Veterinary Medicines In-use Shelf-life

What is an in-use shelf-life?

An in-use shelf-life is the time period following the first broaching of a container (for example via a needle entering a bung or the unscrewing of a cap) after which any remaining product in the container should be destroyed. Veterinary medicines, human medicines, and increasingly other types of products such as cosmetics and shampoos specify an in-use shelf-life on their labels.

Why is it necessary to have an in-use shelf-life?

An in-use shelf-life is needed to provide assurance of the appropriate quality of the product throughout its use, thereby helping to ensure the safety and efficacy of the product. A product used outside its in-use shelf-life may have insufficient levels of the active substance and this may lead to inefficacy (or in some cases contribute to the development of resistance), it may contain harmful levels of degradation products, or it may be contaminated with micro-organisms which could be harmful.

For example, multi-dose parenteral (injectable) products, are manufactured to be sterile (complete absence of living organisms) and must remain sterile until first use. However, sterility can no longer be guaranteed as soon as the immediate package is broached. Therefore, in order to ensure that multi-dose injectables remain microbiologically safe to use, the product will contain an antimicrobial preservative (unless the formulation itself is self-preserving) and will be assigned an in-use shelf life.

Why don't all medicines have an in-use shelf-life?

Only products which are susceptible to degradation or contamination after first broaching of the pack carry an in-use shelf-life. For example, micro-organisms will not usually survive in non-aqueous environments. Therefore, for a non-aqueous pour-on product which has been shown not to be prone to degradation when exposed to the atmosphere an in-use shelf-life will not be specified.

Why do so many medicines have a 28 day in-use shelf-life?

The in-use shelf-life specified depends on the product, in particular its physical, chemical and microbiological characteristics. The in-use shelf-life is not always 28 days. It may be less than this, for example if the active substance is prone to degradation following exposure to the atmosphere, or it may be longer than this, for example for a product which is very stable and which will not support the growth of micro-organisms (which can be the case for certain oily/non-aqueous injections).

However, many of the multi-dose parenteral (injectable) products do specify a 28-day maximum in-use shelf-life. The main reason for this is that the EU guideline for veterinary medicines[1] on the "maximum shelf-life for sterile veterinary products after first opening or following reconstitution" indicates that, from a microbiological point of view, for aqueous preserved sterile products and non-aqueous sterile products the in-use shelf-life should not normally exceed 28 days. While these are EU guidelines, the vast majority of UK authorised veterinary medicines were authorised when the UK was a member of the EU, therefore the contents of these guidelines remain relevant and form the basis of the current regulatory framework for veterinary medicines in the UK.

There are a number of injectable products authorised in the UK where the in-use shelf-life exceeds 28 days. In these instances, additional microbial challenge studies beyond those set out in the European Pharmacopoeia will have been conducted and subsequently assessed as acceptable by the appropriate regulatory authorities.

Is it possible to extend an in-use shelf-life?

Marketing Authorisation Holders (the companies who produce the product) can apply to the regulatory authority who approve veterinary medicines, the Veterinary Medicines Directorate, in some circumstances to vary their Marketing Authorisation (the licence) to permit a longer in-use shelf-life. However, there will be significant additional costs involved in generating the data, potentially requiring the investigation into the reformulation of the product to use a different preservative system and consequentially conducting additional clinical studies, in

Addition to the significant costs involved in making the changes to the marketing authorisations on a regional or global basis.

Can smaller pack sizes be produced by companies?

Another option to try to avoid wastage of medicines would be for Marketing Authorisation Holders to produce smaller pack sizes, but again this will involve the company investing in changing the Marketing Authorisation and is likely to involve the need for the generation of further data, with the inevitable additional costs that this involves. In the past for medicines where manufacturers had both large and small pack sizes on the market, a frequent problem that was encountered was that the smaller packs were not purchased and used by vets who were attempting to make savings based on economies of scale. As a result, the smaller pack sizes were discontinued.

Conclusions

Animal health companies are aware of the concerns that veterinary surgeons express regarding the general 28-day upper limit and will continue to consider what steps can be taken based on evolving market demands, including reviewing in-use shelf-life and vial sizes where it is feasible to do so, within the constraints of the issues described in this document.

Reviewed October 2023

References:

1. European Medicines Agency, 'Maximum shelf-life for sterile medicinal products after first opening or following reconstitution' (1999). Available at: https://www.ema.europa.eu/en/maximum-shelf-life-sterile-medicinal-products-after-first-opening-following-reconstitution(Accessed 07/10/22).

What is NOAH? NOAH represents the UK animal health industry. Its aim is to promote the benefits of licensed medicines and solutions for the health and welfare of all animals.

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