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Abstract NL Deze handleiding beschrijft de toelatingsbeoordeling van chemische pesticiden. De wettelijke achtergronden, benodigde gegevens, de afleiding van referentiewaarden en de methodiek voor beoordeling van humaan en milieurisico's worden beschreven. De beoordeling werd ontwikkeld in het kader van het Programma voor de Reductie van Risico's door Pesticiden in Ethiopie (PRRP - Ethiopia), gefinancierd door het Nederlandse Ministerie van Buitenlandse Zaken / Ontwikkelingssamenwerking, de Voedsel en Landbouw organisatie van de Verenigde Naties (FAO) en de Federale Republiek van Ethiopie.
De toelatingsbeoordeling bestrijkt zowel humane als milieurisico's. Humane risicobeoordeling gebruikt een eenvoudiger categorisatie (acceptabel versus niet-acceptabel) maar kent het gebruik van hogere trappen in de beoordeling. Milieurisico's worden gekenmerkt als laag, mogelijk, en hoog risico, maar de procedure bevat op dit moment niet de mogelijkheid om hogere trappen in de beoordeling te gebruiken.

Abstract UK This handbook describes the evaluation procedure for pesticides based on chemical substances. It describes the legislative background, data requirements, how reference values are derived, and the methodology for estimation of the risks of the application of pesticides to human health and the environment. The evaluation procedure was developed within the Pesticide Risk Reduction Programme (PRRP) – Ethiopia, a project that ran from the beginning of 2010 up to the end of 2014. The project was funded by the State of The Netherlands (Ministry of Foreign Affairs/Development Cooperation), the Food and Agriculture Organisation of the United Nations (Technical Cooperation Programme) and the Federal Republic of Ethiopia (Ministry of Agriculture).

The evaluation procedure addresses various fields of risk assessment, covering both human toxicology and environmental toxicology. Human risk assessment uses a simpler risk characterization (acceptable versus non-acceptable), but allows the use of higher-tier analyses when non-acceptable risks are identified. Environmental risk assessment uses three categories of risk (low risk – possible risk – high risk), but in its current form does not provide for the use of higher tiers.

Keywords: Pesticides, registration, evaluation, Ethiopia

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List of abbreviations

Abbreviation	Explanation
a.i.	Active ingredient
ADI	Acceptable Daily Intake
AOEL	Acceptable Operator Exposure Level
ARfD	Acute Reference Dose
ATSDR	Agency for Toxic Substances and Disease Registry
AUC	Area Under the Curve
CF	Conversion Factor (residue definition) / Correction factor (OECD calculator)
cGAP	Critical Good Agricultural Practice
CXL	CodeX alimentarius maximum residue Level
DF	Default value
dw	Drinking water
DWS	Drinking Water Standard
EC50	Effect Concentration, causing 50% effect
ECMWF	European Centre for Medium-Range Weather Forecasts
EFSA	European Food Safety Agency
EHC	Environmental Health Criteria monographs
EHNRI	Ethiopian Health and Nutrition Research Institute
ERA	Environmental Risk Assessment
ETE	Estimated Theoretical Exposure
ETR	Exposure Toxicity Ratio
EU	European Union
EuroPEARL	PEARL model for use on European scale
EuroPOEM	European Predictive Operator Exposure Model
FAO	Food and Agricultural Organisation
FIR	Food Intake Rate
FOCUS	Forum for Co-ordination of pesticide fate models and their USe
GAP	Good Agricultural Practice
GHS	Globally Harmonized System for Classification and Labelling
GLP	Good Laboratory Practice
GPMT	Guinea Pig Maximisation Test
HR	Highest Residue
IARC	International Agency for Research on Cancer
IEDI	International Estimated Daily Intake
IESTI	International Estimated Short Term Intake
IPCS	Internation Programme on Chemical Safety
IPM	Integrated Pest Management
IPR	Intellectual Property Rights
ITMDI	International Theoretical Maximum Daily Intake
IUPAC	International Union of Pure and Applied Chemistry
IVM	Integrated Vector Management
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPM	FAO/WHO Joint Meeting on Pesticide Management
JMPR	FAO/WHO Joint Meeting on Pesticide Residues
LD50	Lethal Dose, causing 50% mortality
LLNA	Local Lymph Node Assay
LO(A)EL	Lowest Observed (Adverse) Effect Level
log Pow	The logarithm of the octanol-water partition coefficient Pow
LOQ	Limit Of Quantitation
LP	Large Portion
MAF	Multiple Application Factor
MAFF	Japanese Ministry of Fisheries and Food
MoA	Ministry of Agriculture
MRL	Maximum Residue Level
NOEC	No Observed Effect Concentration
NO(A)EL	No Observed (Adverse) Effect Level
OECD	Organisation for Economic Cooperation and Development
PEARL	Pesticide Emission Assessment at the Regional and Local scale
PEC	Predicted Environmental Concentration
PHED	Pesticide Handler Exposure Database
PHI	Pre-Harvest Interval
PHRD	Plant Health Regulatory Directorate (of the Ministry of Agriculture)
PNEC	Predicted No Effect Concentration
POEM	Pesticide Operator Exposure Model, model for estimation of operator exposure
PPE	Personal Protective Equipment

PPP	Plant Protection Product
PRIMET	Pesticides Risks in the tropics to Man, Environment and Trade
PRZM	Pesticide Root Zone Model
PRRP	Pesticide Risk Reduction Program (Ethiopia)
QA	Quality Assurance
RUD	Residue per Unit Dose
RPE	Reduction of Personal Exposure, resulting from the use of PPE
SANCO	EU Directorate General for Health and Consumers
SD	Standard Deviation
SEARCH	Southern and Eastern Africa Regulatory Committee for Harmonization of Pesticide Registration
SG	Suspendable Granule (formulation type)
SP	Suspendable Powder (formulation type)
STMR	Supervised Trial Median Residue
sw	Surface water
TC	Transfer Coefficient
TMDI	Theoretical Maximum Daily Intake
ToIU	Table of Intended Uses
TOXSWA	TOXic substances in Surface WAters
TRIPS	Trade Related Aspects of Intellectual Property Rights
UF	Uncertainty Factor
US EPA	United States Environmental Protection Agency
WG	Wettable Granule (formulation type)
WHO	World Health Organisation
WHO-GEMS	World Health Organisation – Global Environment Monitoring Scheme
WHOPES	World Health Organisation Pesticide Evaluation Scheme
WP	Wettable Powder (formulation type)
WTO	World Trade Organisation

Preface

The Pesticide Risk Reduction Programme (PRRP)-Ethiopia ran from the beginning of 2010 up to the end of 2014. It was funded by the State of The Netherlands (Ministry of Foreign Affairs/Development Cooperation), the Food and Agriculture Organisation of the United Nations (Technical Cooperation Programme) and the Federal Republic of Ethiopia (Ministry of Agriculture).

Its main objectives were:

1. To develop a legal framework for the registration and postregistration of pesticides (regulation, directives and guidelines).
2. To develop a proper pesticide registration system for Ethiopia and capacity building on dossier evaluation.
3. To develop a well-functioning postregistration system (including monitoring, procurement guideline, inspection, storage of pesticides, capacity building and training).
4. To develop a formal consultation platform that will support PHRD with advice on (post) registration issues.
5. To execute an impact assessment of the new (post) registration system.

The PRRP project is intended to serve as a pilot project for other African countries and regions.

This evaluation manual has been written as part of Work Package B2.1 of the PRRP project. The goal of WP B2.1 of PRRP Ethiopia was to further develop the technical and scientific evaluation capacity to ensure sound pesticide management in Ethiopia at the pesticide registration stage, focussing on plant protection products.

Within WP B2.1 a total of fourteen workshops and training sessions were organised. In six workshops improved guidelines for efficacy testing and statistical analysis of the trials were developed, which were incorporated into the new Directive on Pesticides of Ethiopia (developed with assistance of the FAO and Falconsult). This resulted in the development of twenty crop-pest specific protocols for the evaluation of efficacy.

In a further series of seven workshops with representatives of the Plant Health Regulatory Department (PHRD) of the Ministry of Agriculture of Ethiopia and other stakeholders, the dossier evaluation system has been expanded. Protection goals were set and prioritised, and risk assessment procedures were developed. Moreover, capacity building and specific training sessions on dossier evaluation were organized (see www.prrp-ethiopia.org, Activities and Outputs, Dossier Evaluation).

The existing SEARCH data requirements have been improved and the assessment of human health and of environmental hazard and risks have been developed. These assessments, and the data necessary to perform them, are described in this manual. The human health and environmental risk assessment procedures have been implemented in a software tool, PRIMET-Registration_Ethiopia, that will enable the PHRD to perform risk evaluations in a reproducible, user-friendly and transparent way. Details of PRIMET-Registration_Ethiopia are given in a separate manual which can be freely downloaded, together with the software, from www.pesticide.models.eu. The final training on dossier evaluation, held in September 2014, was specifically aimed at the use of PRIMET-Registration_Ethiopia.

Many people have contributed to the workshops, the development of the efficacy testing protocols and the development of the risk assessment procedures. From the Netherlands the main contributors were Paulien Adriaanse, Joost Lahr, Mechteld ter Horst, John Deneer, Louise Wipfler and Jos Boesten (all employed at Alterra), as well as Peter van Vliet, Marloes Busschers, Caroline van der Schoor (employed at the Ctgb), Harold van der Valk (FALCONSULT) and Paul de Boer and Jan-Hendrik Krook (Linge Agroconsultancy). The main contributors from Ethiopia (PHRD) were Alemayehu Woldeamanual, the late Gizachew Assefa (former work package expert of WP B2.1) and Berhan Melese (Ph.D. student at Wageningen University, sponsored by the PRRP-Ethiopia project). The efficacy testing protocols were developed by representatives of several Ethiopian Institutes of Agricultural Research (EIARs). Major Ethiopian contributions to the development of the surface water and groundwater scenarios for drinking water production were given by Dr. Engida Zemedagegenhu of the Water Works Design and Supervision Enterprise-Ethiopia as well as the late Dr. Dereje Gorfu of the EIAR.

