Central African Economic and Monetary Community (CEMAC)
Executive Secretariat

Common Regulation on the Registration of Pesticides in the CEMAC zone

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APPENDICES

APPENDIX 1

Common pesticides registration procedure for Central African States

First step
- The applicant shall submit a complete registration application file to the Permanent Secretariat of the Central African Pesticides Registration Committee (CPAC). The Permanent Secretariat shall provide each applicant with the model registration application file.
- The CPAC Permanent Secretariat shall register the application file and issue a receipt to the applicant.
- The applicant shall pay a file examination fee.
- The CPAC Permanent Secretariat shall verify all the documents of the file and, where any essential information is lacking, notify the applicant to complete the missing documents.
- The CPAC Permanent Secretariat shall submit the file to CPAC experts.

Second step
- CPAC shall study the file and may:

1- decide to register the pesticide in Central Africa for 10 (ten) years;
2- grant a provisional sale authorization (PSA) for a two-year period pending further studies;
3- retain the file under study pending additional information;
4- refuse to register the pesticide.

A pesticide that has been registered or one that has been granted a PSA shall be issued a unique number valid for all CPAC member States.

Third step
- The CPAC Permanent Secretariat shall transmit the results of the deliberation to the applicant and to member States.
- The Permanent Secretariat shall publish the list of registrations and PSAs in a CPAC periodical.

Appendix 2

Composition of pesticide registration application file

The application file shall comprise all information necessary to assess the efficiency of the pesticide and the foreseeable hazards that such a pesticide might pose to man, non-target animals and the Central African environment as a whole. It shall include all information on the identification and the physico-chemical properties of the product and the active ingredient, toxicology, effects on the environment and wildlife, the residues as well as information on the safety measures on the use of the product.

The application file for pesticide registration in Central Africa shall include the following items:
1) an application for the registration of the commercial product;
2) a specification sheet;
3) a technical package;
4) an analytical file;
5) a toxicology file;
6) the original label or scale model;
7) a reference sample of the active ingredient(s) contained in the commercial product and a sample of the commercial product;
8) an attestation or a registration certificate in the country of origin and/or any other countries in similar agro-ecological zones.

All documents submitted shall be in French (or in English).

Due to the huge volume of conducted studies, the file shall comprise only abstracts of these studies. However, the complete studies shall be made available to CPAC on request.

The file shall comprise an impartial report giving an acceptable justification for CPAC in case some specific data or information not deemed necessary on account of the nature or use of the product, are proposed. This shall also apply where it is not scientifically necessary or technically feasible to provide such data or information.

Part 1: application for registration of a commercial product

It shall comprise the following:
1- the name and address of the applicant;
2- the name and address of the manufacturer of the product;
3- the name and address of the patent holder;
4- the brand name of the product;
5- the form of presentation of the product;
6- the detailed chemical (or biological) composition of the product;
7- the properties and intended uses of the product;
8- the conditions of use;
9- the dosage and concentration;
10- a summary of the toxicological file relating to the acute toxicity of the formulation and active substance(s);
11- the toxicological classification of the formulation (according to WHO classification);
12- the admissible daily intake, Maximum Residue Limit (MRL) and a suggested waiting period for the Central African zone;
13- precautions to be taken before, during and after using the product;

14- symptoms of intoxication in animals, and in man where possible;
15- measures to be taken in case of intoxication;
16- the nature, content and size of packaging;
17- storage precautions;
18- shelf life of the product;
19- recommendations for eliminating expired products and packaging;
20- list of countries with similar ecologies where the product is approved, and authorizations for use in those countries;
21- if need be, a sufficient quantity of the formulated product to be used for experimental purposes in Central Africa.

Part 2: Specification sheet

It shall comprise:

1 For the formulation

1.1. brand name;
1.2. name and address of manufacturer;
1.3. type of formulation;
1.4. aspect;
1.5. composition;
1.6. minimum and maximum contents in active substances;
1.7. actual or approximate mass density;
1.8. inflammability;
1.9. corrosive potential;
1.10. acidity or alkalinity;
1.11. water content;
1.12. wettability;
1.13. suspension content;
1.14. emulsion persistence;
1.15. fineness of particles;
1.16. fluence;
1.17. kinematic viscosity;
1.18. miscibility with hydrocarbons;
1.19. known incompatibilities;
1.20. nature, size and content of packaging, and description of closing mechanism;
1.21. stability in storage.

2. For technical grade products
2.1. origin: name and address of manufacturer, address and place of manufacture;
2.2. aspect;
2.3. mass density;
2.4. minimal purity;
2.5. possible variations of the composition.

3. For active substances
3.1. international common name and synonyms ;

3.2. chemical identity by international classification;
3.3. empirical chemical formula, structural chemical formula, and molecular mass;
3.4. aspect;
3.5. mass density;
3.6. fusion, boiling and decomposition points;
3.7. vapour pressure;
3.8. volatility;
3.9. sulfonation index and distillation properties;
3.10. solubility in water and organic solvents;
3.11. coefficient of mixture with water and an appropriate non-miscible solvent;
3.12. absorption spectrum: ultraviolet, visible and infrared
3.13. chemical stability;
3.14. metabolite(s) left by active substance(s) following use of the product: state if it is/they are toxic or phytotoxic;
3.15. all other relevant properties.

Where the formulation is combined with several active substances, the above information shall be furnished separately for each active substance.

Part 3: technical package

It shall comprise:
1. a statement on the behaviour of the active substance(s);
2. a study on the action of the commercial product for which registration is sought, its lasting effects, phytotoxicity, selectivity, and unforeseen or undesirable side effects;
3. directions for use: indicate dosage, time, stage and frequency of use;
4. limits for use: indicate limits for use in order to make product harmless to crops, animals or the substrate treated as well as to persons applying it, consumers and the next crop in the rotation;
5. a statement on known incompatibilities of the pesticide with others.

Part 4: analytical file

It shall comprise:
1. methods of extracting, identifying and dosing the active constituents in the commercial product;
2. methods of extracting and dosing the residues from the active substances and metabolites that are classified as residues;
3. a method of studying residues in plants and food which are likely to be contaminated;
4. a method of studying the degradation of the active substance(s) in a treated plant or food crop;
5. a study on the behaviour of the active substance(s) and their conversion products in the soil and in water.

Part 5: toxicology file

It shall include:

1. *study on the toxicity of the formulation*:

1.1 Acute toxicity;
1.1.1 LD_{50} by oral route;
1.1.2 LD50 through the skin;
1.1.3 LC_{50} by inhaling;
1.2 Irritation of the skin;
1..3 Irritation of the eye.

2. *Study on the toxicity of active substance(s)*

2.1. Acute toxicity
2.1.1. LD_{50} by oral route
2.1.2. LD_{50} through the skin
2.1.3. LC_{50} by inhaling
2.2. Irritation of the skin
2.3. Irritation of the eye among rabbits
2.4. Sensitization
2.5. Sub-chronic toxicity
2.5.1. Toxicity by oral route
2.6. Chronic toxicity by oral route
2.7. Mutagenicity and its effects on DNA
2.7.1. In vitro
2.7.2. In vivo
2.8. Carcinogenicity
2.9. Teratogenicity and embryotoxicity
2.10. Effects on reproduction
2.11. Neurotoxicity
2.12. Other studies could be required as warranted by the results of the toxicity tests or the chemical structure and properties of the substance.
2.13. Animal metabolism

3. Summary of observations of the toxicity of the product to humans

4 Study of the environmental impact of the product

4.1 Toxicity to birds;
4.1.1 Acute toxicity;
4.1.2 Diet;
4.1.3 Reproduction
4.2 Toxicity to reptiles
4.1.1 Acute toxicity
4.1.2 Chronic toxicity

4.3 Toxicity to aquatic organisms
4.3.1 Toxicity to fish
4.3.1.1 acute toxicity study;
4.3.1.2 long term toxicity
4.3.2 Toxicity to invertebrates
4.3.3 Toxicity to algae;
4.3.3.1 acute toxicity test;
4.3.3.2 supplementary studies;
4.4 Toxicity to useful arthropods;
4.4.1 Toxicity to bees;
4.4.1.1 acute toxicity by oral route;
4.4.1.2 acute toxicity through contact;
4.4.2 Toxicity to natural enemies of depredatory invertebrates (auxiliaries)
4.5 Toxicity to soil organisms;
4.6 Evolution and behaviour in the environment;
4.6.1 Evolution and behaviour in the soil;
4.6.1.1 rate and means of degradation;
4.6.1.2 absorption and desorption;
4.6.1.3 mobility;
4.6.1.4 importance and nature of related residues;
4.6.2 Evolution and behaviour in water, the soil and the air;
4.6.2.1 rate and means of degradation
4.6.1.1 absorption and desorption;

5 Study on bio-accumulation of active substances

6 Recommendations relating to therapy and precautions.

6.1 Diagnosis and symptoms of poisoning;
6.2 First aid in case of intoxication and contra-indications;
6.3 Therapy and antidotes;
6.4 Safety measures;
6.4.1 Transportation precautions;
6.4.2 Storage precautions;
6.4.3 Precautions in case of fire outbreak;
6.4.4 Precautions for handling packaging;
6.4.5 Precautions in case of leakage or accidental spill;
6.4.6 Recommendations for decontamination of application material, clothing and protective equipment;
6.4.7 Instructions and/or proposals to feature on the packaging;
6.5 Recommandations on the disposal of expired products and packaging.

