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**Guidelines for Specifying the Shelf Life
of Plant Protection Products**

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1. INTRODUCTION

The shelf life and the quality of plant protection products are to a large extent dependent on the conditions under which they are stored. Therefore, manufacturers routinely conduct both accelerated and real-time storage stability tests to ensure that products are fit for the intended purpose. Regulatory authorities must be provided with relevant information with which they can make an evaluation of the quality of a product on behalf of the end user. The aim of this paper is to harmonise industry's approach to storage stability testing.

2. BACKGROUND

The stability of a formulated product on storage may be influenced by many factors and therefore, its determination is a complex problem. The major difficulty stems from the nature of the pesticide market itself, where the transport and storage conditions are not only highly variable but are usually beyond the control of the manufacturer.

Pesticide manufacturers recognize that it is in their own interest to have reliable information on the storage properties of their products. As the distribution of many pesticides is world-wide, the variety of different climatic conditions under which products are likely to be stored must be taken into account during the development of new pesticide formulations. Industry, therefore, carries out storage stability tests under well defined and controlled conditions at both ambient and elevated temperatures. Low temperature studies are normally included for liquid products, particularly if they are to be shipped through, or stored in, areas with cold climates. The goal of these tests is to evaluate the storage properties of a product as well as to identify suitable packaging materials. From the data obtained under these controlled conditions, a prediction of minimum storage stability under proper storage and handling conditions can be made.

In paragraph 10.2.6 of the FAO Code of Conduct it is stated that industry should use labels that are marked with the date (month and year) of formulation of the lot or batch and with relevant information on the storage stability of the product. The FAO/WHO Manual¹ refers to this as the Release Date.

It is normal convention that information on storage stability is given only if the product cannot be stored for at least 2 years in unopened original containers. Most pesticides are applied in the growing seasons following their manufacture and any remaining product is normally used in the following season, i.e. before the product is 2 years old, although many products can be used without problems in subsequent seasons.

If products have exceptionally been stored for more than 2 years or under unfavourable conditions, and their quality is in doubt, then they should be re-analysed in order to make a decision as to their continued suitability for use.

In certain cases where the Supply Chain may be extensive or with certain product types (e.g. Public Health products) it can be desirable to have a product shelf-life statement of greater than 2 years. In order for a shelf-life claim of more than 2 years to be made the manufacturer must ensure that studies demonstrating the stability of the product for these extended periods are available and clearly show to Regulatory authorities that the shelf-life specification continues to be met at the end of the extended storage period. Where such approvals for longer shelf life exists then separate discussions with the relevant authorities on the labelling requirements for these specific products will be required.

3. DEFINITIONS

Formulation	A pesticide preparation containing active ingredient(s) and formulant(s), in a form suitable for practical use.
Finished pack	Primary sales pack that is in contact with the formulation.
Shelf life specification	Specification, within which the properties of a formulation will remain after a minimum of 2 years storage, if no other statement as to storage period is made.
Shelf life	Period of time during which the product remains suitable for use, and within the shelf life specification, when stored in the unopened original container under conditions of the area where it is marketed and following the recommendations of the manufacturer.
FAO/WHO Specifications	International Standards of quality for pesticides evaluated and published by FAO/WHO.
Release date	The date from which the supplier guarantees a shelf-life of at least 2 years, unless stated otherwise, under actual conditions of storage in the area where the technical grade active ingredient or formulation is to be marketed.

Real a.i. content	A.i. content of a lot or batch not including analytical and sampling errors (adequate accuracy requires analysis of a sufficient number of samples).
Real a.i. degradation	A.i. degradation of a formulation not including analytical errors.
FAO tolerances	Tolerances (established by FAO) on the active ingredient content taking into account analytical and sampling errors and the manufacturing variance (see Manual ¹).
Ambient temperature	Average temperature in the region where the product is marketed.
CIPAC methods	Analytical and physical test methods published by CIPAC ² .