1 General introduction

1.1 Introduction

This handbook describes the authorisation evaluation for pesticides based on chemical substances. It describes the legislation background, data requirements, how reference values are derived, and the methodology for estimation of the risks of the application of pesticides to human health and the environment.

The evaluation procedure addresses various fields of risk assessment, covering both human toxicology and environmental toxicology. The basic concept of risk assessment is similar in both fields, comparing an estimated exposure to the level of exposure known to cause toxic effects. However, terminologies differ for historical reasons. Moreover, human risk assessment as described here uses a simpler risk characterization (acceptable versus non-acceptable), but allows the use of higher-tier analyses when non-acceptable risks are identified. Environmental risk assessment uses three categories of risk (low risk – possible risk – high risk), but in its current form does not provide for the use of higher tiers.
The pesticide risks are evaluated for their intended uses as stated in the Table of Intended Uses (ToIU) that is part of the data requirements package as requested by the PHRD from the applicant. Moreover, pesticide risks are only evaluated for Good Agricultural Practices, i.e. (according to the World Health Organization WHO) the 'officially recommended or authorized usage of pesticides under practical conditions at any stage of production, storage, transport, distribution, and processing of food and other agricultural commodities, bearing in mind the variations in requirements within and between regions and taking into account the minimum quantities necessary to achieve adequate control, the pesticide being applied in such a manner as to leave residues that are the smallest amounts practicable and that are toxicologically acceptable.'
The evaluation procedure considers the various protection goals for human health or environment on a one by one basis, so, no overall risk assessments are performed. E.g. the risk for workers may be classified as non-acceptable and the risk for non-target arthropods may be acceptable, but no overall risk assessment of the compound is made. However, if protection goals are composed of several elements an overall risk assessment is made. E.g. the risk for drinking water from surface water is assessed in three scenarios, an overall risk assessment is made by adopting the highest risk assessment of one of the scenarios as the overall assessment for this protection goal: if one (or two) scenario has a non-acceptable risk the protection goal of drinking water from surface water is assessed and summarised as having non-acceptable risk. Another example is the aquatic ecosystem: if one of the elements (e.g. Daphnia) has possible risk and all other elements low risk, the overall risk assessment for the aquatic ecosystem is possible risk.
The reader should be aware that this handbook does not contain any sections on risk management. If a compound is found to exceed one or more risk criteria, it is often possible to mitigate risk to acceptable levels through risk management measures. The principles of risk management are not considered in this manual.

Finally, the authors want to mention explicitly that in this handbook only parent compounds are assessed and not their transformation products, the so-called metabolites. They are aware that there is an urgent need to include metabolite risk assessment, especially for compounds which are toxic for humans. E.g. the entire leaching assessment was started in the late seventies of the twentieth century in the USA due to toxicologically relevant levels of metabolites of aldicarb (aldicarb sulfon and alidicarb sulfoxide) in groundwater at Long Island that was used as source of drinking water by the farmers (see e.g. http://www.who.int/water_sanitation_health/dwq/chemicals/aldicarb.pdf).

Chapter 1 is a general introduction, with information on Ethiopian legislation, FAO/WHO guidelines, data protection and confidentiality of information. Moreover this chapter contains also information to check the quality of data provided by the applicant.

Chapter 2 describes the efficacy assessment of plant protection products and the accompanying data requirements.
In Chapter 3, the human risk assessment is explained. The chapter includes information on hazard and exposure assessment and risk characterisation for occupational health as well as consumer health. It covers the data requirements for mammalian toxicity and residues, derivation of the reference values, and the use of models for exposure estimations.
Chapter 4 gives guidance on the assessment of the risk of pesticides to humans and cattle, resulting from the use of groundwater and surface water as source for drinking water.
The environmental risk assessment is outlined in Chapter 5. It addresses the concern for the potential impact of pesticides on the environment by examining both exposures resulting from pesticide emissions and the effects of such emissions on the structure and function of the ecosystem.

1.2 Legislation and policy background

The importance of pesticides for boosting agricultural production and improving human and animal health has been phenomenal. Whereas there have been enormous gains through the application of pesticides, it was soon clear that the benefits of pesticide use could not be sustained if they continued to be used in a non-judicious way. Their injudicious use would cause negative effects on human beings, non-target animals including fish, birds, natural enemies, beneficial organisms such as bees, earthworms and on plants as well as on soil and water. For this reason, pesticides are among the most rigorously tested and regulated substances in the world, in order to minimize their adverse effects to human and animal health and the environment in general.
Owing to these facts, the Government of Ethiopia has an overall responsibility to regulate the manufacture, formulation, import, transport, storage, distribution, sale, use and disposal of pesticides in line with the International Code of conduct on the distribution and use of pesticides, international conventions and local legislations.
In an effort towards regulating the use and management of pesticides, Ethiopia has developed policies and legal instruments and has also accepted and ratified different international conventions that are critical for sound management of pesticides. Various efforts were made to translate some of the relevant national policies into enforceable laws for sound pesticides management. Since 2004 FAO provided technical assistance for the review of pesticide legislation. This followed the enactment of Pesticide Registration and Control Proclamation No. 674/2010 in August 2010. In early 2013, the full-fledged draft pesticide registration and control regulation that covers virtually all elements of pesticide management has been finalized. This was achieved through the support of FAO and the Pesticide Risk Reduction Program-Ethiopia (PRRP-Ethiopia), which is a joint collaborative project between MoA and the Netherlands' government (through Alterra). This regulation was sent to the Council of Ministers in September 2013 for review and subsequent enactment by the same.
This important work in turn has helped to bring the draft regulation in line with the enacted pesticide proclamation and internationally agreed pesticide registration procedures, data requirements, registration criteria and guidelines for public health and environmental toxicological data that are critical to the decision making process of the registration of pesticides. Moreover, transparency of the registration process was emphasized, as was objectivity in dealing with (matters of) pesticide registration, import and export, competence certificate, licensing, packaging, storage, transportation, packaging, efficacy, labelling use and quality control. This will help Ethiopia to ensure that the entire pesticide management cycle promotes the highest degree of human and animal health and environmental protection.

1.3 Ethiopian data requirements

Ethiopia conforms to the SEARCH (Southern and Eastern Africa Regulatory Committee for Harmonization of Pesticide Registration) data requirements for the registration of chemical pesticides. However the SEARCH application form, active ingredient and formulated product indices and the accompanying guideline has been updated during mid-December 2012 with the assistance of Ctgb registration experts.

Moreover, as it is elaborated above, the data requirements and criteria in connection to chemical pesticides have been given a legal setting for their proper enforcement. A more detailed explanation concerning the use of required data is given in Chapters 3, 4 and 5, which can be used as a guide for Ethiopian pesticide dossier evaluators.

1.4 FAO/WHO guidelines for the registration of pesticides

Other useful information might be found in the FAO/WHO report: International Code of Conduct on the Distribution and Use of Pesticides, Guidelines for the Registration of Pesticides, April 2010:

http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Code/Registration_2010.pdf

The FAO (2010) guidelines indicate that the responsible authority should take the following steps for the assessment of the submitted registration dossier.

- Verification of authenticity: The responsible authority should ensure that an applicant has the rights to submit the registration dossier and the data submitted are authentic.
- Completeness check: The responsible authority should ensure that data in the submitted dossier is complete and in conformity with the officially published data requirements for the intended use of the pesticide.
- Waiving request: The responsible authority should ensure that if there is a request for a waiver from certain data requirements, reasons given are acceptable based on the criteria set.
- Assessment of data quality: The responsible authority should ensure that the data submitted are of acceptable quality and that they comply with the standards required.
- Assessment of registration status in other countries: The responsible authority should ensure that the information is provided and includes information about restrictions.
- Assessment of all technical data: The responsible authority should ensure that the data support the registration for the intended use.
- Risk assessment: The responsible authority should ensure that the risks of using the pesticide according to the proposed label are acceptable.
- Relevance of data: The responsible authority should ensure that all data provided is relevant to the conditions under which the product will be used and to the crops and pests/diseases to which it will be applied.

However, the FAO also recognises that this description of the registration process concerns a comprehensive registration scheme. Many countries will not have the human and financial resources to establish such a scheme in the short term. The FAO provides guidance on the phased introduction of pesticide registration for countries with limited resources.

With the support of the PRRP-Ethiopia project, Ethiopia has already elaborated a detailed process for pesticide registration that includes 14 steps, starting from pre-submission of pesticide dossier meeting until issuance of certification of registration, and approved label and inclusion in the pesticide register and publication on the website. These steps have sufficient legal basis in the draft pesticide registration and control regulation which will be submitted to the Council of Ministers for endorsement in the near future (see the detailed process for pesticide registration in the report of Harold van der Valk et al. Workshop on administration of the Ethiopian Pesticide Registration system, April 2011, Addis Ababa, Ethiopia).

The FAO (2010, Chapter 12) provides more elaborate guidance on the phased introduction of pesticide registration for countries with limited resources. In any case, the actual elements and stages of the registration process applicable in a given country should be published by the responsible authority. For information purposes, Chapter 12 of FAO (2010) is reproduced below.

