

International Pharmaceutical Excipients Council Of The Americas



IPEC-Americas Position Paper Conducting Accelerated Stability on Excipients

Current Issue / Event

During the first quarter 2015, several IPEC member companies reported that requests have been received from certain countries for Accelerated Stability (AS) data on excipient products that already have full long term stability study data. These requests have come from regulatory agencies receiving product registrations in those countries or from excipient user companies exporting finished drug formulation into those countries. There have also been requests for ICH long term, intermediate and accelerated stability data¹, and questions regarding differences between storage statements on Safety Data Sheets (SDSs) and product stability documents.

Purpose of Position Paper

IPEC-Americas has prepared this document to establish its position regarding the necessity of such studies or data. This paper does not address new excipients or excipients that are new chemical entities that do not have a history of storage and transporting. To address these please see the IPEC Excipient Stability Program Guide, 2010.

Supporting Background Information for IPEC-Americas Members / Stakeholders

The primary purpose of an excipient stability study is to provide evidence that the excipient continues to meet specifications from the time of completion of its manufacturing to the retest/re-evaluation or expiry date if maintained in an unopened package under the recommended storage conditions. Stability issues occurring subsequent to the opening of the package are the responsibility of the user or any party carrying out re-packaging processes. (See The IPEC Excipient Stability Program Guide, 2010).

ICH Q1A(R2) Stability Testing of New Drug Substances and Products

The scope of the ICH Q1A(R2) Stability Guideline is intended for APIs and/or finished drug products. The ICH guideline was not intended for nor does it include requirements for excipients.

In addition, the ICH Q1A(R2) is not applicable to excipients because:

1. Finished dosage forms are packaged in small containers, usually the largest of which holds no more than a few kilograms. Excipients are generally provided in a range of package sizes, usually significantly larger than those used for finished dosage forms. Excipient packages include bags, drums, supersacks, and bulk isotainers, holding up to several hundred kilograms.

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2. The temperature and humidity conditions referenced in this ICH Guideline are useful for finished goods that are stored on a pharmacy shelf or in the home under room temperature conditions, while excipients are usually stored in warehouses in widely varying temperature and humidity conditions.

The vast majority of excipients have been successfully packaged, stored and transported throughout the world under a variety of temperature and relative humidity (T/RH) conditions. It is the position of IPEC-Americas members that ICH Stability studies would not add any meaningful stability information for these products. The few excipients that are inherently unstable are handled in special packaging or under known (controlled) temperature and/or relative humidity conditions. These excipients require evaluation under these predefined and specified conditions.

IPEC Excipient Stability Program Guide, 2010

As defined in the IPEC Stability Guide, very stable or stable excipients should not require an expiration date; however, a retest date is typical. By their very nature, changes do not occur in very stable or stable excipients so as to cause a risk to the patient; thus these materials do not expire. However, unstable excipients require the manufacturer to determine how to obtain stability data based on sound scientific principles and to define under what conditions these materials do expire.

Exposure to Extreme Environmental Conditions

Although stability testing program conditions do not cover the entire range of environmental conditions to which the packaged excipient may be exposed, the vast majority of excipients have been in commerce for years and have been stored and shipped around the world with few stability issues attributable to transit or warehouse conditions. It is the belief of IPEC-Americas members that the risk for these products being out of specification due to extremes of environmental conditions is very small.

Safety Data Sheets (SDS) Storage Conditions vs Product Storage Information

With regards to differences between storage statements on SDSs and product stability documents, whereas the statements on SDSs are based on the individual chemical ingredients *these results are not intended to reflect supplier based stability studies or historical information*. Storage conditions on an SDS should not be confused with real-time stability. Storage information from the SDS are often based on product environmental, health and safety (EHS) labeling and may contain phrases that are meant to fulfill SDS and EHS labeling requirements for worker occupational safety and health compliance. These phrases (e.g., "Store in a cool, dry place") are provided as standard language from other sources (e.g., the American National Standards Institute in the U.S.). Such terms and language are not connected with any pharmacopeial requirement or product stability testing program.

IPEC-Americas Position

IPEC-Americas position is as follows:

1. If a product is a new chemical entity or has no long term history of storage and transporting, care must be taken to prove that no stability issues arise during the storage and transporting of these new products. It must be established that they can be handled in warehouses and during transportation with much more testing. (See the IPEC Excipient Stability Program Guide, 2010).
2. ICH Stability Guidelines do not apply to excipients. The guidelines set forth in the IPEC Excipient Stability Guide should be used instead.

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3. For stable excipients (based on the development work, the scientific literature, historical data, etc.) stored in an uncontrolled warehouse, the manufacturer should provide stability data to support the claim that the excipient is stable in the marketed packaging under the conditions likely to be encountered.
4. Stable excipients do not normally expire based on known safety issues. If they have retest dates, they should be retested and recertified to determine whether they continue to meet their specifications.
5. For unstable excipients, stability data must be generated based on accepted scientific principles. If accelerated stability studies are run, they should be carried out under controlled storage conditions.
6. Since accelerated stability is used to support long term stability, when long-term stability data is available, accelerated stability is not necessary.
7. It should be clearly communicated to excipient users what long term stability study conditions that the stability study performed by the excipient manufacturer was based on (e.g. uncontrolled conditions, usually those existing in warehouses).
8. Stability testing under extreme environmental conditions may be justified if the excipients have not been in commerce for years and have not been stored and shipped around the world without any reported stability issues. The susceptibility of the product to these types of conditions should be considered in the development of a stability testing program by the excipient manufacturer.
9. Storage conditions on an SDS should not be confused with real-time stability as information in the SDS is meant to fulfill SDS and EHS labeling requirements for worker occupational safety and health compliance, and is not connected with any pharmacopeia terminology, requirement or product stability testing program.
10. If a product is stored in an environmentally uncontrolled warehouse, the stability study samples should be subjected to similar environmentally uncontrolled conditions to get data that relates to the product's stability.

References:

1. ICH Stability Guide: ICH Q1A(R2), Stability Testing of New Drug Substances and Products <http://www.ich.org/products/guidelines/quality/quality-single/article/stability-testing-of-new-drug-substances-and-products.html>
2. IPEC Excipient Stability Program Guide, 2010 – <https://ipecamericas.org/ipec-store>
Member access click here - must be logged in as a member:
<http://ipecamericas.org/content/download-ipec-guidance-documents-here>