Part 6: Original label or scale model, see Appendix 4

Part 7: Reference sample of active constituent(s) in the commercial product and sample of commercial product.

Part 8: An attestation or a registration certificate in the country of origin or in other countries with a similar ecology to that of Central Africa.

Appendix III
Registration criteria

1 REGISTRATION APPLICATION

It shall comprise:

1.1 Administrative Information

1.1.1 Name and address of applicant;

1.1.2 Name and address of the patent holder;

1.1.3 Name and address of the manufacturer of the formulation and place of manufacture;

1.1.4 Name and address of the manufacturer of the active substance(s) and place of manufacture.

1.2 Identity of the formulation

1.2.1 Brand name of the formulation;

1.2.2 Composition of the formulation: names and proportions

- **Active constituent(s);**
- **Additives;**
- **Inert compounds;**

1.2.3 Type of formulation (see appendix II);

1.2.4 WHO toxicologic classification of the formulation.

1.3 Identity of the active substance(s)

1.3.1 International common name (ISO);

1.3.2 Purity;

1.3.3 Identities and proportions of additives and impurities .

1.4 Intended Uses

1.4.1 type of pesticide
(e.g. insecticide, herbicide)

1.4.2 intended uses
(e.g. cotton plant foliage insects, rice weeds);

1.4.3 list of countries (with similar ecologies) where the formulation is registered and authorizations for use in these countries;

2 ABSTRACT

The purpose of the abstract shall be to provide the Central Africa Pesticides Committee (CPAC) with relevant information on the product to be registered. Data thus provided shall enable CPAC members to have a quick overview on the product to be registered. The same information may later be used to inform users and to compile a Phytosanitary Index for the CEMAC zone.

The applicant shall be required to fill the following data sheet provided for this purpose. Only the essential details should be provided, and if possible, using keywords or model phrases.

Abstract sheet
Name and address of the applicant _____
Brand name of the product _____

Identification of product		
Brand Name		
Common Name of active substances		
Type of Formulation	Content in active substances	
Physico-chemical properties		
Melting point	Boiling point	Mass density
Vapour pressure	pH	Flammability
Solubility in water		
Solubility in organic solvents		
Physical state, odour and colour		
Stability in storage		
Incompatibilities		
Other important properties of the product as deemed by the applicant		
Biological effectiveness		
Scope of use of the product		
Target harmful organism(s)		
Rate of use		
Period and frequency of use		
Waiting period		
Toxicology data		
Technical active matter		
LD50 (oral)	LD50 (skin)	LC50 by inhaling
Irritation of the eye	Irritation of the skin	Sensitization
Carcinogenicity	Teratogenicity	Embryotoxicity
Neurotoxicity	Effects on reproduction	
WHO Classification		
Formulated product	LD50 (skin)	LC50 by inhaling
WHO Classification	Irritation of the skin	Sensitization
Irritation of the eye		
Signs and symptoms of exposition		
Symptoms of intoxication		

Abstract sheet
Name and address of the applicant _____
Brand name of the product _____

First aid measures in case of intoxication
Therapy and antidotes
Safety measures
Transportation precautions
Storage precautions
Precautions in case of fire outbreak
Precautions to be taken for the disposal of surplus stocks and packaging
Recommendations for decontamination of application material, clothing and protective equipment
Safety precautions to be taken before, during and after application of product
Effects of product on the environment
Evolution and behaviour of product in the soil TD50
Evolution and behaviour of product in water TD50
Maximum limit of residues in food stuffs
Toxicity of product to birds oral LD 50
Toxicity of product to fish CL50
Toxicity of product to bees oral LD 50
Toxicity of product to soil organisms CL50

Date of drafting of abstract
Applicant's signature

It shall comprise:

3.1 For the formulated product:

3.1.1 Brand name

3.1.2 type of formulation

3.1.3 physical state, colour and odour

3.1.4 chemical nature of constituents of formulated product and their contents

The titers shall be expressed in grams per kilogram for solid substances or in grams per litre at 20° C for liquids:

- active matter;
- fillers;
- diluents;
- solvents;
- emulsifiers;
- colouring agents;
- additives.

3.1.5 Minimum and maximum contents in active ingredients

3.1.6 Absolute density for liquids or apparent density for solids

Expressed in mass unit per volume at 20° C (e.g. g/l)

3.1.7 Volatility

3.1.8 Flammability

- for liquids: give the flashpoint in degrees centigrade and indicate the method used;
- for solids: specify if the product is flammable and indicate the flammability conditions;

NB. In case of a flammable product, indicate the sign of the flame on the label.

- **3.1.9 acidity/ alkalinity/ pH**

pH: expressed for a 1% dilution for formulations to be diluted in water. Specify the limits compatible with a good stability of the product:

- acidity: expressed in g/kg of H_2SO_4 ;
- alkalinity: expressed in g/kg of NaOH ;

3.1.10 corrosive potential

Indicate the corrosive effects of the product to material likely to be used for packaging and to material with which the product is likely to come in contact when it is used.

3.1.11 Stability in storage

Indicate the guaranteed stability duration of the product in its commercial packaging and specify the conditions:

- Provide results of an accelerated stability test conducted for two weeks at 54° C;

- Also provide results of long-term stability tests conducted for 12 weeks at 45° C, or for 52 weeks at 37° C. Possibility to use any of the tests: for 2, 4, 8 weeks, or 3 months at 40 ° C / 2 years at room temperature. Indicate the methods used.

3.1.12 Statement of the incompatibilities of the formulated product

Indicate the incompatibilities with materials with which the product is likely to come in contact during its conservation, handling or use.

3.1.13 Stability of the emulsion and its conversion capacity

To be determined for emulsible concentrates. Indicate the method used.

3.1.14 suspension content

To be determined for dispersible powders and concentrates for suspension. Indicate the method used.

3.1.15 Water content

Indicate maximum tolerance content and the method used.

3.1.16 Wettability

To be determined for dispersible powders in water. Indicate method used.

3.1.17 Fineness of particles

To be determined for granules, powders for dusting, dispersible powders and concentrates for suspension. Indicate methods used.

3.1.18 Fluence

To be determined for dusting powders. Indicate method used.

3.1.19 Kinematic viscosity

To be expressed in centistokes (or mm^2/s) at 25, 30 and 40° C, for formulations to be used for ULV spraying. Indicate the method used.

3.1.20 Miscibility with hydrocarbons

Particularly with gas oil and "Solvesso" 200 (or an aromatic solvent with identical features). To be determined for liquids to be used for ULV spraying. Indicate the method used.

3.2 For technical grade active matter:

3.2.1 Physical state, colour, odour

3.2.2 Absolute density (to be determined for liquids) or apparent density (to be determined for solids)

It shall be expressed in mass unit per volume at 20° C (e.g. g/l)

3.2.3 Possible variations of the composition: minimum and maximum purity

3.2.4 Fusion point

3.2.5 Boiling point

3.2.6 Decomposition point

3.3 For pure active ingredients:

3.3.1 international common name
Proposed or accepted by ISO and synonyms

3.3.2 chemical identity
According to international IUCPA nomenclature

3.3.3 empirical chemical formula

3.3.4 structural chemical formula
3.3.4 molar mass

3.3.6 physical state, colour, odour

3.3.7 absolute density (to be determined for liquids) or apparent density (to be determined for solids)

It shall be expressed in mass unit per volume at 20° C (e.g. g/l)

3.3.8 fusion point

3.3.9 boiling point

3.3.10 decomposition point

3.3.11 vapour pressure
It shall be expressed in millibars.

3.3.12 sulfonation index and distillation properties
To be determined for mineral oils.

3.3.13 solubility in water and in organic solvents
At a specified temperature, preferably between the 20 - 25° C bracket.

3.3.14 Partition coefficient
With water and an appropriate non-miscible solvent

3.3.15 absorption spectrums:

- ultraviolet;
- visible;
- infrared;
- nuclear magnetic resonance (NMR);
- mass spectrum (MS).

3.3.16 chemical stability:

- hydrolysis and photolysis rate under specified pertinent conditions;
- half-life according to pH in water solution at 20° C or in an isopropanol/water mixture at a 1:1 ratio.

