A STANDARD PROTOCOL for DERIVING and ASSESSMENT of STABILITY

Part 3 – Oral Liquid Medicines (Solutions, Emulsions, Suspensions and Syrups)

EDITION 1

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This document has been produced on behalf of the NHS Pharmaceutical Quality Assurance Committee, the NHS Pharmaceutical Production Committee and the NHS Pharmaceutical Aseptic Services Group by the NHS Pharmaceutical Research and Development Working Group. Membership is shown below.

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A Standard Protocol for Deriving and Assessment of Stability Part 3 – Oral Liquid medicines

1. Scope

This document is intended to cover stability testing of all oral liquid formulations including suspensions, emulsions, solutions and powders for reconstitution as oral solutions. The document should be considered both when setting out to conduct or commission a stability study and also when reviewing stability data in support of procured unlicensed medicines.

2. Introduction

Oral liquid medicines are often prepared or sourced as unlicensed medicines (Specials) or extemporaneously prepared medicines; these are required to meet a special patient need in such circumstances as paediatrics, for those who cannot swallow tablets or where the dose required is not available in solid dosage forms, or for patients with naso-gastric feeding tubes in place.

These products are often ordered in small numbers and may not be well formulated in order to maximise stability or to meet the patient need. Nevertheless they are critical medicines and need to be of a quality suitable to their usage and meet with specifications throughout their shelf life.

As well as chemical and microbiological stability issues there are also other factors to consider such as the stability of a suspension or emulsion and the ability to re-suspend following storage, including an assessment of the ability to continue to provide accurate dosages.

This protocol, prepared by the NHS Pharmaceutical Research and Development Working Group, a sub-group of the NHS Pharmaceutical Quality Assurance committee and the Production committee, presents a standardised methodology for establishing shelf lives for oral liquid products. It is expected that the principles of the protocol are used when conducting in-house stability trials and when assessing the validity of published stability data or commercially supplied stability data. Evidence of its use should also be requested when products are outsourced and it should form part of relevant tender documents.

The principles informing the protocol are;

2.1 Many products are not commercially available as oral liquids and these often have to be procured or made as Specials or made extemporaneously

2.2 Published stability data may be of limited value because of inappropriate analytical methodology, failure to commit the study for long enough to establish the full life of the product, and improper processing of analytical data.

2.3 Shelf lives are derived from various sources of data including chemical, physical and microbiological considerations. Once allocated the shelf life should be subject to on-going review and revalidation.

2.4 Other considerations such as container integrity and in-use shelf life are also considered within this document

2.5 This protocol applies to all drug substances and oral liquid formulations.

Note that Appendix 2 of this document is supplied to assist procurement staff in assessing the suitability of products to be procured as unlicensed oral liquid preparations to meet the special needs of a patient, including assessment of the shelf life assigned and stability information supplied or otherwise available for the specific product.

3. Analytical Methods

The development, validation, and adoption of analytical methods are beyond the scope of the protocol except to say that methods used must be stability indicating, robust and fully validated. The principles of 'Guidance on the Validation of Pharmaceutical Quality Control Analytical Methods' [1] should be followed, also, where appropriate, ICH Q2 (R1) [2] (implemented as CPMP/ICH/281/95).

Where there is a Pharmacopoeial monograph available then unless it can be fully justified the product must be shown to comply with this monograph throughout its shelf life. An example of where this may be justified is where a pH range has been determined and documented for a particular strength of product, the monograph is open to any strength and concentration affects the indigenous pH. All products must also comply with the British Pharmacopoeia (BP) General Monographs whether or not a specific monograph is present and they should also meet the requirements of the relevant Supplementary Chapters as best practice.

Analytical methodology should be in line with the BP unless an alternative method can be demonstrated to be equivalent to the BP method. Validated changes to the BP methods may be justified where, for example, excipients are required to be resolved from active drug and/or its degradation products.

4. Formulations

Formulations should be suitable both for stability and for the intended population group. Formulations may at times be made by crushing tablets or using the contents of capsules but it is preferable to use pure Active Pharmaceutical Ingredients (APIs) where these are available. Particle size for APIs and other excipients can also be an important factor when considering consistency of formulation and hence reliability of the stability data generated.

If tablets / capsule contents are to be used then the manufacturer of the starting materials and the Product Licence number should be included in the stability testing protocol and any changes to this starting material need to be fully assessed before introduction.