12. Phased development of a pesticide registrationScheme

Countries developing or strengthening their pesticide registration scheme should not only consider the establishment of an appropriate regulatory framework but also the available resources, both financial and human (professional and scientific capacity), necessary for operating such a scheme.
Depending on the resources available, a country should choose the degree of complexity of the registration procedure that suits it best. Countries with limited resources may initially choose a registration scheme requiring less staff or funding. As experience is gained with the evaluation of pesticide registration dossiers, expertise and infrastructure will be built up and the scheme can progressively be strengthened and tailored to the specific conditions of use in the country.

Two stages of the pesticide registration process are particularly resource-intensive. First, the generation of data for the registration dossier, which is carried out mainly by the applicant but which may also involve public research institutions. Second, the evaluation of the dossier, which is primarily done by the pesticide registration body. Phased development of a registration scheme, when resources are limited, therefore tends to focus on optimizing the use of funds and personnel during these two stages. There are various approaches to the phased development of a pesticide registration scheme, which all have their particular advantages and disadvantages. They include, among others:

- *acceptance of registrations in other countries*. If a pesticide has been authorized in a country with a reputable registration system, the responsible authority may decide to register that same pesticide for the same uses based on only a limited evaluation ofthe dossier;
- *use of existing risk assessments*. If risk assessments exist from reputable pesticide registration bodies in other countries or international organizations, the responsible authority may use such assessments as a starting point for the risk evaluation of a pesticide that has been submitted for registration under comparable use conditions. This is sometimes referred to as a 'bridging approach' to risk assessment;
- *mutual acceptance of data*. If relevant data of good quality have been generated in other countries, the responsible authority may waive the requirement for local data generation. This is particularly relevant for efficacy trials, residue data and environmental field studies, all of which likely require the involvement of national (public) research institutions;
- *prioritize specific groups of pesticides*. In the early stages of development of the registration scheme, the responsible authority may focus on more in-depth evaluation of pesticides which are either likely to be used in high volumes, or by many different groups of users, or on high-value crops that may pose moderate-to-high risk to human health or the environment. This approach would also valuable for the prioritization of pesticides for re-registration;
- *prioritize specific protection goals*. When evaluating a pesticide for registration, its risk for many groups of non-target organisms (e.g. fish, birds, soil organisms) and several human exposure conditions (e.g. consumer, applicator, worker, bystander) is assessed. In the early stages of development of the registration scheme, the responsible Authority may limit data requirements and/or more thorough evaluation to protection goals that are considered high priority for the country;
- *set up fast-track registration channels*. For certain groups of pesticides, (temporary) fast-track registration channels may be set up, which either limit the data requirements or simplify and shorten the dossier evaluation process. The responsible authority may, for instance, temporarily allow fast-track registration for pesticides that have been used on a large scale in the country, and for a long time, without adverse effects or insufficient efficacy having been reported; for pesticides expected to pose very low risk (see 4.4); for minor use products (see 8.4); or for active ingredients or products that already have been authorized in the country on another crop or for another use (see 8.3).

These options for phased development of a registration scheme are not mutually exclusive, and in practice several of the above approaches are generally implemented at the same time. As expertise is built up over time, or as more resources become available, the registration procedures can be further strengthened, data requirements better tailored to local conditions, efficacy and risk evaluations improved and the coverage of the scheme made more comprehensive.

It is generally better to operate a pesticide registration scheme effectively with recognized, but politically accepted, limitations, than to set up a complex system intended to cover all eventualities, which cannot be implemented with the available resources.

Some other aspects explicitly mentioned by the FAO (2010) are reproduced below:

Risk–benefit analysis
According to the FAO (2010) the responsible authority should also use risk–benefit analysis as one of the principles in the consideration for registration of a pesticide. Under certain circumstances, this analysis may have to include evaluation of the potential impact of using the pesticide compared with that of not using it, or comparison of potential risks and benefits of the product under evaluation with other already registered pesticides or locally available pest management options.
In considering the need for a pesticide, the responsible authority should weigh the benefits against the risks the pesticide would pose if it were to be used under local conditions.
Relevant questions that should be considered are whether: the pest(s) for which the pesticide is to be used against is a problem; suitable (non-chemical) or lesser toxic and cost-effective chemical alternatives are available; there is a need for its use in resistance management; or the use of the pesticide is compatible with IPM or IVM. Besides human health and environmental risks there also may be economic risks, for instance if maximum residue limits for certain pesticides on export crops have been set at detection level in the country of destination.

Pesticide classification
All products should be classified according to their hazard, in accordance with the Globally Harmonized System for Classification and Labelling (GHS). As long as this system is not fully implemented, products can be classified according to the WHO hazard classification or any national regulation. Responsible authorities particularly in developing countries should consider the use of colour bands, warning statements and pictograms to reflect the different hazard classes of pesticides to minimize risks posed by pesticides.

Pesticide labelling
Draft labels submitted by applicants should be evaluated based on the requirements and criteria set for registration and should include clear information on the permitted use of the product, dosage and other use recommendations, warning and precautionary statements and description of required personal protection, hazard class, warning statement against the reuse of containers, and instructions on safe disposal or decontamination of empty containers. The responsible authority should also ensure that the approved labels are written in the major language(s) of the country and also include the registration number, lot or batch number, warning and precautionary statements, date of release of lot (month and year).

Highly hazardous pesticides
Compounds meeting the criteria of carcinogenicity, mutagenicity or reproductive toxicity categories 1A and 1B of the Globally harmonized system of classification and labelling of chemicals (United Nations, 2009; http://live.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html) can be regarded as highly hazardous pesticides (JMPM, 2008). The Joint Meeting on Pesticide Management (JMPM) has issued a general recommendation that pesticides meeting the criteria for highly hazardous pesticides should not be registered for use unless:
- A clear need is demonstrated;
- There are no relevant alternatives based on risk–benefit analysis; and
- Control measures, as well as good marketing practices, are sufficient to ensure that the product can be handled with acceptable risk to human health and the environment (JMPM, 2008).

1.5 Quality of data

The data provided by the applicant should be of high quality and reliability: the studies should be conducted according to internationally accepted test guidelines, and with an acceptable code of Good Laboratory Practice (GLP).

1.5.1 Test guidelines

Whenever possible, all toxicity studies must be conducted in accordance with the OECD Guidelines for the Testing of Chemicals or other recognised test guidelines e.g. US Environment Protection Agency (EPA), Japanese Ministry of Fisheries and Food (MAFF), and comply with the principles of Good Laboratory Practice (GLP).

OECD test guidelines:
http://www.oecd.org/env/chemicalsafetyandbiosafety/testingofchemicals/oecdguidelinesforthetestingofchemicals.htm

WHO Pesticide Evaluation Scheme (WHOPES). Guidelines for testing.
http://www.who.int/whopes/guidelines/en/

US EPA test guidelines:
http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm

Japanese MAFF test guidelines:
http://www.mhlw.go.jp/english/topics/foodsafety/residue/dl/01.pdf

Older studies (1970's or older) are usually performed before the introduction of the international validated test protocols. These studies can still be similar to the test protocols guidelines, and could contain valuable information, depending on the study design and performing laboratory.

1.5.2 Good laboratory practice (GLP)

Data should be generated in accordance with sound scientific and experimental procedures and experiments performed after 25 July 1993 must have been performed in accordance with the guidelines of Good Laboratory Practice (GLP), since by then all OECD countries had adapted these guidelines.

GLP is a quality system concerned with the organisational processes and conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported. The GLP regulation has no influence on the scientific aspects of study conduct, but does impact study quality, through aspects such as record keeping, thus ensuring that any study can be easily 'reconstructed' from the raw data records of the study.

Generally, open literature does not meet internationally recognized testing guidelines or GLP regulation and is therefore usually considered as supplementary information.

WHO has published a handbook on GLP:
http://www.who.int/tdr/publications/documents/glp-handbook.pdf

1.5.3 How to check studies for OECD and GLP compliance

In the application form, the applicant has to indicate whether the study was performed according to international test guidelines (and which ones), and whether the study was conducted under GLP.

Quick scan:
In the study report, the test guideline is most easily checked by looking for a statement signed by the study director, indicating in accordance to which test guideline the study was performed. The report should also indicate if there were deviations or amendments to these guidelines. Sometimes, the test protocol or guidelines are mentioned on the first page.
The GLP status can be checked by looking for a Quality Assurance statement in the study report, which must include the dates of several internal QA inspections of the study. The GLP statement must be signed by the QA officer. Ideally, an official GLP certificate is included in the report.

Detailed evaluation:
The identity of the tested substance and the tested product, and the purity of the tested substance should be clearly stated for each study. In the context of the influence that impurities can have on toxicological behaviour, it is essential that for each study submitted, a detailed description (specification) of the material used be provided. Tests should be conducted using active substance of the specification to be used in the manufacture of preparations to be authorized, except where radiolabelled material is required or permitted.

The OECD test guidelines for various types of study can be found on:
http://www.oecd.org/env/chemicalsafetyandbiosafety/testingofchemicals/oecdguidelinesforthetestingofchemicals.htm

Section 4 contains the guidelines for studies of health effects. Click on the English version under health effects. Thereafter, by clicking on 'Title', the test guidelines will appear according to ascending Guideline number. Similarly, section 2 contains the guidelines for studies of environmental (biotic) effects, and section 1 contains guidelines for studies of physico-chemical properties.

1.6 Data protection and confidentiality

According to FAO (2010, chapter 5.5 of the registration guideline) pesticide registration authorities will receive many documents, materials and a wide range of data from companies wishing to register their products. Companies submitting such data for registration of a pesticide have an interest in ensuring that this information, which is costly to generate and which may be used unfairly by competitors, is suitably protected. At the same time, good public policy and national legislation strive to reconcile competing interests, and to provide sufficient incentives for such data to be generated in the first place, ensuring that follow-on producers have reasonable opportunities to enter the market and providing for the possibility of making all or part of the data concerned accessible to the public.