Where the formulation is combined with several active ingredients, this information shall be provided separately for each active ingredient.

Biological effectiveness tests shall be conducted with the formulated product. The purpose of such tests shall be to provide sufficient data necessary to assess the level, duration, and uniformity of control, protection or expected effects of the formulated product as compared to other appropriate reference products where they exist.

These tests shall require that the objectives, materials and methods used be specified, as well as the references of the institutions having conducted the tests.

The results obtained from these tests should be sufficient to enable an assessment of the biological effectiveness of the formulated product.

The biological effectiveness file shall include:

4.1 Results of the effectiveness tests

4.1.1 Test requirements

A test must, in principle, be based on three objects:

- the tested product;
- the reference product;
- an untreated biomonitor.

It must show the degree of effectiveness of the formulated product, for which registration is sought, on the targeted harmful organisms.

The formulated product must be tested under conditions where it is evident that the harmful organism is present in levels capable of affecting output, quality, etc.

For each formulated product being submitted for registration, the applicant shall present the results of experiments conducted in one or more countries of the CEMAC zone and covering, as the case may require, the following ecological zones:

- Sahelian zone;
- Sudano-Sahelian zone;
- Guinean zone
- Forest zone

The number and type of tests shall be as follows: minimum three years

- First year: one test in station and under operational conditions;
- Second year: one test in station and one test under operational conditions;
- Third year: one test under operational conditions.

In the case where the harmful organisms targeted by the formulated product submitted for registration constitute a problem in all these four ecological zones, the tests shall cover all the zones. On the other hand, if the harmful organisms are only specific to one, two or three of the zones, the applicant shall only be required to present the results from those specific zones.

As specifically concerns locust control, a Sudano-Sahelian zone shall be necessarily taken into account in assessing the biological effectiveness.

CPAC may decide to grant a PSA on the basis of reliable results obtained during the first two years of the tests sequence. Moreover, in certain cases, repetition in space might replace a repetition of independent tests in time.

For registration, however, the applicant shall be required to present the results of experiments conducted over a period of at least three years, in one or more CEMAC countries and covering, as the case may be, the targeted ecological zones.

4.1.2 Report contents

Reports on the studies on the biological effectiveness of the formulated product submitted for registration must be presented in conformity to the Framework Protocols and Specific Protocols of CPAC. In the case where these protocols are not available for a given combination (crop/harmful organism), the reports shall comply with the EPPO Directives on effectiveness data required for registration of pesticides.

4.2 A summary of:

4.2.1 The action mechanism of the active ingredient(s)
E.g. biochemical, physiological

4.2.2 A description of the pathway/route
E.g. repulsion, ingestion, inhalation, contact, systemic

4.2.3 Directions for use

4.2.3a a description of the field of application of the formulated product
E.g. farm, greenhouse, garden, storage of plant or animal products

4.2.3b a specification of each field of application
E.g. for farm use: vegetable crop, cotton crop, grain, horticultural crop

4.2.3c a description of the target organism

E.g. insects, weeds, fungi, nematodes, bacteria, with specification on family, group and genus.

4.2.3d a precision on the application rate, period, stages and frequencies
Include the directions for use recommended for the application of the product.

4.2.3e a precision on the effects of the application of the formulation on output, plant quality, plant or animal products
Organoleptic and commercial quality, aptitude for conservation, transformation and transportation.

4.2.4 Limits for use

4.2.4a An indication on limits for use in order to ensure safety for:

- Crops;
- Animals;
- Substrate treated;
- Persons applying the products;
- Consumers;

4.2.4b An indication of time frames to be respected between the last application of the product and:

- The sowing or planting of the crop;
- The sowing or planting of the next crop in the rotation;
- Access of workers to treated plots of land;
- Access of animals to treated areas;
- Harvesting.

4.2.5 Incompatibilities of the product with other pesticides

4.2.6 Information on the onset or eventual development of a resistance

Nota Bene: **A Provisional Sale Authorization or Registration shall be issued for the fields of application and harmful organisms for which the biological effectiveness tests results are satisfactory.**

It shall comprise:

5.1 Formulated product

The methods of extraction, identification and dosage of the active ingredient(s) contained in the commercial product.

5.2 Residues

5.2.1

The methods of extraction and dosage of the residues of the active ingredient(s) and its/their metabolites classified as residues.

5.2.2

The methods of studying residues in plants and food which are likely to be contaminated (e.g. meat, fat, milk, eggs, stored food, food products).

It shall comprise:

1 a study on the toxicity of the active ingredient(s);

2 a study on the toxicity of the formulated product;

3 a summary of observations of the toxicity of the formulated product to humans;

4 recommendations on therapy and precautions.

The objectives, materials and methods used, as well as the results obtained and references for these studies shall be specified.

6.1 Study on the toxicity of the technical grade active ingredient(s).

Abstracts of the studies shall be supported by references and experiment reports clearly stating the methods used and the vehicle through which the toxic was administered. Studies shall be conducted separately for each of the active ingredients used in the composition of the product.

6.1.1 Acute toxicity

The study shall include the following points:

6.1.1a LD_{50} by oral route

To be conducted among two animal species, including a rodent, males and females, after administering a single dose.

6.1.1b LD_{50} through the skin

Among rabbits or rats, after applying a single dose;

6.1.1c LC_{50} by inhalation

It shall be carried out when the active substance:

- Is a gas, particularly a liquefied gas;
- Is to used as a fumigant;
- Is to be incorporated in a smoke generator;
- Is an spray can;
- Has a vapour pressure $>1x10^{-2}$ Pa and is to be incorporated in preparations intended to be used enclosed space such as storerooms or greenhouses;
- Is to be incorporated in powder preparations containing a significant proportion of particles of a diameter of <50 M (>1% based on weight);
- Is to be incorporated in preparations intended to be applied according to a process producing a significant proportion of particles or droplets of a diameter of <50 M (>1% based on weight).

6.1.2 Irritation of the skin

It shall be conducted among rabbits according to recognized standard methods.

6.1.3 Irritation of the eye

It shall be conducted among rabbits according to recognized standard methods.

6.1.4 Sensitization

The study shall be conducted under any condition, except where the substance is a known sensitizer. It shall be conducted according to recognized standard methods and the results shall clearly indicate if the active substance is allergenic or not.

6.1.5 Chronic toxicity by oral route

In all cases, the animal species used shall be specified. The duration of the study (28 or 90 days) should help to determine the nature of side effects, their reversibility or not and to set the non-observable effect dose.

6.1.6 Chronic toxicity by other routes

Supplementary studies on toxicity through the skin or by inhalation might be required to assess the exposure of the operator.

6.1.7 Genotoxicity

The study on genotoxicity should provide at the minimum, results of the two experiments at each stage. *In vitro* and *in vivo* studies are recommended on somatic cells while *in vivo* studies are recommended on germ cells. The other tests to be conducted shall be subject to the interpretation of results sat each stage.

6.1.7a *In vitro* studies

In vivo mutagenesis tests must always be conducted (bacterial test relating to genetic mutation, clastogenic tests in mammalian cells and mutagenesis tests in mammalian cells).

The following tests might be used:

- Ames test on strains of *Salmonella typhimurium* and/or *Escherichia coli*, with and without activation of hepatic cells by microsomal enzymes;
- Punctual mutation test on *Escherichia coli* and/or on *Saccharomyces cerevisiae*, with and without activation of hepatic cells by microsomal enzymes;
- Punctual mutation test on lymph cells of rats or Chinese hamsters, with and without activation of hepatic cells by microsomal enzymes;
- test on human fibroblasts;
- test on the hepatic cells of rats to identify an eventual unscheduled DNA synthesis;
- test on *Saccharomyces cerevisiae* cultures on mitosis and gene conversion;
- "Pol-A1" test on DNA deterioration among *Escherichia coli* mutants with and without activation of liver by microsomal enzymes;
- "Rec-Assay" test on strains of *Bacillus subtilis* to identify an eventual harmful effect on the DNA.

6.1.7b *In vivo* studies (somatic cells)

The following test may be used:

- Analysis of the metaphase of cells of bone marrow in rodents;
- Micronucleus tests among rodents;
- Unscheduled DNA synthesis test;
- spot test among rats.

6.1.7c *In vivo* studies (germ cells)

The following test may be used:

- dominant lethality test among rats;
- test on hamster (cytogenetics study of Spermatogonia) ;
- test on the Chinese hamster (study on the exchange of sister chromatids and chromosome aberrations) ;

- lethal recessive mutation test on *Drosophila melanogaster*

6.1.8 Long term toxicity / Carcinogenesis

Long term toxicity and the carcinogenicity of every active substance must be determined. If, in certain exceptional cases, it is declared that such tests are not necessary, these declarations must be fully justified.