Further information on formulations, excipients etc. can be found in the following reference sources

British Pharmacopoeia and Pharm Europa
Handbook of Extemporaneous Dispensing (Jackson, Lowey)[3].
Handbook of Pharmaceutical Excipients[4].
EMA List of excipients of known effect[5].
Pharmaceutical Codex[6].

5. Containers

5.1 General considerations

In general the container used for the stability study should be the one proposed to store the product. Any secondary packaging which could have an impact on product stability should also be part of the pack put onto stability testing; this may be where the secondary packaging offers light protection or where it is a barrier to oxygen.

It may be possible to extrapolate data between different containers as long as the physical properties of the container are well understood. Critical physical properties include oxygen permeability, water permeability (water loss), light permeability, material constitution and possible extractables and the potential to adsorb materials. Any extrapolation must be evaluated and fully justified.

It is preferable to use child resistant closures where these are available, although legally these are only required for a small range of liquid medicines.

5.2 Glass containers

The type of glass must be included in the stability protocol. Amber glass should be used where light protection is necessary

5.3 Plastic Containers

It is now more usual to use plastic containers for storage of oral liquids; the type of container and closure should be discussed within the protocol. The properties of the container should be well understood and opaque plastic containers can present an issue for visibility of the product during release and later where re-suspension may be difficult.

Leachables data should be available for the plastic bottles, but with certain solvents or other excipients it may be that extractables data will need to be generated as part of the stability study

5.4 Unit Dose Presentations

These can largely be treated as above although it may be that a new container has to be used for each time point of the stability study, hence the uniformity of dose on packaging will need to be carefully assessed. Dose uniformity in these cases is a one off exercise as this will not change as a result of on-going storage; ability to re-suspend may still be an issue though.

6. Storage Conditions

Standard storage conditions are given in Table 1 below. Relative humidity control is not likely to be significant for oral solutions, although will be so for powders for reconstitution and may need consideration depending on the permeability of the container type. For aqueous solutions where storage times are comparatively short it will be possible to conduct studies without relative humidity control, however, the properties of the container do need to be assessed and understood (e.g. water loss by weight loss on storage).

Frozen storage is not normally appropriate for oral solutions, suspensions and emulsions.

1. Refrigerated in the absence of light	5ºC +/- 3ºC
2. Room temperature in the dark	25ºC +/- 2ºC
3. Elevated temperature	Representing accelerated stability data for products to be stored at room temperature. Normally 40ºC +/- 2ºC
4. Room temperature in the light	At ambient temperature, exposed to continuous fluorescent light
5. Frozen	Frozen at -20 ºC +/- 5ºC

Table 1 – A summary of stability testing temperature requirements

7. Storage Protocols

Conditions referred to in this section are referenced in Table 1 above.

7.1 Room Temperature stored products

Ideally oral liquids should be able to be stored at room temperature although some will need refrigerated storage for stability reasons and others (particularly for in-use stability) for microbiological reasons.

Products stored at room temperature should ideally also be subjected to accelerated testing at 40°C

7.2 Refrigerator stored products

Products requiring refrigerated storage should ideally be tested at both refrigerated temperatures and at an accelerated temperature of 25°C in order to fully understand any impact of storage at ambient conditions.

7.3 Products stored frozen

For products which have to be stored frozen, the process of defrosting must be documented and fully validated for its impact on stability, together with the stability of the product once defrosted, which can be either Table 1 Condition 1 (Refrigerated) or Condition 2 (Room Temperature) as appropriate.

7.4 Consideration of light exposure

The effect of light on the stability of a product needs to be assessed unless light exposure is eliminated in normal usage. The properties of the container in terms of light permeability across the whole spectral range needs to be well understood. Table 1 Condition 4 is appropriate if the product shelf life is dependent on light induced degradation. Further details as to the techniques to be used can be found in ICH Q1(B)[7].

7.5 Contact with closure

The protocol should include some containers stored on their side so that the effect of contact with the closure can be assessed.

7.6 In-use stability data

Stability studies for oral liquids should include consideration of in-use shelf life from a microbiological viewpoint but also in terms of chemical stability considering the risk of spoilage. In use storage should match the label requirements for the product and should simulate normal handling.

