

THE UNIVERSITY OF ADELAIDE

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Shelf-Life: Designing and Analysing Stability Trials

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BY

ANDREAS KIERMEIER

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Abstract

All pharmaceutical products are required by law to display an expiry date on the packaging. The period between the date of manufacture and expiry date is known as the label shelf-life. The label shelf-life indicates the period of time during which the consumer can expect the product to be safe and effective.

Methods for determining the label shelf-life from stability data are discussed in the guidelines on the evaluation of stability data issued by the International Conference for Harmonization. These methods are limited to data that can be analysed using linear model methods. Furthermore, in the situation where a number of batches are used to determine a label shelf-life, the current regulatory method (unintentionally) penalizes good statistical design. In addition, the label shelf-life obtained this way may not be a reliable guide to the properties of future batches produced under similar conditions.

In this thesis it is shown that the current definition of the label shelf-life may not provide the consumer with the desired level of confidence that the product is safe and effective. This is especially the case when the manufacturer has performed a well designed stability study with many assays. Consequently, a new definition for the label shelf-life is proposed, such that the consumer can be confident that a certain percentage of the product will meet the specification by the expiry date. Several methods for obtaining such a label shelf-life under linear model and generalized linear model assumptions are proposed and evaluated using simulation studies.

The new definition of label shelf-life is extended to allow a label shelf-life to be obtained from stability studies that make use of many batches, such that a proportion of product

over all batches can be assured to meet specifications by the expiry date. Several methods for estimating the label shelf-life in the multi-batch case are proposed and evaluated with the help of simulation studies.

Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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