Long term studies which have been conducted and reported, and which have been incorporated with other data and important information on the active substance, shall be sufficient to identify the resulting effects from repeated exposure to the active substance and sufficient particularly to detect harmful effects resulting from exposure to the active substance, and equally to identify the target organs, establish a dose-response relationship, identify changes in the symptoms and manifestations of toxicity observed and determine the undetectable-effect dose.

Likewise, carcinogenesis studies coupled with other relevant data and information shall be sufficient to enable the assessment of hazards to humans who have been subjected to repeated exposure to the active substance, and sufficient particularly to identify the carcinogenic effects resulting from exposure to the active substance, determine the types and specificity of the induced tumors, establish the dose-response relationship and, for non-genotoxic carcinogens, to identify the maximum dose without harmful effects.

6.1.9 Teratogenicity and embryotoxicity

Experiments shall be carried out among two animal species, including rabbits, and the product shall be administered by oral route during a clearly determined period of the organogenesis.

6.1.10 Effects on reproduction

Studies shall be carried out on at least two generations, with a mating, preferably among rats. Observations shall include fertility (males and females), pre- and post-natal effects on the young and the increase of sensitivity to the product during the generations. The apportioning of administered doses shall be such that at least one dose shall be likely to have an effect following the results of the other toxicity tests.

6.1.11 Delayed Neurotoxicity

The studies shall provide sufficient data to examine whether the active substance can cause a deferred neurotoxicity after acute exposure. These studies shall be conducted for active substances of an identical or relative structure to substances likely to induce a delayed neurotoxicity (e.g. organophosphorous pesticides).

6.1.12 Toxico-kinetic studies

The studies shall be conducted among rats (single doses for two concentrations and repeated studies for one single concentration) on absorption, distribution and accumulation in the body, biotransformation, elimination, etc., of the tested active substance and its metabolites.

6.1.13 Other studies

Other studies could be required as warranted by the results of the toxicity tests or the chemical structure and properties of the active substance.

- Studies on the immuno-toxicological potential;
- Studies on the toxicity of the active substance(s) on animal species other than those previously mentioned;
- Studies on eye abnormalities (cataract) conducted among ducklings;
- Studies on the inhibition of the cholinesterase (plasma, erythrocytes, brain);

- Studies on the toxicity of isomers, solvents, charges, additives, impurities and other by-products contained in the formulation;

6.2 Study on the toxicity of the formulated product

The required toxicity studies shall help to indicate the toxicity class of the formulated product according to WHO classification.

Abstracts of the studies shall be supported by references and experiment reports clearly stating the methods used and the vehicle through which the toxic was administered.

6.2.1 Acute toxicity

The study shall include the following elements:

6.2.1a LD_{50} by oral route

Among male and female rats or mice, after administering a single dose.

6.2.1.b LD_{50} through the skin

Among rabbits or rats, after applying a single dose.

6.2.1c LC_{50} by inhalation

For certain formulations, after a single exposure of the animal according to recognized standard methods. The preferable animal species to be used for this test shall be the rat. The test could also be conducted among any other species provided for under recognized standard methodologies.

Formulations for which LC_{50} is required include the following:

- A gas, particularly a liquefied gas;
- A smoke formulation or fumigant;
- An aerosol;
- A powder containing a significant proportion of particles of a diameter of <50 M (>1% based on weight);
- A formulation applied by aircraft in cases where exposure through inhalation is pertinent;
- A formulation likely to contain an active substance whose vapour pressure is $<1x10^{-2}$ Pa and is to be used in an enclosed space such as storerooms or greenhouses;
- A formulation intended to be applied according to a process producing a significant proportion of particles or droplets of a diameter of <50 M (>1% based on weight).

6.2.2 Irritation of the skin

The study shall be conducted among rabbits, according to recognized standard methods. This test shall not be necessary if it is established that the product is corrosive.

6.2.3 Irritation of the eye

The study shall be conducted among rabbits, according to recognized standard methods. This test shall not be necessary in the case where the product causes a strong irritation of the skin.

6.2.4 Sensitization

The study shall be conducted according to recognized standard methods and the results shall clearly indicate whether the product is allergenic or not.

6.2.5 Data on exposure

This shall include data aimed at protecting workers against risks of exposure to the products.

6.2.5a Assessment and measure of exposure of the operator

An assessment of the exposure of the operator, under the proposed conditions of use, shall be made through the use of an appropriate numerical model. The assessment shall be made in the assumption where the operator is not using any individual protective equipment and in a second assumption where the operator uses efficient protective equipment available on the market.

The efficacy data on exposure concerning the principal exposure route(s) shall be reported if the risk assessment indicates that a threshold value on health has been exceeded.

6.2.5.b Assessment and measure of exposure of persons present

People present might be exposed to the products during application. An assessment of the exposure of such persons shall be made for each application method. The assessment shall be made in the assumption where the persons present are not wearing any individual protective equipment. Protection measures for persons present may be required where the assessments show a preoccupying situation.

6.2.5c Assessment and measure of exposure of workers

Workers might be exposed following the application of products, by entering treated farms or premises, or by handling plants or plant products on which residues persist. Sufficient data shall be reported to provide a selection basis for appropriate protection methods, including waiting time and time to keep away from the treated premises.

In the case where skin exposure is the main exposure route, an absorption test through the skin shall, if it is not already available, be a useful replacement test to fine-tune the assessment.

6.2.5d Skin absorption

It shall be conducted where skin exposure is a significant exposure route and where risk assessment indicates that a threshold value on health has been exceeded.

6.2.5e Available toxicology data on non active substances

Modalities for a specific information system on possibly hazardous non active substances shall be fixed. The applicant shall provide maximum available information to this end.

6.3 Summary of observations on the toxicity of formulated product to humans

The studies shall lay emphasis on the summary of observations (where they are available) carried out on the toxicity of the product to humans, especially with regard to the medical records of the workers handling the product, the direct clinical observation of cases of deliberate or accidental poisoning and reported cases of hypersensitivity. Where the data is available, the nature of metabolites in humans shall be specified. If possible, the dangerous dose for humans shall be assessed from all these data.

The following shall be indicated:

- Signs and symptoms of intoxication in the case of intoxication in humans;
- Emergency measures and contraindications in the case of accident and/or malaise;
- Therapy, antidote and emergency treatment;
- Safety measures for storage and transportation;
- Decontamination procedures.

6.4 Recommendations for therapy and precautions

Recommendations shall include the following elements:

6.4.1 Diagnosis and symptoms of poisoning

6.4.2 First aid emergency measures in case of intoxication and contraindications

6.4.3 Therapy and antidotes

Treatment(s) to be administered by physician shall be described and, should the need arise, the antidotes and their modes of administration shall be indicated as well as the contraindications;

6.4.4 Safety measures

6.4.4a Precautions to be taken for transportation;

6.4.4b Precautions to be taken for storage;

6.4.4c Precautions to be taken in case of fire outbreak;

6.4.4d Precautions to be taken in handling packaging;

6.4.4e Precautions to be taken in case of leakage or accidental spillage;

6.4.4f Recommendations for decontamination of application material, clothing and protective equipment;

6.4.4g Instructions and/or proposals to feature on the packaging.

Nature of risks: Precautions to be taken before, during and after application aimed at ensuring safety in the use of the pesticide.

It shall include:

1 studies on the behaviour and evolution of the pesticide in the environment

2 studies on the effects of the pesticide on non-target organisms.

Since these studies are quite voluminous, the applicant shall only provide sufficiently detailed abstracts (objective of the study, materials and methods used, results obtained and references of the study) so as to facilitate comprehension of the studies. However, the complete reports of certain studies might be requested by CPAC.

The requirement to carry out environmental studies shall depend on several factors: the field and mode of utilizing the product, probability of exposure of the environmental compartment or the non-target organism and the results of studies carried out earlier on. Certain basic studies shall always be required, while others, more comprehensive, shall be demanded in the case where risk assessment based on the basic studies shall warrant the necessity.

The studies shall be conducted in conformity with internationally recognized protocols of directives, such as those of the OECD, the European Union, or SETAC. **For each study, reference shall be made (in the file) to the protocol and/or directives applied.**

Studies required in this chapter include the minimum requirements for a PSA and registration. However, the applicant may provide information and/or results of supplementary studies describing the environmental effects of the product submitted for registration.

7.1 Behaviour and evolution of the pesticide in the environment

7.1.1 Evolution and behaviour in the soil

7.1.1a Means of degradation in the soil

Laboratory studies

Laboratory tests shall be conducted in order to identify the process involved (chemical and biological degradation), the relevant compounds of the product present in the soil (active substance, metabolites, reaction products, etc.) as well as the extractable or non extractable residues. The tests shall be carried out in at least one soil type of the CEMAC zone. The results shall be presented in the form of schematic diagrams.