Preservative Efficacy Testing (PET)[8] should be part of the protocol for preserved multi-use products. For unpreserved multi-use products in-use periods are normally the responsibility of the end user who may better understand the local conditions of handling and anyway should be kept to a minimum (maximum seven days refrigerated). Any in use period assigned to the product must be supported with data to assess the impact of a microbiological load, possibly using a modified method loosely based on the Preservative Efficacy Test. Consideration should also be given to supplying the product in unit dose forms.

8. Concentrations

Before formulating a product, advice needs to be sought on standard dosages and solutions should be of standard concentration(s) to allow safe clinical use. If a range of concentrations is to be made each should be tested separately although for simple solutions a high and low concentration can be tested and results interpolated to intermediate concentrations.

9. Study period and sampling periods

Sampling times are study specific and the intrinsic stability of the system will decide the overall study period.

The study should be carried on for sufficient time to allow the critical parameter (i.e. that which will control the shelf life of the product) to reach beyond the appropriate confidence interval of its specification limits.

A minimum of 4 time points plus the initial data is needed. It is worth noting that increasing the number of time points can help minimise the 95% confidence interval which otherwise may restrict the allocated shelf lives. This is particularly applicable to studies with suspensions where between-day repeatability may be higher than for other product types.

In the case of the critical parameter being API concentration, it is desirable for the study period to allow the concentration to fall to a value which allows proper understanding of the reaction kinetics. This may not be possible for stable materials (however, see point 2.3).

Consideration should be given to carrying out accelerated stability studies particularly for products expected to be or known to be relatively stable. Condition 3 (40ºC) is the temperature normally selected for this purpose. The impact of the raised temperature on the physical aspects of stability of emulsions and suspensions needs to be carefully considered.

10. Sample Numbers

For licensed products and regularly manufactured specials there should be a programme of on-going stability work. It is required that three independent batches have been studied for licence submissions.

In general, for studies for products made as Specials or to be extemporaneously prepared, it is usual to carry out the initial stability assessment on a single batch, however, this must include at least three replicates (independent containers).

In general for oral liquids individual units may be regarded as a batch and multiple samples taken from them with the container being replaced in storage conditions after sampling. Note that samples should be removed in a controlled manner to minimise the risk of microbiological contamination and prevent spoilage.

For unit dose containers it will be necessary to prepare a fully mixed bulk before filling into the storage container to ensure all such containers contain an identical homogenous solution or suspension.

The three samples must be tested at each time point in triplicate, note that for some products testing may need to include even more replicates in order to fully understand the implications of the results.

Each sample should be reported independently or by including a standard deviation with the mean result. For example, for samples tested in triplicate this should be reported as an average and standard deviation for each sample together with the overall population mean and variance for the three samples. Ideally, for assay of the active ingredients and other critical excipients, samples should be reported as a percentage of the starting concentration, in this way small variations in initial concentration have no significance. For an example of how to express results please see Appendix 1.

11. Testing Protocols and methodologies

The minimum testing protocol should include;

Appearance - colour, clarity, particulate formation, creaming/cracking for emulsions, ease of re-suspension for suspensions
API concentration
pH
Degradation product concentration and / or a risk assessment of the properties of the expected degradation products.

Additional parameters are to be included where applicable, for example:
Uniformity of dosage (for suspensions and emulsions)
Dissolution (for suspensions)
Excipient concentrations
Container extractables and leachables.
Viscosity

Microbiological considerations
Total Viable Counts (TVC) initially and end of shelf life
Preservative Efficacy Testing (initial and end of shelf life / end of in-use shelf life)
In-use microbiological data
Absence of specific organisms where specified

11.1 Appearance

This should include the macro appearance of the product in the container if possible, for example looking at levels of suspension settlement and ease of re-suspension, but also examination of the withdrawn dose for changes in appearance, formation of particles and changes in organoleptic properties. Emulsions may show evidence of phase separation although often they may be readily re-dispersed on shaking.
In opaque bottles it may be difficult to view the product itself in the container but care should be taken that the macroscopic examination will detect any problems with suspension settlement or creaming / cracking of emulsions.

11.2 Assay

In general stability indicating HPLC methods will be required for the assay of active substances and degradation products as well as critical excipients such as preservatives and antioxidants. Degradation products may be determined using quantitative or semi-quantitative tests (such as TLC). Where quantitative methods are used, unknown degradation compounds are assessed by measurement of peak area as a percentage of principal/active analyte peak.

11.3 pH

The pH is likely to be critical to the stability of the active substance but is also critical to the activity of preservative systems and any change in pH is likely to be indicative of other chemical changes in the formulation.