4. OUTLINE OF THE PROPOSAL

To obtain accurate information on the shelf life of a product, it is necessary to conduct both accelerated and real-time storage stability tests with a representative sample of the product being evaluated. In order to develop sufficient data on the formulation, chemical and physical properties tests must be performed after storage at elevated temperatures at appropriate time intervals in either glass or a simulated or actual finished packaging material to be able to draw meaningful conclusions.

In general, it is sufficient to perform a storage stability study with one representative lot or batch of the formulation. In case of different type of packaging materials, it is recommended to perform for each pack a separate study unless it can be clearly justified that one pack type can be extrapolated to another. Conducting such studies on different pack types with one single representative batch of formulation is also acceptable.

For each temperature linked to a given storage time one separate sample is needed. This means for a storage stability study in a given container the number of samples needed is equal to the number of different temperature/time testing points. To document the shelf life of a product the manufacturer, after having carried out the storage stability studies, will:

- Supply actual results to support this stability claim. The stability data may be based on accelerated tests until real-time storage tests at ambient temperature become available. Tests will be based on CIPAC² methods, if applicable.

- Make label statement of release date (month and year) and relevant storage stability information of the product based on paragraph 10.2.6 of the FAO Code of Conduct.

5. SHELF LIFE & FITNESS FOR USE

During storage formulated products can undergo chemical and physical changes. The rate at which products undergo changes depends very much on the nature of the active ingredient(s), the formulation type, the packaging and, the storage conditions. The product remains fit for use as long as these changes have no adverse effects on application, biological performance, and on operator, consumer and environmental safety. The purpose of the shelf life specification is to define appropriate limits to comply with the above requirements.

The shelf life specification must provide limits for the active ingredient content and the key physical properties of the product.

Where a formulation has a shelf-life of less than 2 years, this must be fully justified and the label must identify both the manufacturing date and the 'use by' date.

5.1. Active ingredient content

The manufacturer must guarantee that at the time of manufacture the average production value of a formulation is not below the nominal content.

It is generally accepted that a deviation of +/- 10% of the nominal active ingredient content will not significantly influence the biological performance. This is not to be confused with the FAO tolerance ranges, which do not include an allowance for degradation or an overage.

5.2. Physical properties

The specification on physical properties should be based on CIPAC² methods when appropriate and provide limits that ensure that the formulation can be handled and applied without difficulties. If internal company methods or other methods are used they should be justified and described in the study report.

The FAO/WHO Specification Manual¹ provides guidelines, for each specific key formulation type, on the physical test parameters required to be tested before and after storage.

5.3. Packaging

The effect of the formulation on the primary pack and vice versa is important and therefore, a statement on the stability of the packaging material may be required.

6. STORAGE STABILITY TESTING

Storage stability programmes include accelerated as well as real time tests.

Accelerated tests are performed at elevated temperatures in an attempt to get information on the shelf life of a formulation in a relatively short time. Accelerated testing involves extrapolations from higher to lower temperatures and from shorter to longer storage periods. Since formulations are complex mixtures and elevated temperatures can initiate a degradation pathway that may not be operational at lower temperatures, there is uncertainty involved in such extrapolations, unless the formulation proves to be very stable under all conditions.

Real-time testing does not require extrapolations, but cannot produce adequate results in a short time. The storage is normally performed at ambient laboratory temperature for at least 2 years on a single batch of formulation. Depending on the formulation and packaging material testing under standardized relative humidity or by exposure to light may be required.

If a shelf-life of more than 2 years is required on particular products then storage at ambient laboratory temperature must continue and the formulation tested to ensure the shelf-life specification is met at the end of the proposed maximum extended period.

6.1. Accelerated tests

At the initial stages of a registration process a complete set of real-time data is usually not available. In this case data from accelerated tests should be provided. Since the final packaging material may not yet be known when stability testing is initiated the samples may be stored in experimental containers.

The normal storage regime is 2 weeks at 54°C as referred to in the Manual¹, but certain flexibility in choosing test conditions is necessary due to the different nature of products, e.g. a lower temperature if the active ingredient in a solid formulation melts below 54°C.