The aerobic degradation means shall always be described except where the possibility of soil contamination is excluded (e.g. treatment of enclosed spaces, treatment of products in storage, internal domestic use and veterinary products).

The description of the means of anaerobic degradation shall only be required in cases of anaerobic conditions (e.g. the treatment of surface water, irrigation or drainage zones, etc.).

The photodegradation means shall always be described except where the possibility of deposition on the soil surface is excluded (e.g. the treatment of enclosed spaces, treatment of stored food internal domestic use and veterinary products).

The tests shall be conducted with technical grade active substance. However, studies shall also be conducted with the exact formulation to be registered where the extrapolation of results from the active substance is not possible (e.g. for slow-release formulations).

Field studies
Field studies shall generally not be required.

7.1.1b Degradation rate in the soil

Laboratory studies
The aerobic degradation rate in the soil shall be assessed in at least three soil types of the CEMAC zone. The studies shall enable the determination of the TD_{50} and TD_{90} for each soil type.

The aerobic degradation rate shall always be assessed except where the possibility of soil contamination is excluded (e.g. treatment of enclosed spaces, treatment of products in storage, internal domestic use and veterinary products).

The description of the means of anaerobic degradation shall only be required in cases of anaerobic conditions (e.g. the treatment of surface water, irrigation or drainage zones). The test shall be conducted on the same soil used for the study on the means of degradation (see 7.1.1a).

The tests shall be conducted with a technical grade active substance. However, studies shall also be conducted with the exact formulation to be registered where the extrapolation of results from the active substance is not possible (e.g. for slow-release formulations).

Standard studies shall be conducted at 20° C and they shall be acceptable. However, given that the degradation rate might be faster because of high temperature, supplementary studies at 25-30° C shall be encouraged for a better assessment of the impact of temperature on the degradation of the pesticide.

Field studies
Dissipation
A study on dissipation in the soil (TD_{50}, TD_{90}) shall always be required, except where the possibility of soil contamination is excluded (e.g. treatment of enclosed spaces, treatment of products in storage, internal domestic use and veterinary products).

The study shall be conducted with a technical grade active substance, in the CEMAC zone or under similar environmental conditions. The study shall equally be conducted with the formulation where it is not possible to extrapolate the results from studies with the above mentioned active substance (e.g. slow-release formulations).

Residues
A study may be required to determine the rate of residues during harvesting, sowing or planting of the next crops. It shall, in general, be required when the TD_{50} (laboratory) is superior to one third of the period spanning from the application to harvesting and when absorption of the residue by the next crop is possible.

The study shall be conducted with a technical grade active substance, in the CEMAC zone, or under similar environmental conditions. The study shall equally be conducted with the formulation where it is not possible to extrapolate the results from studies with the above mentioned active substance (e.g. slow-release formulations).

Accumulation
A study of the accumulation of the active substance and metabolites in the soil may be required where the product is persistent (TD_{90} > 12 months) where repeated applications are considered.

The study shall be conducted with a technical grade active substance, in the Sahel zone, or under similar environmental conditions. The study shall equally be conducted with the formulation where it is not possible to extrapolate the results from studies with the above mentioned active substance (e.g. slow-release formulations).

7.1.1c Adsorption / desorption in the soil

Laboratory studies
The data provided should be enough to determine the adsorption coefficient of the active substance, metabolites and degradation and reaction products, with a toxicological and environmental effect, or representing more than 10% of the original active substance. The magnitude of the residues shall be evaluated.

The study shall be conducted in at least three soil types of the CEMAC zone.

The adsorption and desorption capacity shall always be assessed, except where the possibility of soil contamination is excluded (e.g. treatment of enclosed spaces, treatment of stored food, internal domestic use and veterinary products).

The study shall be conducted with a technical grade active substance.

Field studies
Field studies shall generally not be required.

7.1.1d Mobility in the soil

Laboratory studies
The data provided should be sufficient to assess the mobility and leaching potential of the active substance and, if possible, metabolites and degradation and reaction products, having a toxicological and environmental effect, or representing more than 10% of the original active substance.

The study shall be conducted in at least three soil types of the Sahel zone.

The mobility in the soil shall always be assessed, except where it can be assessed from adsorption/desorption data, or where the possibility of soil contamination is excluded (e.g. treatment of enclosed spaces, treatment of stored food, internal domestic use and veterinary products).

The tests shall be conducted with technical grade active substance. However, studies shall also be conducted with the exact formulation to be registered

where the extrapolation of results from the active substance is not possible (e.g. for slow-release formulations).

Field studies

A field study of mobility may be required where it is not possible to extrapolate the results from the above laboratory studies (e.g. for slow-release formulations). The study shall be conducted with the formulated product in the CEMAC zone or under similar environmental conditions.

7.1.1e Assessment of foreseeable concentrations in the soil

An assessment of the foreseeable concentrations in the soil shall be provided. It shall correspond to a single application of the product (the highest application dose) for which registration is sought. In addition, an assessment of these concentrations shall be done for the maximum number of applications at the highest dose, during a crop season.

The assessments shall be made for each soil type. In addition to the concentration of the active substance, the estimations shall include the concentrations of metabolites and the degradation and reaction products having a toxicological and environmental effect.

7.1.2 Evolution and behaviour in water

7.1.2a Means of degradation in aquatic environment

Laboratory studies

Laboratory tests shall be carried out in order to identify pertinent compounds of the product present in water, in seabed sediments and on suspended matter (active substance, metabolites, reaction products, etc.), as well as the processes involved (hydrolysis, photochemical and biological degradation). The results obtained shall be presented in the form of schematic diagrams.

The means of degradation in an aquatic environment must always be described, except where the possibility of water contamination is excluded (e.g. treatment of enclosed spaces, treatment of stored food, internal domestic use and veterinary products).

The tests shall be conducted with a technical grade active substance.

Field studies

Field studies shall generally not be required.

7.1.2b Degradation rate in aquatic environment

Laboratory studies

Laboratory studies shall be conducted in order to assess the degradation rate of the active substance. Tests on the hydrolysis rate, the photochemical degradation rate and the biological degradation rate shall be conducted.

The degradation rate in the aquatic environment must always be described, except where the possibility of water contamination is excluded (e.g. treatment of enclosed spaces, treatment of stored food, internal domestic use and veterinary products).

The tests shall be conducted with a technical grade active substance.

Field studies
Field studies may be required where it is not possible to extrapolate the results from the above laboratory studies. They shall be conducted with the formulated product in the CEMAC zone or under similar environmental conditions.

7.1.2c Assessment of foreseeable concentrations in water

Assessments of the foreseeable concentrations in surface water and underground water shall be provided. They shall correspond to the highest application dose and the number of applications of the product for which registration is sought.

In addition to the concentration of the active substance, the estimations shall include the concentrations of metabolites and the degradation and reaction products having a toxicological and environmental effect.

7.1.3 Evolution and behaviour in the air

As of now, there are no specific requirements for the assessment of the evolution and behaviour of the pesticide in the air.

7.1.4 Definition of the residue

It is necessary to propose a definition of the residue in the soil, water or air, taking into consideration their toxicological and environmental levels and effects. The definition of the residue shall be used for environmental and toxicant monitoring.

7.2 Effects of the pesticide on non-target organisms

7.2.1 Toxicity to birds

7.2.1a Acute toxicity by oral route

Of the technical grade active substance
The acute LD_{50} of the technical grade active substance by oral route shall be determined for two bird species at least. The appropriate species shall include the pigeon, the Japanese quail, the duck, and the *Bengalius* sparrow. For the Sahel zone, the warbling silverbill *(Lonchura malabarica*) shall be acceptable. The species shall be chosen with regard to their feeding behavior and exposure risks.

Studies shall be required for all areas of use, except for products specifically intended for internal domestic use (e.g. aerosol bombs, coils) and those used in the treatment of enclosed spaces and stored food.

Of the formulation
A study of the acute toxicity by oral route with the formulated product shall only be required where the TERa[1] or the TERst[2] of the active substance is between 10 and 100. In addition, a study with the formulated product shall be required where the product is composed of several active substances and the results of the studies on mammals show that the toxicity of the formulated

[1] **TERa** (acute toxicity/exposure ratio) = LD_{50} (mg active substance/kg body weight) / ETE (estimated theoretical exposure) (mg active substance/kg body weight).

[2] **TERst** (subacute food toxicity/exposure ratio) = LC_{50} (mg active substance/kg food) / ETE (estimated theoretical exposure) (mg active substance/kg food).

product is higher than expected on the basis of the additivity of the toxicity of active substances separately.

The study shall be conducted with the most sensitive species determined in the studies with the active substance.

7.2.1b Palatability / acute toxicity by oral route

A study on palatability shall be conducted for granulated formulations, pellets, poison baits and treated seeds. In addition, the study shall be done (with an appropriate food) for all formulations with a TERa<10.