11.4 Uniformity of dosage (for suspensions)

It is important that suspensions are capable of delivering a consistent dose throughout their shelf life and in-usage period. The British Pharmacopoeia specifies limits for homogeneity of suspension to be applied to unlicensed suspensions, and which are applied to suspension left undisturbed over a period of twenty four hours. An assessment of homogeneity should also be made at the end of the shelf-life of the product.

It may also be necessary to simulate use by routinely shaking the bottle at pre-defined intervals as part of the assessment of in-use shelf life.

11.5 Dissolution

Dissolution testing is required for oral suspensions using pharmacopoeial methods and is a British Pharmacopoeial requirement for unlicensed suspensions. It is important to assess that dissolution is not affected by on-going storage of the product throughout its shelf life. Hence dissolution testing should be included at the start and the final time point of a stability study for suspensions.

Note that difficulties in performing dissolution testing on oral suspensions have been noted with some formulations, hence such testing needs to be carefully thought out, designed and validated.

11.6 Viscosity

Viscosity is an important measure for oral liquid preparations particularly for suspensions and the physical stability of these and when considering preparations for naso-gastric administration. A change in viscosity during storage would be an indicator of a more fundamental physical change in a preparation.

11.7 Preservative Efficacy Testing

Effective preservation is an important aspect of product stability for multi-use presentations of oral liquids. For preserved oral liquids Preservative Efficacy Testing (PET) should be carried out as a minimum at the beginning and end of the shelf life and at the end of the in-use shelf life for this aspect of the stability study. The BP methodology should be followed for this test[8], any non-compliance with the BP suggested limits that is accepted must be fully justified. It should be noted that often PET is the rate limiting step when assigning both shelf life and in-use shelf life to a product.

For unpreserved preparations then these should ideally be presented in unit dose form, if a statement is to be made about in-use shelf life for an unpreserved multi-dosage presentation this should be supported with data from a modified PET or similar test.

11.8 Microbiological testing

For unpreserved systems the total microbial count at the beginning and end of shelf life and any in-use shelf life should be measured and its implications for the product shelf life considered.

Initial testing may also be required for absence of specific micro-organisms as specified in the BP monograph or where materials at risk of such contamination are included in the formulation

11.9 Powders for solution / suspension

For products presented as powders for dissolution / suspension then the stability study needs to cover their post reconstitution (in-use) shelf life in the same way as above. The stability and acceptability of the powder formulation may need to involve making up the solution or suspension at each time point and carrying out the raft of tests on the freshly made product.

12. Allocation of Shelf Lives

12.1 Analysis of data

A simple plot of analytical results against time is not acceptable for assigning shelf life. There are various options available for data handling and generally the one selected will depend on the data set. A simplified statistical approach is suggested, where the one-sided lower 95% confidence limit of the slope is used to calculate the time to reach 90 or 95%, as appropriate, of the labelled content (see 11.2 below). This may be calculated using a spreadsheet.

The principles of ICH Q1E (Evaluation of Stability Data)[9], implemented as CPMP/ICH/420/02, should be followed where appropriate, however, this document does offer flexibility of approach and the above approach would be acceptable for many studies.

The method favoured by ICH Q1E is where analytical data is subjected to linear regression analysis after determination of the appropriate relationship between critical parameter and time. An appropriate method of shelf life calculation, for an attribute which is known to decrease with time, utilises the lower one-sided 95% confidence limit of the regression, and calculation of the time required for the critical parameter to reach the specification limit. For example if Active Pharmaceutical Ingredient (API) loss is the critical

parameter, the lower 95% confidence limit of the time to reach 90 or 95%, as appropriate, of the labelled content is the physico-chemical shelf life.

This technique, however, requires specialised statistical software and unless the distribution of data around the regression line is carefully analysed using a statistical approach and is expertly interpreted, then significant errors could occur. The method can only be used if clear statistical conditions and expert knowledge of the analytical system are applied. The potential errors are particularly exacerbated in short-term studies which are often used with oral liquid formulations, particularly the in-use part of the studies.

It is often not desirable to use a statistical approach where little or no degradation occurs over the course of the study. As mentioned in section 9, a well-designed study should allow for a significant level of degradation to allow good understanding of the reaction kinetics, however, this is not always possible for stable materials. It is likely for these products that the shelf life will be assigned for other reasons (e.g. length of study, physical stability of suspensions, microbiological risks etc.).