Many different types of data exist, for which there are different mechanisms and levels of protection. There is also wide variability in the way in which individual countries protect such data as a separate category of intellectual property rights (IPRs) in their domestic legislation. For Members of the World Trade Organization (WTO), the protection of undisclosed information is mandatory under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), contained in Annex 1C of the Agreement Establishing the World Trade Organization (WTO).
In an attempt to achieve a balance between competing interests, and to promote public interest in the development of such data by firms and reference to them by regulatory authorities, WTO Members are required to provide for two ways of protection of undisclosed test or other data pursuant to Article 39.3 of the TRIPS Agreement. The first is against unfair commercial use, where:

- The data have to be submitted as a condition of marketing approval for pharmaceutical or agricultural chemical products;
- Those products utilize new chemical entities;
- The origination of the data involves considerable efforts; and
- The data is undisclosed.

The second form of protection of test data is against disclosure, except where necessary to protect the public, or unless steps are taken to ensure the data are protected against unfair commercial use.

The TRIPS Agreement does not state how protection against unfair commercial use should be implemented by WTO Members. Some form of protection of test data has generally been implemented into national legislation. For example, a number of WTO Members provide for a fixed period of exclusivity during which neither regulatory authorities nor third parties can rely on the data submitted by the originator company for regulatory approval purposes without the originator's consent. Other WTO Members have implemented approaches to data protection that do not provide for a specific period of exclusivity.

Countries may take different approaches as to which government authorities should be responsible for data protection. However, for data on agricultural or public health pesticides, the pesticide registration authority is usually responsible for developing and administering pertinent national legislation, including its adherence to international obligations on intellectual property rights. Where appropriate, pesticide authorities should consult the national office with general responsibility for intellectual property rights, in order to ensure a consistent approach regarding the protection, handling and access to registration data, materials and documents.

For WTO Members, it can be expected that relevant national laws and regulations, and their administration, reflect the minimum standards established by the TRIPS Agreement as set out above. Countries that are not members of WTO may have legislation on intellectual property or rules in place that should be adhered to. Where no such legislation or rules exist, pesticide registration authorities are advised to use the TRIPS Agreement, and the specific choices taken by different WTO Members, as a point of reference. Details of the diverse national approaches of many countries to implementing TRIPS standards on data protection have been notified to WTO and are available upon request from the WTO Secretariat.

Use of existing evaluations of the same active ingredient and/or product
In case the applicant has the ownership of the data or can fully justify the right to use the data for his application for registration, elements of existing registrations can be used for new applications based on the same active ingredient. However, if the data were to be owned by a different owner and the applicant could not justify his right to use these data, the responsible authority should not use the data and evaluation from the first registrant for approval of the product of the second applicant (FAO, 2010).

Moreover, the draft Ethiopian pesticide registration and control regulation have given a legal basis for data protection and confidentiality by including requirements under article 21 and 22 which are shown below.

Article 21: Data protection

1. Notwithstanding the national legislation on data protection and industrial property rights, data submitted to the Ministry for pesticide registration, as specified under Article 8, will be given exclusive protection status for a period of:.

a. Ten years, for new products, from the moment of first registration;
b. Two additional years for new uses of a registered pesticide, from the moment of first request for re-registration..

2. The total period of data protection for a registered product cannot exceed 14 years.
3. During the periods specified in sub-articles 1 and 2, the data cannot be used by an applicant without written consent from the first registrant.

Article 22: Confidentiality and data access

1. Pursuant to Article 14 of the Proclamation, the information included in the pesticide dossier will be disclosed and made accessible to the public, including:
   a. Contact details of the applicant;
   b. The identity of the pesticide, including;
      (i) Active ingredient
      (ii) Formulation
      (iii) Concentration
      (iv) Co-formulants of toxicological or environmental concern;
   c. Intended uses;
   d. Toxicity and environmental effects;
   e. Behaviour and fate on crops and in the environment;
   f. Physical hazards;
   g. Disposal methods;
   h. First aid measures and treatment of poisoning;
   i. Any other information that the Ministry considers relevant to ensure appropriate information.
2. As an exception to sub-article 1) and, at the request of the applicant, the Ministry may grant confidentiality and remove from the public dossier, the information on:
   a. The details of the product formulation;
   b. The manufacturing process;
   c. The specification of impurity of the active substance except for the impurities that are considered to be toxicologically, ecotoxicologically or environmentally relevant;
   d. Results of production batches of the active substance including impurities;
   e. Methods of analysis for impurities in the active substance as manufactured except for methods for impurities that are considered to be toxicologically, ecotoxicologically or environmentally relevant;
   f. Links between a producer or importer and the applicant or the authorisation holder;
   g. Information on the complete composition of the formulation;
   h. Names and addresses of persons involved in testing on vertebrate animals;
   i. The studies or parts of the studies in sub-article 1.l) when the studies include information on the processes used in the manufacturing or processing of a pesticide or disclose a portion of the mixture;
3. Notwithstanding intellectual property rights, the Ministry may decide to disclose the information under i), when there is an overriding public interest.
4. Applicants who want to claim confidentiality of the information in sub-article 2 shall identify and mark the information claimed as confidential as 'CONFIDENTIAL INFORMATION'. All pages containing such information should be stamped 'CONFIDENTIAL.'

2 Efficacy

2.1 Introduction

Article 3 of Schedule 2 of the Pesticide Registration and Control Regulation stipulates that 'Pursuant to Article 5.1b of the Proclamation, the Ministry shall evaluate the efficacy of the pesticide, including verification that the proposed claims and use recommendations on the product label reflect the actual performance of the product while providing a clear benefit to the user. A pesticide shall only be registered if the proposed use:

a. produces a clear and meaningful benefit to the user when compared to an untreated control, a reference product and other available pest management approaches, as appropriate;
b. does not result in unacceptable phytotoxic effects on the crop, or unacceptable effects on the quality or yield of the crop or its produce, unless the risk of such effects can be minimized using locally realistic risk mitigation measures;
c. is accompanied by a realistic resistance management scheme, unless it can be shown that the risk and speed of resistance development of the pest to the pesticide is negligible;
d. does not result in unacceptable adverse effects on succeeding or adjacent crops, unless the risk of such effects can be minimized using locally realistic risk mitigation measures.'

Therefore, upon authorisation of a plant protection product there are three essentials to be fulfilled with respect to its efficacy. Firstly, the use of a product should be **beneficial**. The positive effects (generally the control of a pest) should outweigh the negative effects that may occur on the plants or plant products. Then, it should be ascertained that the use of the product is **correct**. The amounts of product should be determined that have to be applied to achieve the benefit of the product under a broad range of circumstances but they may not be excessive in order to minimise the exposure of humans and environment to the product. Also the way the applications are performed (method, timing, frequency, etc.) should ensure the beneficial effects of the product when it is applied by the end-users. In addition, the implementation of a product may not lead to high risk on resistance development so that its use is **sustainable**.

The criteria set in this document refer to those specified in the Directive and apply to both chemical and biological pesticides in open field, covered and indoor situations. The exact claim(s) to evaluate are specified in the Table of Intended Uses (ToIU) which is to be provided by the applicant when applying for registration.

For the decision making on the aspect of efficacy no strict rules can be given. Efficacy evaluation requires expertise, understanding of the specific situation related to the claim and is based on assessments of the risks involved. It is impossible to cover each and every specific situation in this evaluation manual.

2.2 Efficacy data

In order to be able to assess the benefit of a product, data from efficacy field trials is required. The aim of the efficacy trials is to generate sufficient data to make an evaluation possible of the level, duration and consistency of control, protection or other intended effects of the plant protection product.
For more guidance on the execution of efficacy trials one is referred to the Directive and its Annexes A - D. Existing pre-verification and verification efficacy trial protocols for various Ethiopian crop-pest combinations are published on the web site of the Ethiopian Ministry of Agriculture (http://www.moa.gov.et/) and on the web site of PRRP-Ethiopia (www.prrp-ethiopia.org).

The efficacy (effectiveness and crop safety) is compared to an untreated control and one or more reference products. The untreated control is included to quantify the level of control and to verify the pest pressure in the trial. The reference product acts as a positive control, to check if the trial setup and execution succeeded and to relate the observed efficacy of the test product to that of a known previously recommended product. A reference product should have a registration for the tested use and should preferably have the same characteristics as the test product with respect to active substance, formulation, application methods etc. If no appropriate reference product is available, the comparison to the untreated control is sufficient. For biopesticides (especially in the first years of the implementation of the new registration system) it will not be possible to find an appropriate reference product since no biopesticides are yet registered and the characteristics of these products are often very specific. In such cases chemical plant protection products can serve as the positive control of a trial. Foremost, it is up to the researcher to argue the choice of the reference product.

For the effectiveness claim of a product a distinction is made between two factors: control and reduction. The trial results should correspond to the respective claim. A product that suppresses the development of a target pest and is to be applied in an IPM where a certain level of damage is tolerated, will not claim the 'control' of that target pest. When 'control' is claimed, it should be verified that the treatment with the product indeed keeps or kills the target pest below the damage threshold level. Again, this may differ per situation and involves expert judgement.

2.2.1 Quantity

In first instance, the number of successful efficacy trials needed for evaluation depends on the formal registration status of the product. In the following paragraphs the principal number of trials is given for each situation. However, to determine the exact required number of successful trials a provision is in force in which the following aspects are taken into account. The Ministry shall determine the number and types of efficacy trials to be conducted.