For consumption cases, the acute LD_{50} by oral route shall be determined for at least one bird species. The appropriate species may be taken from the list given under 7.2.1a, taking into consideration their feeding behaviour and the treated substance.

The study shall be conducted with the formulated product.

7.2.1c Subacute food toxicity

Of the technical grade active substance

The LC_{50} and the subacute food NOEC shall be determined at one bird species. The species studied shall be chosen on consideration of their feeding behaviour and exposure risks. The species mentioned under 7.2.1a shall in general be acceptable for the study.

Studies shall be required for all areas of use, except for products specifically intended for internal domestic use (e.g. aerosol bombs, coils) and those used in the treatment of enclosed spaces and stored food.

The subacute food study shall be conducted with the technical grade active substance.

Of the formulation

A study with the formulated product shall equally be required where the formulation is composed of several active substances and the results of the studies on acute toxicity (7.2.1a) show that the toxicity of the formulated product is higher than expected on the basis of the additivity of the toxicity of active substances separately.

In case of consumption of the formulation in the palatability test (see 7.2.1b), a subacute toxicity study shall be required with the granules, pellets, poison baits or treated seeds.

7.2.1d Sub-chronic and/or reproductive toxicity

Data on the sub-chronic or reproductive toxicity may be required:

- Where there exists a prolonged exposure risk due to the frequency and methods of applying the formulation;
- Where there are indications that the substance is accumulating;
- Where harmful effects may be considered in the light of experiments carried out with similar products or results of acute and subacute toxicity tests of the active substance;
- Where the long term effects of the active substance can not be predicted due to absence of knowledge on the relationship between its chemical structure and its toxicity.

The sub-chronic and/or reproductive studies shall be conducted with the technical grade active substance.

7.2.1e Cage or field studies

The study should enable an assessment of the nature and scope of the risk involved in the use of the product, under practical conditions, in the CEMAC zone.

Where the TERa and TERst >100, and where sub-chronic and/or reproductive studies with the active substance do not show the existence of risks, cage or field studies shall not be necessary.

For any other case, an informed opinion shall be required to decide if it is necessary to conduct cage or field studies in CEMAC zone.

As an indication, these studies shall normally be required by CPAC:

- Where the TERa and TERst <10, or where the TERlt[3] <5 (except where the final assessment is possible on the basis of the palatability study);
- For products intended for large scope aerial or land treatments (e.g. locust control, control of vectors), except it can be deduced from the above studies that the risk to birds is negligible.

The cage or field studies shall be conducted with the formulated product.

Results of studies carried out in other ecological regions and/or in similar climatic regions may replace, in certain cases, the requirement for a study in the Sahel region.

7.2.2 Toxicity to reptiles

NOTE: Given that standardized protocols are not yet available for these tests, laboratory data on reptiles shall not, as of now, be required.

7.2.2a Acute toxicity

The LD_{50} by oral route (and eventually through the skin) shall be determined for one reptile species at least.

The study shall be required for products intended for soil treatment, farm treatment (land and aerial) and water treatment.

7.2.2b Subacute food toxicity

The subacute food LC_{50} shall be determined for one reptile species at least.

7.2.2c Sub-chronic and/or reproductive toxicity

- Data on the sub-chronic or reproductive toxicity may be required: Where there exists a prolonged exposure risk due to the frequency and methods of applying the formulation;
- Where there are indications that the substance is accumulating;

[3] **TERlt** (long-term food toxicity/exposure ratio) = NOEC (mg active substance/kg food) / ETE (estimated theoretical exposure) (mg active substance /kg food).

- Where harmful effects may be considered in the light of experiments carried out with similar products or results of acute and subacute toxicity tests of the active substance;
- Where the long term effects of the active substance can not be predicted due to absence of knowledge on the relationship between its chemical structure and its toxicity

The study shall be required for products intended for soil treatment, farm treatment (land and aerial) and water treatment.

7.2.3 Other studies on land vertebrates

Studies on secondary poisoning, tests with other vertebrate species, or other necessary studies to assess the risk of the product for vertebrates, may be requested by CPAC, either for the delivery of a PSA or for registration.

7.2.4 Toxicity to fish

7.2.4a Acute toxicity

Of the active substance

The LC_{50} after 96 hours shall be determined for at least two appropriate fish species. Only the species recommended by standard methodologies shall be used, including at least one tropical species (e.g. catfish, carp). The Sahel species *Oreochromis niloticus* ("tilapia") may also be used.

The studies shall be obligatory for the following areas of use of pesticides: soil treatment, farm treatment (land or aerial), external domestic use, water treatment, rodenticides. They may be required for all other areas of use where there is a possibility of exposure of water with the product.

The study shall be carried out with technical grade active substance.

Of the formulation

Laboratory studies on fish with the formulation submitted for registration shall be required where the risk of the pesticide can not be predicted from the studies with the active substance. This may be the case for formulations with several active substances, or formulations containing substances likely to increase the toxicity of the active substance (e.g. certain solvents, dispersants, etc.).

Studies with the formulation shall always be required for products intended to be applied directly on water. These studies may also be required where there exist a high risk of contamination of surface water.

Where one of the three groups of organisms assessed under 7.2.4 to 7.2.6 is much more sensitive to the active substance than the others (a factor of 100, or above), the studies with the formulation shall be conducted only with the most sensitive species. Where applicable, the studies shall be conducted with at least one species of each of the three groups of aquatic organisms (fish, invertebrates, algae).

7.2.4b Chronic toxicity

The study shall be conducted in order to determine the EC_{50} and the NOEC for at least one appropriate species of fish.

A chronic study with an appropriate species of fish shall be required:

- For each product applied directly on water, or very near to surface water, (e.g. aquatic herbicides, treatment of rice in the presence of water, certain vector control treatments {e.g. mosquitoes, black flies}, anti-avian treatment), where the TD50> 2 days;
- Where there are indications of accumulation of the active substance;
- Where results of short-term toxicity studies warrant such a study.

The study shall be conducted with the technical grade active substance.

7.2.4c Bioaccumulation

Where a product is suspected to be bioaccumulable (Log P_{ow} > 3), a study on bioaccumulation among fish shall be required in the case where the formulated product is intended for the following fields of use: soil treatment, farm treatment (land or aerial), water treatment, rodenticides. They may be required for all other areas of use where there is a possibility of exposure of water with the product.

In the light of the results of this study, complementary tests on bioaccumulation may be required.

The study shall be conducted with the technical grade active substance.

7.2.5 Toxicity to aquatic invertebrates

7.2.5a Acute toxicity

Of the active substance

The determination of the acute EC_{50} for at least one appropriate organism species shall be required. The study may be conducted with the standard species *Daphnia magna*, or with one of the Sahelian species *Caridina africana* (Crustacean), *Streptocephalus sudanicus* (Crustacean) or *Anisops sardeus* (aquatic insect).

The studies shall be obligatory for the following areas of use of pesticides: soil treatment, farm treatment (land or aerial), external domestic use, water treatment, rodenticides. They may be required for all other areas of use where there is a possibility of exposure of water with the product.

In the case of direct exposure of water with the pesticide, a study on at least one species of each of the following three groups of invertebrates shall be required: aquatic insects, aquatic crustaceans, and aquatic shellfish.

The studies shall be conducted with the technical grade active substance.

Of the formulation

Laboratory studies on aquatic invertebrates with the formulation to be registered shall be required where the risk of the pesticide can not be predicted from the studies with the active substance. This may be the case for formulations with several active substances, or formulations containing substances likely to increase the toxicity of the active substance (e.g. certain solvents, dispersants, etc.).

Studies with the formulation shall always be required for products intended to be applied directly on water. In this case, a study on at least one species of each of the following three groups of invertebrates shall be required: aquatic insects, aquatic crustaceans, and aquatic shellfish.

These studies may also be required where there exists a high risk of contamination of surface water.

Where one of the three groups of organisms assessed under 7.2.4 to 7.2.6 is much more sensitive to the active substance than the others (a factor of 100, or above), the studies with the formulation shall be conducted only with the most sensitive species. Where applicable, the studies shall be conducted with at least one species of each of the three groups of aquatic organisms (fish, invertebrates, algae).

7.2.5b Chronic toxicity

Determination of the EC_{50} and NOEC, for at least one appropriate aquatic invertebrate species, preferably the *Daphnia magna.* (After developing standard protocols for the chronic tests, the study may also be conducted with a Sahelian species such as *Caridina africana* or *Streptocephalus sudanicus.*)

A chronic study with an appropriate aquatic invertebrate species shall be required:

For each product applied directly on water, or very near to surface water, (e.g. aquatic herbicides, treatment of rice in the presence of water, certain vector control treatments {e.g. mosquitoes, black flies}, anti-avian treatment), where the TD50> 2 days;

Where results of short-term toxicity studies warrant such a study.

