Accelerated Stability Assessment Study for Nicorette® Lozenge

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Introduction

It is crucial to develop a pharmaceutical product with good stability performance. In order to gain approval from regulatory agency, maintain the quality throughout its shelf life and ensure its efficacy and safety. It is essential to determine which factors affect stability performance during early stage of product development. However, the traditional stability study is very time-consuming and costly as multiple formulations in various packaging options are typically evaluated during product development. It is a lengthy, expensive, labor-intensive and uncertain task for R&D.

In order to improve the product understanding, identify the potential stability trend, select the most cost effective packaging material, predict the product shelf life and reduce the uncertainty and risk during product development, GSK evaluated Accelerated Stability Assessment Program and ASAPprime™ stability modeling software, developed by FreeThin Technology Inc. The accelerated stability data can be collected within two to four weeks and used for shelf life projection, stability trend detection and packaging selection.

ASAPprime™ factors in humidity sensitivity factor (B) into the traditional Arrhenius equation for solid dosage forms. ASAP study is normally conducted in five to six conditions in two weeks. Either potency and/or degradant level can be used to calculate Lشا (isolation frequency). Ea (activation energy) and B (humidity sensitivity factor) using ASAPprime™ stability software. Then, those three constants are used to predict the shelf life of the product, project the stability trend, and select the most cost effective packaging materials.

Objective

To evaluate the accelerated stability assessment program and ASAPprime™ stability software for Nicorette® lozenge

Methods

- Tested samples – Nicorette® peppermint lozenge
- ASAP study
  - Table 1 - Isoconversion points
    - Table 2 - Arrhenius constants
  - Table 3 - Validation of ASAP predicted shelf life

Results

Figure 1 – difference between designed and actual conditions

Figure 2 – Accelerated stability

Figure 3 – Moisture sorption isotherm

Conclusions

- Moisture sorption isotherm indicates a significant moisture uptake (B). High humidity sensitivity factor (B) indicates that the potency of Nicorette® lozenge is highly sensitive to the humidity. The adsorbed moisture disturbances buffer in the lozenge and allows nicotine to dissociate from polyacryltes and convert from ionic nicotine to free nicotine which is known to be volatile and escape along with moisture during storage period.

The single unit container closure system with high barrier function (i.e. hot-lam) and the multiple does container with desiccant are required to protect Nicorette® lozenge from moisture and to achieve the desired shelf life. Validation of ASAPprime™ predicted shelf life could only be achieved when MVTR value of formed blister at given condition was available.

Table 3 – Validation of ASAP predicted shelf life