Most importantly, the possibilities for extrapolation can reduce the number of trials needed. The technical possibilities for extrapolation (between crops and pests; *e.g.* from aphid control in wheat to aphid control in barley) are based on expertise and require knowledge and experience of the specific situation. In the Directive the criteria for the acceptance of pesticide efficacy data generated outside Ethiopia are described. Extrapolation of data from abroad is not possible for biopesticides because the isolates, the target pest species and environmental circumstances are too specific.
Local efficacy data from trials carried out in Ethiopia that is submitted at the pre-evaluation stage is also taken into account. These trials must have been performed by institutes (EIAR) or universities acknowledged by the Ministry of Agriculture.

Moreover, the risks involved with the claimed use also determine how the required number of trials is adjusted. In a situation where a pest can be disastrous (*e.g.* locusts) and a decreased level of control cannot be permitted, additional trials may be necessary to sufficiently cover that risk.
On the other hand, knowledge on the active ingredient of the concerned product, argumentation, laboratory trials and literature may be used to lower the number of trials for assessing the risks involved with using the product.

New product
When a new active substance or newly formulated product (non-generic) is submitted for registration, there shall be two stages of testing for each relevant crop-pest combination. The first stage is the pre-verification stage in which three successful trials have to be completed. These trials may be performed within one year. Since herbicides impose a higher risk and are used for the control of several species, the minimum number of trials is set to four for herbicides.
Following pre-verification trials, a verification trial is performed in the next year or season, using large scale plots on three different growing areas which are considered as a replicate or in one growing area with at least three replicates. A growing area is defined as a zone within Ethiopia consisting of one or more agro-ecologies where the crop and pest are common.

Formulation change
When, based on equivalence criteria (according to physical/chemical properties), the change of a formulation of a product is 'major', the new and old formulation should be compared in at least one verification trial ('bridging') using large scale plots on three different growing areas which are considered as a replicate or in one growing area with at least three replicates.

Generic products
A new pesticide product that contains the same active ingredient – in a similar concentration and in a similar formulation – as an already registered pesticide product may be evaluated for equivalence. If the two products are considered equivalent by the Ministry, and registration is requested for the same crop/pest combinations, only verification trials need to be performed consisting of large scale plots on three different growing areas which are considered as a replicate or in one growing area with at least three replicates. The new product then has to adopt the exact claim and label text of the reference product ('bridging').

Extension of use
When additional uses are applied for an already registered product (new crops or target pests) and these cannot be substantiated by means of extrapolation (for effectiveness and/or crop safety), it is regarded as a new use and both pre-verification and verification trials are required. E.g., only the crop safety has to be tested when for effectiveness extrapolation is possible but the extension of use concerns a more sensitive crop.

Minor uses
There can be several reasons to expect that a specific use of a product is of low relevance in practice. The pest can be very specific and occur very locally or during a short period of the year, or the crop is grown on a small scale and of low economic importance. In that case the claim may be authorised as a 'minor use' which does not require any efficacy data. Minor uses have to be indicated on the product leaflet, accompanied by a warning that no effectiveness and crop safety data have been generated for that particular use.

Certain claims cannot be taken into consideration for a minor use. The claimed pest must be specific to the claimed crop and may not also occur in other similar crops *e.g.* aphids do not only infest rye but can occur on all cereal crops. This is to prevent long lists of separate crops in the claim and product leaflet. Also, it should be reasonable to assume efficacy against the target pest. The product should be registered for the use against the target pest or similar organisms. In principle, it is up to the applicant to propose and motivate such a minor use.

2.2.2 Quality

A successful trial meets up to a number of quality criteria. It is the responsibility of the researcher to fulfil these requirements and account for them in the reporting of the trials.
Whenever possible the efficacy trials should be conducted according to the appropriate efficacy testing protocol. If no appropriate testing protocol is available, a new one should be written for that crop-pest combination or an existing one should be modified to fit that combination. When it concerns a biopesticide, a guideline for writing test protocols for biopesticide testing has been developed . Newly developed testing protocols should be handled as soon as possible, *i.e.* at the next research review meeting. Furthermore, treatments should be carried out in accordance with the claim specified in the Table of Intended Uses (method, dose rate, frequency, pest stage, etc.).

Several other quality aspects are related to the exact location of the trial. The trial field should be laid out on a site which is representative for the practical situation. The circumstances within the trial plot must be uniform *e.g*. equal planting density, not partly shaded. The pest infestation should be evenly distributed over the plots. If a certain gradient occurs or heterogeneity is expected within the trial field, appropriate measures should have been applied *e.g.* blocking, adjusting plot size, increasing replicates, choice of untreated control, transformation of data, etc. The pest pressure should also be high enough. The minimum required level of infestation/infection differs for each situation and depends on the characteristics of the product (preventative/curative) and the pest and crop (damage threshold). Although in practice it might be difficult to achieve, the presence of other (non-target) pests may not interfere with the assessments, *i.e.* the observed damage should be ascribed to the target pest with certainty. Further, the data and results of the trials have to show consistency.

Pre-verification trials
In the pre-verification trials the product should be tested at, at least one lower dose rate (50% -and preferably also 75%- of the proposed dose rate) and preferably also at one dose rate which is higher than the claimed dose rate. This is for justification of the dose rate which should assure the benefit of the product without being excessive. Applications are performed according to the claim (ToIU). In order to quantify the efficacy of a product an untreated control is included in the trial. Treatments with one or more reference products are included to verify that the trial has been carried out properly and for comparing the efficacy of the test product. The treatments in the pre-verification tests should be arranged in a statistically suitable design with typically four replications.

Verification trials
Verification trials are conducted on large scale plots on three different growing areas which are considered as a replicate or in one growing area with at least three replicates. Statistics should be performed. In order to quantify the efficacy of a product an untreated control is included in the trial. Treatments with one or more reference products are included to verify that the trial has been carried out properly and for comparing the level of efficacy of the test product. At this stage it is suggested that a visit by the Pesticide Research Committee to the trial must be made if possible.

More than one active substance
When a product contains more than one active substances the benefit of that combination should be justified. The reason for combining two or more active substances can be a broadening of the spectrum of activity (*e.g.* a herbicide that contains an active substance against broadleaf weeds and an active substance against grass weed species), managing the resistance risk (active substances of different chemical classes) or to reduce the amount of either active substance (known as synergism). If necessary, this should be demonstrated by including treatments with the single active substances separately in the efficacy trials. When a single active substance is already registered, this product should be included in the efficacy trials and applied at the recommended dose rate.

2.2.3 Results

The minimum level of effectiveness required to support the given claim as defined in the ToIU is arbitrary. In principle the test product should demonstrate efficacy, at least equal to that of the reference product. However, it is justified to accept a lower level of control (or reduction) when the test product, compared to the reference product:

- Gives less, or no adverse effects (*e.g.* phytotoxicity).
- Has a broader spectrum of activity (more species are controlled).
- Broader period of application (*e.g.* more life stages controlled).
- Reduces the risk on resistance development (new mode of action, possibility to alternate).
- Can be used in ipm (often biopesticides).

2.3 Adverse effects

2.3.1 Phytotoxicity

The aim of the efficacy trials is to generate sufficient data to enable an evaluation of the possible occurrence of phytotoxicity after treatment with the plant protection product. Assessments on phytotoxicity should be made in all trials and preferably on different cultivars. Occurrence of phytotoxicity should be recorded and described and if it is not observed this should also be reported. An unacceptable degree of phytotoxicity may result in rejection of the tested product. The acceptability of phytotoxicity depends on the situation and the type of the damage observed. In flowers or other crops with ornamental value phytotoxicity is more critical than on arable crops where a certain level of damage can be tolerated as long as the development of the crop is not impaired.

When a herbicide is tested it may be feasible to require the inclusion of a handweeded untreated object and a treatment of a handweeded object at double the dose rate (to assess the risk of overlapping sprays).

When a significant level of phytotoxicity is recorded measures should be taken. Harmful effects on the crop may be accepted when adverse effects on yield can be exonerated (by taking the trials to harvest). Another option is to include a warning sentence (*e.g.* perform small scale test applications before large scale use) or to cover risks of crop damage by including a restriction sentence (*e.g.* not on young plants) on the label.

2.3.2 Yield

The aim of the efficacy trials is to generate sufficient data to enable evaluation of possible occurrence of yield reduction or loss in storage of treated plants or plants products and possible adverse effects after treatment with the plant protection product on transformation processes or on the quality of products.

Quality
Assessments on visible residues should be made in all trials when relevant (*e.g.* flowers, fruit crops). Occurrence of visible residues should be recorded and quantified and if it is not observed this should also be reported.

Data on the quality of yield (*e.g.* taint, odour, sugar content) is required when there are indications for an increased risk, based on the observations in the trials, the characteristics of the product (*e.g.* when the active substance is known to have a strong odour), the use pattern of the product (*e.g.* directly on the harvested product) or knowledge on similar active substances (known to cause adverse effects). Of course, these data may also indicate that further data on the quality of yield is not necessary.

Studies on taint can be accepted from abroad when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence. Another option is to cover the risk by including a restriction sentence on the label.

Processing procedures
Data on the processing procedures (*e.g.* fermentation, baking, brewing) is required when there are indications for an increased risk, based on the characteristics of the product (*e.g.* persistent active substance, a biopesticide based on a yeast, fungicide in a crop that is fermented later on), the use pattern of the product (*e.g.* directly on the harvested product) or knowledge on similar active substances (known to cause adverse effects). Of course, these data may also indicate that further data on processing procedures is not necessary.
Studies on processing procedures (on first instance laboratory tests) can be accepted from abroad when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence. Another option is to cover risk by including a restriction sentence (*e.g.* not to be used for processing purposes) on the label.