Other approaches may be used, particularly the Confidence Bound or Maximum Rate method, which can be calculated with a spreadsheet.

12.2 Acceptance criteria

The Pharmacopoeial specification for a product is a shelf life specification to which the product must comply throughout its shelf life. The pharmacopoeial monograph should be checked when assigning acceptance criteria to preparations which must comply with the monograph at the end of their shelf life. It is also expected that a margin of safety is included in this assigned limit. Where loss of the active ingredient is the critical parameter, a loss of between 5 and 10% , as indicated in the monograph where available, is likely to constitute the maximum shelf life. Where the drug concerned has a narrow therapeutic index then a maximum loss of 5% as the parameter for shelf life definition would be more appropriate. It is acknowledged that for some preparations, including some antibiotic suspensions, the BP limits are wider than 90 – 110%.

It is important that, when using semi-permeable containers, the impact of water loss is accounted for when calculating API concentrations. Water loss will have a concentrating effect on solutions and therefore could mask degradation if not accounted for. In these cases the two-sided confidence limits of the slope may be appropriate and should be calculated and compared to both the upper and lower specification limits.

Knowledge of degradation products will be critical, the structure and identity and toxicology, metabolism and clinical effects need to be understood. It may be that the level of a degradation product is the critical parameter, hence, where it can be justified; the level of a degradant may be the key parameter in assigning shelf life.

Other critical excipients such as antimicrobial preservatives, antioxidants etc. may also adsorb, degrade or be used up during the shelf life or in-use shelf life and these may become the limiting parameter for shelf life determination, as may preservative efficacy tests and microbiological contamination levels.

In the case of suspensions, physical measures including the ease of re-suspension and hence the uniformity of dose may be the limiting factor.

13. Stability Study Reports

Stability study reports should be submitted following the agreed format outlined below.

Introduction
• Giving the reasons why the study was undertaken.

Literature Search
• Describing how this was undertaken and summarising relevant published prior work.

Analytical Methods
• Describing the development, validation, and/or adoption of analytical methods used. The specificity of the method together with its ability to detect degradants must be described.

Formulation
• Describing the formulation used, including all excipients and the rationale for their choice.

Container
• Describing the containers used, and the rationale for their choice.

Storage Conditions
• Describing the storage conditions used, and the rationale for their choice.

Concentrations
• Describing the concentrations studied, along with the rationale for their choice.

Storage Protocols
• Describing the storage protocols used and the rationale for their choice.

Sample Numbers
• Describing the number of samples and batches tested, along with the rationale for their choice.

Testing Protocols
• Describing the test protocols used and the rationale for their choice.

Results
• Detailed description of all analytical results. It is suggested that results are presented as a percentage of initial concentration, actual initial concentrations should be given in the report.

Discussion
• Scientific critique and evaluation of the results.

Allocation of Shelf Lives
• Description of the methods used to calculate shelf lives and the rationale for their use.
• Description of proposed shelf lives determined from the study.

Conclusions
• Overall conclusions from the study.

14. Extrapolation of data

It may be necessary to extrapolate from an external (published) study to cover individual circumstances. In general it is not acceptable to extrapolate data from one formulation to another unless the impact of the change on the overall stability profile is well understood. Furthermore, studies should not be extrapolated to other concentrations outside the range studied. It may be possible to extrapolate to different container types as long as the properties of the product and container are well understood. Whenever data is extrapolated then there should be a degree of safety margin to the shelf life assigned. If the product is going to be routinely made then an in-house stability study should be considered at the earliest opportunity.

Glossary

MA Marketing Authorisation

API Active Pharmaceutical Ingredient

References

1. Guidance on the Validation of Pharmaceutical Quality Control Analytical Methods - NHS PQA Committee March 2005.

2. ICH Q2(R1) Validation of Analytical Procedures: Methodology - International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

3. Handbook of Extemporaneous preparation (Jackson and Lowey) Pharmaceutical Press

4. Handbook of Pharmaceutical Excipients (Rowe) Pharmaceutical Press

5. EMA List of excipients of known effect.

6. Pharmaceutical Codex (Lund) Pharmaceutical Press

7. ICH Q1B Photostability Testing of New Active Substances and Medicinal Products.

8. British Pharmacopoeia 2014 Appendix XVIC – Efficacy of antimicrobial preservation

9, ICH Q1E Evaluation of Stability Data - International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

