Emanation rate studies

Factors which may affect validity of **emanation rate studies**:

- study not conducted in compliance with Good Laboratory Practice (GLP)
- failure to conduct power calculations to determine the required number of replicates
- inadequate sample sizes.

1. Purpose of the study

For the purposes of the prequalification assessment, emanation studies are conducted to investigate the in-use active ingredient (AI) release properties of a spatial emanator product and the impact of temperature on the emanation rate.

The study is intended to characterize the proposed spatial emanator product by means of chemical analysis to determine the retention/release of AI over a time series developed in relation to the intended duration of useful life of the product. The study should be designed to also characterize changes in the rate of release over the intended useful life.

2. Requirement for submission of emanation rate studies

A minimum of one emanation rate study is required for Module 3 submissions.

The emanation rate study must be GLP-compliant.

3. Considerations

3.1 Product test samples

Baseline quality checks should be performed to ensure compliance of samples with the manufacturing release specifications of the product.

Packed, unopen product test samples should be taken for testing from across the five batches which were fully characterized for other Module 3 data generation.

Product test samples should be stored in accordance with the manufacturer recommendations prior to initiating the study.

3.2 Methods for AI determination

Internationally validated methods, for example, CIPAC or equivalent, must be used for the quantification of AI from product samples.

In cases where a new or amended extraction or preparation method is required, an independently validated method should be developed and submitted to support the assessment of AI quantification of samples. New or augmented methods must then be internationally validated for use as the reference method for manufacturing release specifications and other forms of product testing.

3.3 Test method

The tests must be conducted in a controlled environment.

Product test samples should be opened and deployed in a manner representative of the intended directions for use.

AI determinations should be conducted over a time series developed and proposed based on the product design and intended useful life. The number of time points should be selected to ensure that the remaining AI concentration in the reservoir can be characterized over the intended life of the product up to the complete loss of AI or cessation of entomological effect.

For products with a prolonged intended useful life, extrapolation approaches may be used to model the loss of AI from the reservoir based on supporting information which substantiates the continuity of the release rate regardless of reservoir concentration.

For example:

> *For a passive spatial emanator intended to emit AI for up to 1 month, samples should be taken for chemical analysis on days: 0, 1, 3, 5, 10, 15, 20, 25, 30, 35.*
>
> *For an active spatial emanator using an impregnated reservoir intended to emit AI for up to 15 days (assuming 24 hours of use), samples should be taken for chemical analysis on days: 0, 1, 3, 5, 10, 15, 20.*

3.4 Variables

3.4.1 Temperatures

The study should include test arms to investigate the emanation rate at different temperatures. Generally, it is important to characterize the emanation rate at temperatures between 20–50 °C, for example, including test arms of 20, 30, 40 and 50 °C. The intent of this approach is to determine how temperature may impact the emanation rate so as to better characterize the potential useful life of the product in different environmental settings.

For active spatial emanators, it may not be necessary to characterize the emanation rate of the product at all temperatures. A justification with supporting data may be submitted which demonstrates that the emanation rate is not temperature dependent.

3.4.1 Air flow/air exchange

Depending on the product design, manufacturers may need to consider including an investigation of the impact of air flow/air exchange on the emanation rate within the study.

If a single air flow/exchange is selected, justification should be provided.

3.5 Number of replicates

In accordance with the requirements for the analysis of five replicates in each of the five batches, five replicates should be measured at each time point in each arm of the study.

4. Submission of proposed protocols

Considering the variety of potential product designs, applicants are strongly encouraged to submit a PQ200 application with the proposed protocol for the emanation rate study.

5. Related documents

- WHO PQT/VCP Implementation Guidance - IG – Manufacturing release specifications