Quantity
Yield quantity can be measured as a part of effectiveness assessment when the pest has a direct effect on yield (*e.g.* fungi on cereals ears). The necessity for these assessments is indicated in the specific efficacy testing protocols.

Other reasons to require data on yield are indications for an increased risk, based on the observations in the trials (phytotoxicity), the characteristics of the product (*e.g.* herbicide), the use pattern of the product (*e.g.* directly on the harvested product) or knowledge on similar active substances (known to cause adverse effects). Of course, these data may also indicate that further data on yield is not necessary. Yield data is generated by taking the efficacy trials to harvest.

2.3.3 Resistance

Information on resistance development may come from laboratory trials, from practice (worldwide) and theory. The applicant should provide sufficient data to make a risk assessment possible. That includes data on the pest, the active substance and conditions of use. A risk analysis and -if applicable- a management strategy should be suggested by the applicant (*e.g.* maximum number of applications, restrict use to most important period or the requirement to alternate). The EPPO guideline 'PP1/213(3) Resistance risk analysis' can be used to set up this section and it may be useful to use the guidelines of the resistance action committees (IRAC, FRAC and HRAC).
It is up to the evaluator to have consistency in the resistance management strategies (*e.g.* among products based on the same active substance).

2.3.4 Adverse side effects

Succeeding crops
The aim of the efficacy trials is to generate sufficient data to enable evaluation of possible adverse effects of a treatment with the plant protection product on succeeding crops. Data on the succeeding (sowing the following cropping season) or replacement (re-sowing a failed crop) crops is required when there are indications for an increased risk, based on the observations in the trials (phytotoxicity) or the characteristics of the product (*e.g.* persistent active substance, slow release product) or the use pattern of the product (*e.g.* in annual crops). Of course, these data may also indicate that further data on succeeding crops is not necessary. Testing of effects on succeeding crops is mandatory for herbicides unless it can be argued that this is not necessary.

Data from the environmental risk assessment can be used for this risk assessment (PEC values and EC10). Also, (indoor) studies from abroad can be accepted when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence. When high risks exist for adverse effects on (certain) succeeding crops these may be covered using a restriction sentence on the label.

Adjacent crops
The aim of the efficacy trials is to generate sufficient data to enable evaluation of possible adverse effects of a treatment with the plant protection product including adjacent crops. Data on adjacent crops is required when there are indications for an increased risk, based on the observations in the trials (phytotoxicity) or the characteristics of the product (*e.g.* volatile active substance). Of course, these data may also indicate that further data on adjacent crops is not necessary (*e.g.* indoor application).

Data from the environmental risk assessment can be used for this risk assessment (non-target data, ED50 and drift values). Also, (indoor) studies from abroad can be accepted when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence. When high risks exist for adverse effects on (certain) adjacent crops, these may be covered with a restriction sentence on the label.

Propagation purposes

The aim of the efficacy trials is to generate sufficient data to enable evaluation of possible adverse effects of a treatment with the plant protection product on plans or plant products to be used for propagation. Adverse effects on plants or plant products that are to be used for propagation purposes are not accepted. In Ethiopia this is an important issue as many (small scale) farmers use the harvested seeds for the next cropping season. Data on propagation purposes (sowing harvested seeds from efficacy trials) is required when there are indications for an increased risk, based on the observations in the trials (phytotoxicity). Of course, these data may also indicate that further data on processing procedures is not necessary.

Beneficials

Possible adverse effects on beneficials (*e.g.* honeybees) should be reported when observed in the efficacy trials. In principle, this aspect is covered in the environmental risk assessment.

3 Human risk assessment

This chapter provides guidance on the assessment of the risk of a plant protection product on human health (occupational and consumer). It describes the data requirements for estimation of the human toxicological effects and the data requirements for the aspect residues, and how reference values are derived. Guidance for the estimation of the risk for operators, workers and consumers of treated crops is described.

3.1 Introduction

Toxicity is an inherent property of all substances. All chemical substances can produce health effects at some level of exposure. Risk is the likelihood that an adverse health effect will result from an exposure to a particular amount (dose) of a chemical. Therefore, risk is a function of both toxicity and exposure.

The risk assessment process can best be described in a 3 step procedure: hazard assessment, exposure assessment, and risk characterisation.

- **Step 1 - Hazard assessment**
  Examines whether a substance has the potential to cause harm to humans, and identifies the dose-response and the lowest relevant No Observed (Adverse) Effect Level (NO(A)EL)
- **Step 2 - Exposure Assessment**
  Examines what is known about the frequency, timing, and levels of exposure to a substance
- **Step 3 - Risk Characterization**
  Examines how well the data support conclusions about the nature and extent of the risk from exposure to pesticides.

Risk characterization is the final step in assessing human health risks resulting from exposure to pesticides. It is the process of combining the hazard, dose-response and exposure assessments to describe the overall risk posed by a pesticide. It explains the assumptions used in assessing exposure as well as the uncertainties that are built into the dose-response assessment. The strength of the overall database is considered, and generalized conclusions are drawn.

RISK = HAZARD x EXPOSURE.

This means that the risk to human health from pesticide exposure depends on both the hazard (toxicity of the pesticide) and the likelihood of people being exposed. At least some exposure and some toxicity are required to result in a risk. For example, if the pesticide is very poisonous, but no people are exposed, there is no risk. Likewise, if there is ample exposure but the chemical is non-toxic, there is no risk. However, usually when pesticides are used, there is some toxicity and exposure, which results in potential risk.

Effects vary between animals of different species and from person to person. To account for this variability, uncertainty factors are built into the risk assessment. These uncertainty factors create an additional margin of safety for protecting people possibly undergoing exposure.

3.2 Protection goals

The following protection goals are selected for the situation in Ethiopia:
- Operators.
- Workers.
- Consumers.

Since the exposure of operators and workers is expected to be higher than what is expected for bystanders/flag men and residents, only operators and workers are considered at this stage in the occupational health risk assessment.

Not yet included in the risk assessment are therefore:
- Bystanders / flag men.,
- Residents.

The detailed protection goal for operator exposure is defined as follows:
1. What should be protected?
   →All pesticide operators, i.e. all pesticide applicators, mixers and loaders.
2. Where should this be protected?
   →In all field and greenhouse crops where pesticides are applied through spraying.
3. How strict should it be protected?
   →No sub-chronic effects on the health of the operators are acceptable, i.e. no exceedance of the Acceptable Operator Exposure Level (AOEL) is allowed.

The detailed protection goal for worker exposure is defined as follows:
1. What should be protected?
   →All pesticide workers, i.e. all persons entering the sprayed field for e.g. harvesting, weeding.
2. Where should this be protected?
   →In all field and greenhouse crops where pesticides are applied.
3. How strict should it be protected?
   →No sub-chronic effects on the health of the workers are acceptable, i.e. no exceedance of the Acceptable Operator Exposure Level (AOEL) is allowed.

The detailed protection goal for consumer exposure through food is defined as follows:
1. What should be protected?
   →All consumers of agricultural commodities.
2. Where should this be protected?
   →Throughout Ethiopia, for all agricultural commodities that have been treated with the pesticide.
3. How strict should it be protected?
   →No acute or chronic effects on the health of the consumer, i.e. no exceedance of the Acceptable Daily Intake (ADI) or the Acute Reference Dose (ARfD) is allowed.

3.3 Hazard assessment, data requirements

3.3.1 Introduction

The use of pesticides may result in human exposure. Such exposure may occur via different routes: oral, dermal and inhalatory. It is therefore important that the intrinsic human toxicological properties of each active substance and product are evaluated and established.

The information on the toxic effects and kinetics of a substance is mainly based on the results of experimental toxicological research performed with different laboratory animal species. Besides toxicity data on the active substance and the formulation, data on metabolites may also be required if human exposure to such metabolites occurs via e.g. consumption.

The information provided for the active substance, and combined with information provided for one or more formulations containing the active substance, must be sufficient to permit an evaluation of the risks for man, associated with the handling and use of pesticide containing the active substance, and the risk for man arising from residual traces remaining in food and water. In addition, the information provided must be sufficient to:

- Classify the formulation as to hazard.
- Establish a relevant acceptable daily intake (adi) level for man.
- If applicable, establish a relevant acute reference dose (arfd) for man.
- Establish acceptable operator exposure level(s) (aoel).
- Permit an evaluation to be made as to the nature and extent of the risks for man animals (species normally fed and kept or consumed by man) and of the risks for other non-target vertebrate species.

3.3.2 Data requirements for the active ingredient

The FAO (2010) indicates that responsible authorities should, whenever possible, make use of data that have been released publicly, and that preferably have been peer-reviewed, when considering an application for registration. In this way, duplication of work and inefficient use of resources can be minimized. Mutual acceptance of data by several regulatory authorities on topics such as efficacy and residues, among others, is recommended whenever a sound basis can be established to ensure that the data is relevant to the situation being considered.
In addition, hazard assessments are generally applicable globally and are available from published sources, including the peer-reviewed assessments of the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) or other reputable national or regional registration authorities. These may be used in the evaluation of a dossier, as long as data propriety is adequately taken into account.

Table 3.1
Examples of evaluations that may be used as starting points or checks for the risk assessment.