Document History	Issue date and reason for change
Version 1	Issued August 2014
Version 2	
Version 3	
Version 4	

Appendix 1

Example of reporting of results from stability trials
For three replicates each tested in triplicate the report at each time point should be presented as:-

Replicate 1 100.3% +/- 1.3%
Replicate 2 99.6% +/- 0.7%
Replicate 3 100.7% +/- 0.5%
Population mean 100.2% variance 0.21%

For three replicates each tested in duplicate the report at each time point should be presented as:-

Replicate 1 99.7% – 100.3%
Replicate 2 100.1% - 101.1%
Replicate 3 99.4% - 100.6%
Population mean 100.2% variance 0.31%

Note that the Variance is defined as the average of the squared differences from the mean. In this second case it is calculated based on the population n=6. In the case of the first data set above it is calculated from the replicate means, hence n=3.

Appendix 2

Checklist for assessment of stability data for procured oral liquid Specials
The following checklist is provided as a quick guide to assessing the suitability of procured oral liquid Specials from the stability assessment viewpoint. This should be used alongside other assessment tools for unlicensed products.
Preparation:……
Supplier / Manufacturer:…….

1) Formulation	1.1) Is the formulation specified in the product specification	Yes (go to 1.2) / No (return to supplier for specification)
	1.2) Is the formulation fit for purpose and for the patient / patient group	Yes (go to 1.3) / No (source a suitable formulation)
	1.3) Is it a validated formulation (BP / USP NF)	Yes / No (Record and proceed)
2) Shelf life assigned	2.1) What shelf life is assigned by the manufacturer	
	2.2) Is this based on a stability study	Yes (go to 3.1) / No (go to 2.3)
	2.3)Is it based on an expert assessment of stability based on related product information (extrapolation)	Yes (assess whether this is suitable and whether risks can be mitigated)/ No (go to 2.4)
	2.4) Is the shelf life arbitrarily applied based on no data	Yes (consider the risk of formulation / stability failure on criticality and use of the product
3) Stability study report	3.1) Is the stability study based on the exact formulation to be procured	Yes (go to 3.2) / No (get an expert opinion on the suitability of extrapolation)
	3.2) Does the report follow the format outlined in this document	Yes (go to 4.1) / No (assess the impact of the lack of information)
4) Stability study	4.1) Storage temperatures / Does this support the product storage directions assigned to the product procured	Storage Temperature Accelerated storage temperature Acceptable (go to 4.2) / Not acceptable (get an expert opinion on suitability of extrapolation)
	4.2) Study storage period / does this exceed the applied shelf life	Yes (go to 4.3)/ No (assess suitability)
	4.3) Is storage in contact with the closure included (Inverted / on its side)	Yes (Go to 4.4) / No (assess the impact, ensure storage is always upright
	4.4) Replicates – does the study include at least three replicates (separate samples) tested in triplicate	Yes (Go to 4.5) / No (consider the robustness of the data presented)
	4.5) Is an in-use shelf life specified and is this supported by the data provided	Yes (Go to 5.1) / No (in-use shelf life will be the responsibility of the user to assign)

5) Analytical techniques / results	5.1) Stability indicating assay of the active ingredient	Satisfactory / Not satisfactory / Not tested
	5.2) Assay and identification of degradation products	Satisfactory / Not satisfactory / Not tested
	5.3) Assay of preservatives / critical excipients	Satisfactory / Not satisfactory / Not applicable / Not tested
	5.4) Dissolution testing for suspensions	Satisfactory / Not satisfactory / Not applicable / Not tested
	5.5) Appearance /ease of re-suspension for suspensions / pH / Viscosity	Satisfactory / Not satisfactory / Not tested
	5.6) Uniformity of dosage (suspensions and emulsions)	Satisfactory / Not satisfactory / Not applicable / Not tested
	5.7) Microbiology / Preservative Efficacy Testing	Satisfactory / Not satisfactory / Not tested
	Overall assessment of data presented	Satisfactory (Go to 6.1) / Not satisfactory (Go back to supplier with concerns)
6) Data analysis	6.1) Does the data presented support the shelf life assigned (with a suitable safety margin)	Yes / No (Go back to the supplier with concerns / consider assigning an in-house shortened shelf life)

Summary of risks

Assessment of stability study for
……..

The data supplied: Provides assurance that the product will be suitable, safe and efficacious / Does not provide suitable assurance

Approved:……..Date:……

Additional risk reduction measures