Alternative storage conditions as listed in the Manual¹ or in CIPAC² MT 46.3 may be used to support the initial stability statement (4 weeks at 50°C, 6 weeks at 45°C, 8 weeks at 40°C, 12 weeks at 35°C, 18 weeks at 30°C).

If no significant chemical or physical changes occur in the accelerated tests the conclusion is that the product will most likely comply with the shelf life specification of 2 years. If changes are observed it may be difficult to draw meaningful conclusions based on accelerated tests alone and additional storage data will be needed.

6.2. Real-time testing

Data on the formulation intended for sale should be supplied demonstrating stability for at least 2 years at ambient temperature (see definition section 3) in the finished pack or in one similar (e.g. smaller volume but same material).

Because of high temperatures in the summer there is often a tendency to overestimate average temperatures. Correct values are available from meteorological stations. In temperate climate, where the temperature in the winter drops below the freezing point, it is considered that warehouses may be slightly heated. To imitate the latter case by storage tests at constant temperature, the tests would have to be carried out at a few degrees (normally 1 to 4) over the meteorological average.

With these corrections the following laboratory test temperatures for various climatic zones are appropriate:

- moderate / temperate climate: 18 - 22°C
- hot climate: 23 - 27°C
- very hot climate: 28 - 31°C

It is recommended to store test samples at 20°C, at ambient laboratory temperature or at 30°C to generate both chemical and physical data when the storage test is initiated and after 2 years. If the sales geography requires an extended shelf-life beyond 2 years then chemical and physical data should be generated at the appropriate extended time point.

Intermediate time intervals of 3, 6, 9 and 12 month should be examined for chemical data only if required to support a shelf life declaration of less than 2 years.

The samples should be stored under thermostatic conditions ($t \pm 2^\circ\text{C}$). If it is not possible to control the temperature then the variation should be measured during the test period and reported.

If the product meets the shelf life specification after the 30°C test, then the conclusion is that it remains suitable for use for at least 2 years under all

practical conditions. If this is not the case different shelf life declarations may be needed for various climatic zones.

6.3. Cold stability

Liquid formulations, in which the a.i. could crystallize or in which phase separation could take place, should also be tested using CIPAC² method MT 39.3 at 0°C or lower, if required, to determine their cold stability. After storage at 0 ± 2°C for 7 days, the formulation must continue to comply with the requirements of appropriate clauses for initial dispersion, stability of emulsion or suspension, and wet sieve test. If the product is irreversibly damaged at 0°C this should be indicated on the label.

6.4. Suitability of packaging materials

Packs need to be examined to ensure that no significant interaction with the formulation affecting the stability of the packaging material; has taken place during storage.

For products packed in water soluble packaging (WSP) additional tests are required to ensure the product disperses satisfactorily in the spray tank and do not cause any problems with poor homogeneity and/or sieve or nozzle blockages. These tests, involving adding appropriate amounts of the WSP during suspensibility and wet sieve tests, are described in more detail in the FAO/WHO Specification Manual¹ and CIPAC Handbooks².

7. SPECIFIC FORMULATION REQUIREMENTS

In sections 1 to 6 general information on storage stability and the determination of a.i. degradation and changes of physical properties during storage has been given. Specific requirements of physical properties to test in a range of important formulation types are given in the FAO/WHO Specification Manual¹.

As defined, the product, when stored at ambient temperature, must comply within the limits of the specification for at least 2 years, if no statement is made on the label. The limits for the a.i. content should include the manufacturing variance and the real degradation, if any, obtained from storage stability studies.

Besides appearance and a.i. content the relevant physical properties should be specified as written in the FAO/WHO Specification Manual¹. When setting the limits the accuracy of the test methods should be taken into account.

REFERENCES

1. Manual on Development and Use of FAO and WHO Specifications for Pesticides, March 2006 revision of the First Edition (available only on internet:
<http://www.fao.org/agriculture/crops/corethemes/theme/pests/pm/jmps/manual/en/>)
2. Collaborative International Pesticides Analytical Council (CIPAC) Handbooks (<http://www.cipac.org/cipacpub.htm>)