-use date is not later than 14 days for liquid preparations exposed to cold temperatures and 7-21°C (45-70°F) for oral liquids.

The beyond-use date is not later than the intended duration of therapy. The beyond-use date is not later than 14 days for liquid preparations exposed to cold temperatures and 7-21°C (45-70°F) for oral liquids.

**Conclusion**

For numerous reasons, stability-indicating methods are critical to pharmaceutical development. These methods are used for different purposes depending on the compound under study. The methods are used for different purposes depending on the compound under study. The methods are used for different purposes depending on the compound under study.

**References**


Sterile BUDS

Quality

Expiration

BUD Level

Sterile

30 Days

90 Days

120 Days

Nonsterile BUDS

Quality

Expiration

BUD Level

Nonsterile

30 Days

90 Days

120 Days

Figure 1: Flow chart that can be used for assigning beyond dates of nonsterile and sterile compounded preparations.

Sterile BUDs
- Active ingredient from a manufactured product
- BUD within 30 days of manufacture expiration date
- BUD is only applicable if a manufacturing testing program is in place
- BUD = Beyond use date

Nonsterile BUDs
- Active ingredient from a nonmanufactured product
- BUD within 30 days of being dispensed
- BUD = Beyond use date

Sterility
- Prepared from ingredient
- BUD = Beyond use date
- BUD = Beyond use date

The information in this document is the intellectual property of QUEST Educational Services, Inc. Reproduction in whole or in part is not allowed without the consent of the publisher. The content and opinions of this article are those of the author and are for educational purposes only. The material is based on review of multiple sources of information, it is not assessed at the time of its manufacture.

1. Evaluate test methods used to establish beyond-use dates for a preparation.
2. State when and why the beyond-use date should be assigned.
3. Identify the importance of documentation in the assignment of beyond-use dates.
4. Formulate recommendations for beyond-use date assignment.
5. Assign a default beyond-use date if no data is available, based on USP Chapters <795> and <797>.

Sterile products
- Uses of compounded sterile products
- Uses of compounded nonsterile products

INTRODUCTION

One of the most important activities of a compounding pharmacist is the assignment of a beyond-use date for a compounded preparation. It is essential that the date be sensibly determined from either laboratory testing or using official standards.

GOALS AND OBJECTIVES

After reading and studying the article, the reader will be able to:

1. Evaluate test methods used to establish beyond-use dates for a preparation.
2. State when and why the beyond-use date should be assigned.
3. Identify the importance of documentation in the assignment of beyond-use dates.
4. Formulate recommendations for beyond-use date assignment.
5. Assign a default beyond-use date if no data is available, based on USP Chapters <795> and <797>.

Send this completed form in for CE credit Today!

Please print address clearly below OR offer an address label here if available.

Name ______________________________ ______________________________

City ____________________________ State __________ Zip ______________

Primary State Licensee ______________________________

License No. ______________________________

Phone 1 ( ) ______________ Phone 2 ( ) ______________

Email Address ______________________________

To receive credit, send completed registration form and test answer sheet (original or a photocopy of the page) to: QUEST EDUCATIONAL SERVICES, INC., P.O. BOX 1092, GROTON, CT 06340. One contact hour (0.1 CEU) awarded for a passing grade.

*Please note that QUEST Educational Services, Inc. will not need CE credit approval from any State Board of Pharmacy.

Disclaimer
The content and opinions of this article are those of the author and are for educational purposes only. The material is based on review of multiple sources of information, it is not assessed at the time of its manufacture.

Primary State Licensee ______________________________

License No. ______________________________

Phone 1 ( ) ______________ Phone 2 ( ) ______________

Email Address ______________________________

To receive credit, send completed registration form and test answer sheet (original or a photocopy of the page) to: QUEST EDUCATIONAL SERVICES, INC., P.O. BOX 1092, GROTON, CT 06340. One contact hour (0.1 CEU) awarded for a passing grade.

*Please note that QUEST Educational Services, Inc. will not need CE credit approval from any State Board of Pharmacy.

Figure 1: Flow chart that can be used for assigning beyond dates of nonsterile and sterile compounded preparations.