The study shall be conducted with the technical quality active substance.

7.2.6 Toxicity aquatic algae

7.2.6a Effects on growth

Of the active substance

The determination of the EC_{50} and the NOEC for the growth of algae shall be required. In general, the study shall be conducted with green algae (e.g. *Scenedesmus subspicatus* ou *Selenastrum capricornutum*).

The studies shall be obligatory for the following areas of use of pesticides: soil treatment, farm treatment (land or aerial), external domestic use, water treatment, rodenticides. They may be required for all other areas of use where there is a possibility of exposure of water with the product.

In the case of a herbicide, a study on at least a second species of another group of algae (e.g. diatoms or blue-green algae) shall be required.

The study shall be conducted with the technical grade active substance.

Of the formulation

Laboratory studies on algae with the formulation to be registered shall be required where the risk of the pesticide can not be predicted from the studies with the active substance. This may be the case for formulations with several active substances, or formulations containing substances likely to increase the toxicity of the active substance (e.g. certain solvents, dispersants, etc.).

Studies with the formulation shall always be required for products intended to be applied directly on water. These studies may also be required where there exists a high risk of contamination of surface water.

Where one of the three groups of organisms assessed under 7.2.4 to 7.2.6 is much more sensitive to the active substance than the others (a factor of 100, or above), the studies with the formulation shall be conducted only with the most

sensitive species. Where applicable, the studies shall be conducted with at least one species of each of the three groups of aquatic organisms (fish, invertebrates, algae).

7.2.7 Other studies on aquatic organisms

Studies with other aquatic organisms, with fish juveniles, microcosm/ mesocosm tests, or field studies may be required by CPAC, either to deliver a PSA or for registration. Expert opinion shall always be required in order to determine the need.

Studies that shall normally be required by CPAC include:
For every herbicide, studies on aquatic plants shall be required;
Where there exists a real risk of contamination of estuaries or marine areas, studies on aquatic estuary species shall be required;
Where there exists a real risk of persistence of the product in sediments, studies on organisms living in the soil shall be required.

7.2.8 Toxicity to bees

7.2.8a Acute toxicity

At least one acute toxicity test by oral route and an acute toxicity test by contact for bees shall be required.

The study shall be required for all areas of use, except where exposure of bees can be excluded. This shall be case for treatment of seeds and the soil with non-systemic compounds, treatment of enclosed spaces and stored food, rodenticides, internal domestic use and veterinary use.

The study shall, in general, be conducted with the formulated product, but any study conducted with the technical grade active substance may also be accepted. Where the formulation contains more than one active substance, the study shall always be conducted with the formulated product.

7.2.8b Toxicity of residues

A laboratory or cage study on the toxicity of residues on crops may also be required where the QHC[4] > 50. An informed opinion shall be required to decide the relevance of such assessment.

The study shall be conducted with the formulation.

7.2.8c Toxicity to larvae

A feeding test of the brood of bees may be required in order to assess the toxicity of the product to larvae.

This study shall always be required where the active substance is likely to act as an insect growth regulator.

The study shall, in general, be conducted with the formulated product, but any study conducted with the technical grade active substance may also be accepted. Where the formulation contains more than one active substance, the study shall always be conducted with the formulated product.

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[4] **QHC** (hazard-contact quotient) = application dose (kg/ha) / acute LD_{50} by contact (µg active substance/bee)

7.2.8d Cage, tunnel or field tests

A cage, tunnel or field test may be required in order to assess the risk of the product under relatively natural conditions.

This study may be required where the QHC and the QHO[5] > 50. An informed opinion shall be necessary to decide the relevance of such assessment.

The study shall be conducted with the formulation.

7.2.9 Toxicity to natural pest enemies

Data on the toxicity of the product shall be required on 4 parasitoid or natural pest enemy species. In principle, the tests shall be conducted on a species representing each of the four major natural enemy groups: predators living on/in the soil, predators living in vegetation, predacious mites and parasitoids. At least one of these species should be of the CEMAC zone; the other data may come from temperate or tropical species.

Where the product is intended for use within the framework of integrated pest management in CEMAC zone, all of the tests shall be conducted with the species of the sub-region.

The studies shall be required for all areas of use, except where exposure of the natural pest enemies is excluded. (e.g. treatment of seeds with non-systemic compounds, rodenticides, internal domestic use and veterinary use).

The study shall, in general, be conducted with the formulated product, but any study conducted with the technical grade active substance may also be accepted. Where the formulation contains more than one active substance, the study shall always be conducted with the formulated product.

7.2.10 Toxicity to soil invertebrates

7.2.10a Acute toxicity

The determination of the acute toxicity of the product to non-target earthworms or termites may be required to assess the risk of the pesticide to soil organisms.

For products intended to be used mainly in semi-arid or arid zones (e.g. locust control), the study shall be conducted with termites. Test protocols are now available for *Psammotermes* and *Odontotermes*. For products intended for use in more humid zones, the study shall be conducted with the earthworm. Temperate species shall be accepted in this case.

The study shall be required for all areas of use, except where exposure of the soil invertebrates is excluded. This shall be case for the treatment of enclosed spaces and stored food, internal domestic use, rodenticides and veterinary use).

The studies shall be conducted with the technical grade active substance or with the formulation. They shall be required with the formulation where it is impossible to extrapolate from the results obtained with the active substance (e.g. for slow-release formulations and formulations containing more than one active substance).

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[5] **QHO** (hazard - oral quotient) = application dose (kg/ha) / acute oral LD_{50} (µg active substance/bee)

7.2.10b Other studies

Other studies with soil invertebrates (sub-lethal effects or field tests) may be required where the results of acute toxicity tests show a long term hazard. This might be the case with relatively persistent products (e.g. TD_{90} > 90 days).

7.2.11 Toxicity to non-target soil micro-organisms

The studies shall be conducted in order to assess the impact of the pesticide on soil respiration and nitrogen conversion. Where the pesticides are intended for the sterilization of the soil, the studies shall aim at determining the recovery rate after treatment.

The study shall be required for all areas of use, except where exposure of the soil micro-organisms is excluded. This shall be case for the treatment of enclosed spaces and stored food, internal domestic use, rodenticides and veterinary use).

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The studies may be conducted with the active substance or with the formulation.

It shall include:

1. Studies on metabolism and transformation of residues
2. Studies on the residual rate
3. Studies on the exposure of the consumer

8.1 Studies on the metabolism and transformation of residues

8.1.1 Studies of residue metabolism in plants

The studies shall involve crops or group of crops on which the pesticide to be registered shall be used in CEMAC zone. The studies shall be conducted within the CEMAC zone, but data from other climate zones may also be accepted, provided that the categories of plants studied are the same or are very similar to those treated in the CEMAC zone.

Studies on the metabolism in the plant shall be required for at least three crops, except where it can be justified that a different metabolism is very unlikely, or if the registration of the pesticide is sought for less than three crops. Where registration is sought for different categories of crops, the studies shall be typical of such categories. Five main categories of crops are recognized for this purpose:

- Root vegetables;
- Leafy vegetables;
- Fruits;
- Legumes and oil seed crops;
- Cereals.

Where the results show that the metabolism of the pesticide may be variable, studies on more than three plant categories shall be required.

The studies shall be conducted with the technical grade active substance.

Studies shall always be required, except where it is possible to prove that no residue shall remain on crops or agricultural products intended for consumption by humans or animals. However, studies shall not be required where it can be proved that the crop to be treated shall not be destined for human or animal consumption.

CPAC shall encourage the presentation of abstracts of metabolism studies in plants already assessed and approved by international bodies like the WHO/FAO Joint Meeting on Pesticide Residues (JMPR) or the Commission of European Communities.

8.1.2 Studies on the metabolism of residues in farm animals

These studies shall be conducted with lactating ruminants (e.g. cow, goat or she-camel) or poultry in egg-laying period.

The studies shall be conducted within the CEMAC zone, but data from other climate zones may also be accepted, provided that the categories of animals studied are the same or are very similar to those that will be exposed to the pesticide in the CEMAC zone.

The studies shall be conducted with the technical grade active substance.

These studies shall be conducted where the pesticide is applied directly to animals or to buildings housing them. In addition, the studies shall be required where significant residues may exist in animal feed. A pesticide residue shall be considered significant when its concentration level is superior to 1 mg/kg in animal feed.

CPAC shall encourage the presentation of abstracts of metabolism studies in animals already assessed and approved by international bodies like the WHO/FAO Joint Meeting on Pesticide Residues (JMPR) or the Commission of European Communities.

8.1.3 Studies on industrial agro-food processing and/or domestic preparation

Studies on processing shall simulate trade or domestic as closely as possible. In general, at least one study shall be required for each group of agricultural products. However, where the agricultural product is an important fraction of the diet, several studies may be required.