EU data base	http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection&a=1	Useful site, indicating the EU ADI, ARfD, and AOEL, and also presenting other ADI/ARfD such as JMPR if available,
Pesticide Properties DataBase	http://sitem.herts.ac.uk/aeru/footprint/en/index.htm	ADI, ARfD, and AOEL. Usually includes the EU, JMPR and US EPA reference values, if available. In some cases it contained the wrong EU reference values.
Joint Meeting on Pesticide Residues (JMPR) – Monographs and Evaluations	http://www.inchem.org/pages/jmpr.html	WHO. Detailed tox and MRL evaluation reports, more difficult to find the ADI/ARfD. Contains no occupational reference values (AOEL)
USEPA – Pesticide evaluations	http://www.epa.gov/pesticides/regulating/index.htm or http://www.epa.gov/pesticides/reregistration/status.htm	ADI and ARfD for US EPA
European Food Safety Authority (EFSA) – Pesticide Risk Assessments	http://www.efsa.europa.eu/en/pesticides/pesticidesscdocs.htm	EU. Detailed risk assessments for human and environmental health
International Agency for Research on Cancer (IARC) – Monographs on the Evaluation of Carcinogenic Risks to Humans	http://monographs.iarc.fr/	Tox evaluation, focussing on carcinogenicity. Will not include an ADI, ARfD or AOEL
Agency for Toxic Substances and Disease Registry (ATSDR) – Toxicological Profiles	http://www.atsdr.cdc.gov/toxpro2.html	Tox evaluation. Will probably not include an ADI, ARfD or AOEL.
International Programme on Chemical Safety (IPCS): – Concise International Chemical Assessment Documents – Environmental Health Criteria Monographs	http://www.inchem.org/pages/cicads.html http://www.inchem.org/pages/ehc.html	Tox evaluation. Will probably not include an ADI, ARfD or AOEL.

For Ethiopia, the data requirements for the active ingredient are indicated in the active ingredient List 1 of the application form. There is a guideline for the applicant on how to fill in this application form. Where the applicant holds the view that a certain study is not necessary, a relevant scientific justification should be provided for the non-submission of the particular study.
The applicant has to provide the full study reports and a summary of each study including the relevant endpoints such as e.g. the 'No Observed (Adverse) Effect Level' (NO(A)EL), LD50, irritating yes/no, etc. This evaluation results for each study and for each sub-aspect in a toxicologically based endpoint, and finally to the toxicological profile of a substance. The toxicological endpoints derived from the submitted research are the basis for the risk evaluation for operator, worker and for consumers. An overview of the data requirements for toxicology are given in Annex 5, whereas the data requirements for residues are given in Annex 6.
The relevance of various data requirements is indicated in a summarized fashion below.

Reference values
ADI and ARfD are used in the consumer risk assessment; AOEL is used for the occupational risk assessment.

Acute toxicity studies (oral, dermal, inhalation)
These studies provide an estimate of the relative toxicity of a substance by the different routes of exposure and they may serve as a basis for classification and labeling. It is an initial step in establishing a dosage regimen in subchronic and other studies and may provide information on the mode of toxic action of a substance by these routes.

Skin and eye irritation studies
These studies provide information on health hazard (e.g. irritation, corrosion) likely to arise from exposure to the test substance by application to the skin or on the eye. They may serve as a basis for classification and labelling.

Skin sensitisation
There are several methods: Buehler test, Guinea Pig Maximisation Test (GPMT) and the mouse Local Lymph Node Assay (LLNA). They all assess the potential of a substance to cause skin sensitisation, an immunologically mediated cutaneous reaction to a substance. The studies may serve as a basis for classification and labelling.

Reproduction multi-generation study
This study is designed to provide general information concerning the effects of a test substance on the integrity and performance of the male and female reproductive systems, and on the growth and development of the offspring. The test substance is administered daily in graduated doses to several groups of males and females. A properly conducted reproductive toxicity test should provide a satisfactory estimation of a no-effect level and an understanding of adverse effects on reproduction, parturition, lactation, postnatal development including growth and sexual development.

Subchronic toxicity 90 day
This study provides information on health hazards likely to arise from repeated oral exposure over a prolonged period of time covering post-weaning maturation and growth well into adulthood. The study will provide information on the major toxic effects, indicate target organs and the possibility of accumulation, and can provide an estimate of a no-observed-adverse-effect level (NOAEL) of exposure which can be used in selecting dose levels for chronic studies and for establishing reference values, such as the AOEL.

Chronic toxicity
The objective of chronic toxicity studies is to characterize the profile of a substance in a mammalian species (primarily rodents) following prolonged and repeated exposure of at least 1 year. The study will provide information on the major toxic effects, indicate target organs and the possibility of accumulation, and can provide an estimate of a no-observed-adverse-effect level (NOAEL) of exposure which can be used for establishing reference values, such as the ADI. The test is often combined with carcinogenicity testing.

Carcinogenicity
The objective of a long-term carcinogenicity study is to observe test animals during a major portion of their life span for the development of neoplastic lesions during or after exposure to various doses of a test substance by an appropriate route of administration. This Test Guideline is intended primarily for use with rats and mice, and for oral administration. The duration of the study will normally be 24 months for rodents. For specific strains of mice, duration of 18 months may be more appropriate. The test is often combined with chronic toxicity testing.

Neurotoxicity
These studies provide the information necessary to confirm or to further characterise the potential neurotoxicity of chemicals in adult animals (rats). The dosing regimen may be acute (1 day), subacute (28 days), subchronic (90 days) or chronic (1 year or longer). For organophosphates, specific tests are designed to detect delayed neurotoxicity in hens.
The study can be used for establishing reference values, and is often the basis for the ARfD.

Teratogenicity
This study is designed to provide general information concerning the effects of prenatal exposure on the pregnant test animal and on the developing organism; this may include assessment of maternal effects as well as death, structural abnormalities, or altered growth in the foetus. The study can be used for establishing reference values, and is often the basis for the ARfD.

Mutagenicity / Genotoxicity
The primary function of genetic toxicity testing is to investigate, using test cells or organism, the potential of chemical substances to induce mutation in man that may be transmitted via the germ cells to future generations. Scientific data generally support the hypothesis that DNA damage in somatic cells is a critical event in the initiation of cancer. Such damage can result in mutations, and tests to detect mutagenic activity may also identify chemicals that have the potential to lead to carcinogenesis.

Metabolism
These in vivo studies provide information on mass balance, absorption, bioavailability, tissue distribution, metabolism, excretion, and basic toxicokinetic parameters [e.g. AUC], as well as supplemental approaches that may provide useful information on toxicokinetics. Information from toxicokinetic studies helps to relate concentration or dose to the observed toxicity and to understand its mechanism of toxicity. The test substance ('unlabelled' or 'radiolabelled' forms) is normally administered by an oral route, but other routes of administration may be applicable. The study/studies can provide the oral absorption value of the test substance, which is necessary for the setting of the AOEL. If no oral absorption is indicated in the dossier, a default of 100% should be used.

3.3.3 Data requirements for the formulated product

For Ethiopia, the data requirements for the formulated product are indicated in the formulated product (List II) section of the application form. There is a guideline on how to provide the required data. The data requirements are reproduced in Annex 7. The applicant has to provide the full study reports and a summary.
For the behaviour of residues of active substances in formulations, the formulation type used is considered to be of minor importance. In the dossier on the active substance, residue studies are performed with a formulated product, and not with 100% technical active substance. Hence, studies with the specific product for which authorisation is sought, are not required. The application regime used in the studies, should reflect the intended use. The analytical method submitted for the analysis of residues in plant products applies to both the dossier on the active substance as well as the dossier for the formulated product.
For operators and workers the dermal and inhalation routes are the most important routes of exposure. Insight in the extent to which the skin or lung absorbs a substance and/or formulation after exposure to a relevant level is important for calculation of systemic (internal) human exposure (see risk assessment in 3.5). For the uptake via the lungs (respiratory absorption) a default value of 100% is used. However, for the dermal absorption either a default value or study data can be used, which is explained in the following paragraph.

The oral absorption is necessary for the setting of the AOEL and can usually be retrieved from metabolism studies on the active substance. If no oral absorption is indicated in the dossier, a default of 100% should be used.

3.3.3.1 Data from dermal absorption studies

If appropriate, dermal absorption data with a relevant product should be provided (see section 3.5.1). If the study is not performed with the product for which authorisation is requested, the applicant should provide a scientific justification why the tested product is equivalent to the product for which authorisation is requested.

As a pragmatic rule it can be considered that extrapolation is possible within the following groups:
- Liquid oily based formulations.
- Liquid water based formulations.
- Wp/sp formulations.
- Wg/sg formulations.

Moreover, also as a pragmatic rule:
- Liquid oily based formulation data can be used for liquid water based formulations as a worst case.
- Liquid formulation data can be used for solid, e.g. Wettable powders (wp) and water soluble granule (wg), formulations.
- Wp data can be used for wg formulations.

If no extrapolation is possible, the default value (100 or 10%, see 3.3.3.2) will be used.

Insight into the extent to which the skin absorbs a substance and/or formulation after exposure to a relevant level is important for calculation of systemic exposure. There is an OECD Guidance note on dermal absorption (2011)
http://www.oecd.org/chemicalsafety/testingofchemicals/48532204.pdf
and a WHO report on dermal absorption (EHC no 235, 2006)
http://www.inchem.org/documents/ehc/ehc/ehc235.pdf

3.3.3.2 Dermal absorption, default values

If no suitable (animal) experimental data are available, a default value of 100% for dermal absorption has to be assumed as a first step in the exposure calculations. The physicochemical properties of a substance have a major impact on its dermal penetration. Thus, for example, it is widely assumed that for large molecules and those with either a very low or a very high octanol water partition coefficient (log Pow), the skin is much less permeable than it would be for other, smaller molecules. Many authorities, particularly in Europe, consider this factor by reducing the 100% default value to 10% if the molecular weight is greater than 500 and log Pow is either below -1 or above 4. In addition to the use of the 100% and 10% default values, it can be argued that dermal absorption cannot exceed the oral absorption rate. Although the validity of using the physicochemical properties to obtain the default criteria is unclear, at this stage it is a pragmatic way to lower the rather extreme default of 100% in particular cases.