Studies shall not be required in the following cases:

- Where no significant residue is present in the plant or agricultural product; except where the acute toxicity is high or where the Acceptable Daily Intake (ADI) i slow. A pesticide residue shall be considered significant when its concentration level is superior to 0.1 mg/kg in food intended for human consumption;
- Where the agricultural products are consumed raw.

The studies shall be conducted with the formulated product.

8.2 Residual rate studies

8.2.1 Assessment of the maximum residual rate in agricultural products

The tests shall be conducted in conformity with recommended or proposed good agricultural practices, i.e. in respect of the doses, frequencies and methods of treatment, identical or very similar to those proposed for registration. The minimum data to be provided for each test shall be those required by the FAO within the framework of *Codex Alimentarius.*

The studies shall involve crops or group of crops on which the pesticide to be registered shall be used in CEMAC zone. The studies shall be conducted within the sub-region, but data from other similar climate zones may also be accepted, provided that the categories of plants studied are the same or are very similar to those treated in the CEMAC zone.

The studies shall always be conducted where the pesticide is intended to be applied on crops or plant products used as food stuff or animal feed, or where the residues in the soil or in other substrates may be absorbed by these plants.

The results of at least 6 relevant tests shall be provided for each group of crops for which registration is sought. With regard to export agricultural products, a minimum of 3 tests shall always be conducted in the CEMAC zone.

The list of export agricultural products shall be available at the CPAC Permanent Secretariat.

The studies shall be conducted with the formulated product.

CPAC shall encourage the presentation of abstracts of metabolism studies in agricultural products or animal feed already assessed and approved by international bodies like the WHO/FAO Joint Meeting on Pesticide Residues (JMPR) or the Commission of European Communities.

8.2.2 Studies on residues in next crops in the rotation

In a first phase, a theoretical assessment of the residual rate evaluated for the next crop in the rotation shall be sufficient. Where the probability of the presence of residues in the next crop can not be excluded, studies on the metabolism and distribution may be required, eventually on the farm.

Where it is shown that significant concentrations of residues (>10% of the quantity of the applied active substance) subsist in the soil or in the plant products, (e.g. straw) up to the period of sowing or planting of the next crop, it shall then be necessary to study the residues in this next crop.

8.2.3 Index of maximum residue limits

A list of Maximum Residue Limits (MRL) already drawn up by other structures or in other countries shall be provided for the crops and agricultural products concerned in the application for registration or eventually for similar agricultural products. The MRLs of the *Codex Alimentarius* shall always be given.

A specific MRL for the Sahel may be proposed, with detailed justifications.

8.3 Studies on the exposure of the consumer

8.3.1 Waiting period

Proposals for waiting periods between the last treatment and harvesting, or between the last application of the product and the consumption of the stored food, shall always be provided. They shall be entirely justified.

8.3.2 Assessment of exposure

An assessment of potential or real exposure to residues due to diet or other causes shall always be provided. It shall be based on a realistic prediction of ingestion according to the diet or animal feed.

It shall include:

9.1 Packaging

The packaging shall preserve all its qualities throughout the storage of the pesticide.

The material chosen shall be perfectly adapted to the physico-chemical properties of the content according to the local storage conditions, particularly in order to avoid corrosion.

Where the content is intended to be used at very small doses particularly for liquid products, the existence of a measure-stopper shall constitute an additional guarantee for proper dosage and safety in use.

The unit volume of the packaging shall, where possible, be adapted to the area unit to be treated, so that the all of the content should be used once.

Secondary packaging, especially in cartons, shall be as solid as possible to facilitate transportation and storage. Transportation indications shall be printed on the secondary packaging and coarse packaging in conformity with international symbols adopted for air, sea, railway, and road transport.

The applicant shall specify:

- The nature of the packaging materials;
- The net weight;
- The dimensions of the packaging: especially the diameter of openings and the closing mechanism;

- Recommendations for disposing of expired products and packaging.

9.2 Labelling model

The labelling shall be designed as a means of attaining a high level of communication between the supplier and the buyer or the user. It shall comprise, in clear and concise terms, fundamental data for the use of the product in total safety and with guaranteed efficiency throughout its life span.

Every application for registration shall include an original labelling model (or the scale model). The data shall be indicated by the manufacturer using indelible characters, clearly visible and easy to read.

The labelling model shall comply with FAO Directives for proper pesticide labelling.

The labelling shall include the following data:

9.2.1 A description of the content:

9.2.1a brand name of the pesticide

9.2.1b name and content of active substances

9.2.1c type of pesticide
(insecticide, herbicide, etc..)

9.2.1d type of formulation

9.2.1e net content expressed in international measurement units

9.2.2 A clearly visible indication of the hazard
By a toxicological strip and a toxicity symbol in conformity with WHO classification of pesticides

9.2.3 Concise indications for precautions to be taken
For safe handling and proper use of the pesticide

9.2.4 Concise indications for first aid treatment in case of intoxication

9.2.5 Indications on the proper use of the product:

9.2.5a how, when and where to use the product:
Specify the crops, pests, and stages of treatment

9.2.5b contraindications
E.g. **"***do not treat during blossoming***"**

9.2.5c precisions on the waiting periods
Last treatment before harvesting, before consumption…

9.2.6 Name and address of the manufacturer (**"***Pesticide manufactured by ..... "*)

9.2.7 Place of manufacture of the product (country)

9.2.8 Name and address of national or regional distributor where they exist (*"Pesticide distributed by….."*)

9.2.9 Registration number (*"Registration Nr.…..."*)

9.2.10 Date of manufacture or formulation (*"Manufactured on …..."*)

9.2.11 Lot number

9.2.12 Expiry date (*"Best before …..."*)

9.2.13 Stability conditions

9.2.14 Caution notice

9.2.15 indication of legal responsibilities

The manufacturer shall use labels featuring as much as possible internationally accepted symbols and pictograms, in addition to the caution instructions and notices.

The label shall adhere perfectly to the packaging; if possible it shall be impermeable and remain perfectly legible no matter what moment it shall be used.

The label shall obligatorily feature the endorsement: *"Read the label carefully before use*".

9.3 Labels for small packaging

For small packaging (of dimensions less than or equal to100 ml for liquids and less than or equal to 100g for solids), the applicant shall be required to provide a notice. This notice shall include all the requirements of the labelling model.

The label on the packaging shall feature the following data:

9.3.1 a description of the content:

9.3.1a brand name of the pesticide

9.3.1b name and content of active substances

9.3.1c type of pesticide
E.g. insecticide, herbicide

9.3.1d type of formulation

9.3.1e net content expressed in international measurement units

9.3.2 A clearly visible indication of the hazard
By a toxicological strip in conformity with WHO classification of pesticides

9.3.3 Indications on the proper use of the content

9.3.4 Name and address of the manufacturer (**"***Pesticide manufactured by ..... "*)

9.3.5 Registration number (*"Registration Nr.…..."*)

9.3.6 Lot number

9.3.7 Manufacture or formulation date (**"***Manufactured on ..... "*)

9.3.8 Expiry date (*"Best before.…..."*)

9.3.9 Endorsement: *"Read the notice carefully before use*".

Appendix 4
Labelling of phytosanitary products

Given that labelling shall be designed as a means of attaining a high level of communication between the supplier and the buyer or the user, it shall comprise, in clear and concise terms, fundamental data for the use of the pesticide in complete safety and with guaranteed efficiency throughout its life span.
The applicant shall provide the data in the official language(s) of CPAC member States (see Appendix 5) written in indelible characters, clearly visible and easy to read.

The label shall feature the following data:
1 a description of the content;
1.1 brand name of the pesticide;
1.2 name and content of active substance(s);
1.3 type of formulation;
1.4 net content expressed in legal units of measurement
2 a clearly visible indication of the hazard: by use of a coloured toxicological band below the label in compliance with WHO classification of pesticides. In addition, the label shall provide concise indications for precautions to be taken for safe handling and use of the pesticide, as well as eventual first aid measures.
3 directions for the sound use of the content
3.1 how, when and where to use the product on crops, pests, and stages of treatment;
3.2 contraindications;
3.3 waiting time
4 name and address of manufacturer
5 place of manufacture
6 name and address of national or regional distributor
7 registration number
8 physical and chemical incompatibilities with other pesticides
9 date of manufacture or formulation, expiry date and stability conditions and written caution notices.

Since all detailed information cannot be given on the label, the manufacturer shall enclose a specifications sheet or technical notice, which may not exceed four pages, to supplement the information on the physical and chemical description of the active substance(s) and the formulation, toxicological data, detailed directions for use and necessary precautions. Such should include directions for the destruction of the empty container, if they are known. In addition, it would be desirable to add specific information for medical officers, hospitals and poison control centres indicating the recommended antidote in case of intoxication.

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