In summary:
- Dermal absorption value < oral absorption value.
- 10% default dermal absorption value: log Pow < -1 or > 4 and MW > 500.
- 100% default dermal absorption value: all other cases.

3.3.3.3 Dermal absorption, in vitro/in vivo studies

In vitro and/or in vivo research is required if it is expected that the Acceptable Operator Exposure Level (AOEL) will be exceeded when using default values for dermal absorption, and dermal exposure is an important exposure route.

In vivo research (usually performed with the living rat) and/or in vitro research (using pieces of rat skin tissue and human skin tissue), both performed at a relevant dose level, are used for derivation of the dermal absorption for man. In vitro research is performed with the formulation (or a comparable formulation) to study the differences between species (rat/man). If no comparison can be made between species because the required research is lacking, the percentage dermal absorption is derived from the in vivo study with the rat. This is in many cases a worst case assumption because the human skin generally forms a better barrier than the shaven rat skin.

The dermal absorption studies described above must be performed at dose levels that correspond with the exposure expected for operator and worker. The toxicological dossier may also contain dermal toxicity studies, such as, e.g., a 28-day study with dermal administration. Such studies are usually performed at dose levels that are (much) higher than the expected human exposure and they are not suitable for derivation of dermal absorption values for man.

Co-formulants in the test preparation may have a significant impact on absorption and the outcome of a study may be different when another vehicle or formulation is used. Therefore, the dermal absorption study/studies should ideally be performed with the formulation for which registration is requested. A general pragmatic rule, as indicated in the OECD Guidance on dermal absorption is that formulations can be considered similar when the content of each co-formulant is within 25% of the actual concentration of the tested formulation.
In general, the percentage dermal absorption from a less concentrated product is higher than from a concentrated product (the more diluted the formulation, the higher the dermal absorption percentage). Therefore, the content of the active substance should be within the same range as the tested formulation, and not be lower.

Usually different concentrations (dilutions) are tested. These may include a concentrate (or 'neat' formulation) to mimic exposure during e.g. mixing and loading a concentrate. At least one representative use-dilution may be tested to mimic exposure when the chemical is sprayed.
If the formulation applied for has the same/similar composition but has a much lower content of active substance (is further diluted) than the tested formulation, the dermal absorption value from the tested diluted product may be used for the dermal absorption value of the concentrate of the formulation applied for.

3.3.3.4 Dermal absorption, how to use data from studies

Quick way
The most practical way is to rely on the values the applicant has indicated in the application form. If no values are given, the default values can be used.

More detailed evaluation
A practical more detailed evaluation would be to look for similar types of formulations, as long as the content of active substance is within the same range. In general the dermal absorption of liquid oily formulations and/or formulations containing solvents could be considered to be higher than for aqueous formulations. The dermal absorption of liquid formulation could be considered worst case for solid formulations (powders or granules).

If the formulation applied for has the same/similar composition but has a much lower content of active substance (is further diluted) than the tested formulation, the dermal absorption value from the tested diluted product may be used for the dermal absorption value of the concentrate of the formulation applied for.

3.3.4 Classification of the formulation

WHO class

The WHO class must be given as shown in the following table (revised criteria for classification, see the WHO recommended classification of pesticides by hazard and guidelines to classification: 2009 (WHO, 2010)). WHO now uses the Acute Toxicity Hazard Categories from the GHS as the starting point for classification.

It is highly desirable that, whenever practicable, toxicological data for each formulation to be classified should be available from the manufacturer. However, if such data are not obtainable, then the classification may be based on proportionate calculations from the LD50 values of the technical ingredient or ingredients, according to the following formula:

(LD50 active ingredient×100) / Percentage of active ingredient in formulation

For more information see: http://www.inchem.org/documents/pds/pdsother/class_2009.pdf

Table 3.2

WHO-Classification Scheme

WHO class		LD50 for the rat (mg/kg body weight)	
		Oral	Dermal
Ia	Extremely hazardous	< 5	< 5
Ib	Highly hazardous	5-50	5-200
II	Moderately hazardous	50-2000	200-2000
III	Slightly hazardous	Over 2000	Over 2000
U	Unlikely to present acute hazard	5000 or higher	

GHS for skin and eye irritation and skin sensitisation

The FAO/WHO class does not stipulate how to handle formulation which are possible irritants or sensitizers. The GHS system gives the following information.

Skin irritation:

The hazard statement 'H315: Causes skin irritation' is assigned, however, no use of additional personal protective equipment (PPE) is recommended.

Table 3.3

GHS criteria for irritants and sensitizers.

Criteria
(1)Mean value of ≥ 2,3 – ≤ 4,0 for erythema/eschar or for oedema in at least 2 of 3 tested animals from gradings at 24, 48 and 72 hours after patch removal or, if reactions are delayed, from grades on 3 consecutive days after the onset of skin reactions; or (2)Inflammation that persists to the end of the observation period normally 14 days in at least 2 animals, particularly taking into account alopecia (limited area), hyperkeratosis, hyperplasia, and scaling; or (3)In some cases where there is pronounced variability of response among animals, with very definite positive effects related to chemical exposure in a single animal but less than the criteria above.

Skin corrosion:

The hazard statement 'H314 Causes severe skin burns and eye damage' is assigned, additional PPE are recommended: Wear protective gloves/protective clothing and eye protection/face protection.

Table 3.4

Criteria for skin corrosion.

Criteria
Production of irreversible damage to the skin; namely, visible necrosis through the epidermis and into the dermis, following the application of a test substance for up to 4 hours. Corrosive reactions are typified by ulcers, bleeding, bloody scabs, and, by the end of observation at 14 days, by discolouration due to blanching of the skin, complete areas of alopecia, and scars. Histopathology shall be considered to evaluate questionable lesions. Destruction of skin tissue: necrosis through the epidermis and into the dermis in at least 1 tested animal after exposure of less than 3 minutes up to a 4 hour duration.

Eye irritation (reversible effects):

The hazard statement 'H319: Causes serious eye irritation' is assigned, however, no additional PPE are recommended.

Table 3.5

Criteria for eye irritation.

Criteria
if, when applied to the eye of an animal, a substance produces: –at least in 2 of 3 tested animals, a positive response of: –corneal opacity ≥1 and/or –iritis ≥1, and/or –conjunctival redness ≥2 and/or –conjunctival oedema (chemosis) ≥2 –calculated as the mean scores following grading at 24, 48 and 72 hours after installation of the test material, and –which fully reverses within an observation period of 21 days

Eye damage (irreversible effects):

The hazard statement 'H318: Causes serious eye damage' is assigned, additional PPE are recommended: Wear eye protection.

Table 3.6

Criteria for eye damage.

Criteria
If, when applied to the eye of an animal, a substance produces: –at least in one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or have not fully reversed within an observation period of normally 21 days; and/or –at least in 2 of 3 tested animals, a positive response of: – corneal opacity ≥3 and/or – iritis >1.5 calculated as the mean scores following grading at 24, 48 and 72 hours after installation of the test material.

Skin sensitisation:

The hazard statement 'H317: May cause an allergic skin reaction' is assigned, additional PPE are recommended: Wear protective gloves/protective clothing.

Table 3.7
Criteria for skin sensitization.

Assay	Criteria
Local Lymph Node Assay	SI value ≥ 3% (OECD 429) SI value ≥ 1.8% (OECD 442A) SI value ≥ 1.6% (OECD 442B)
Guinea pig maximisation test	≥ 30% of test animals with positive skin reactions
Buehler assay	≥ 15% of test animals with positive skin reactions

Non-approval under the Regulation
The Ethiopian regulation stipulates the following with regard to human and animal health in relation to classification and labelling:

1. Human and animal health
   - 1.1.1. The Ministry shall assess that the pesticide does not cause human and animal health hazards when handled and applied in accordance with the instructions and, to this purpose, will evaluate:
   - 1.1.2. The overall acute and long-term hazards of the pesticide for humans.
     - a. The pesticide will not be registered if:
       - i. the pesticide formulation is classified as or meets the criteria to be approved as classes Ia or Ib of the WHO Recommended Classification of Pesticides by Hazard; or
       - ii. the pesticide meets the criteria of carcinogenicity Categories 1A and 1B of the Globally Harmonized System on Classification and Labelling of Chemicals (GHS); or
       - iii. the pesticide meets the criteria of mutagenicity Categories 1A and 1B of the Globally Harmonized System on Classification and Labelling of Chemicals (GHS); or
       - iv. the pesticide meets the criteria of reproductive toxicity Categories 1A and 1B of the Globally Harmonized System on Classification and Labelling of Chemicals (GHS);

     unless exposure of humans, either directly or through their diet, is likely to be negligible following the intended uses and under locally relevant conditions of use.

This means that with regard to points 1.1.1 a) (ii)-(iv) the classification of the active substances needs to be known. This needs to be indicated by the applicant on the application form. It can also be checked e.g. on the following website:
EU: http://esis.jrc.ec.europa.eu/clp/ghs/search.php

If the pesticide formulation contains a certain amount of the classified active substance, then the pesticide formulation needs to be classified similarly.
The following applies:

Table 3.8

Generic concentration limits of ingredients of a mixture classified as carcinogen that trigger classification of the mixture.

Ingredient classified as:	Generic concentration limits triggering classification of the formulation as:	
	Category 1A carcinogen	Category 1B carcinogen
Category 1A carcinogen	≥ 0,1%	-
Category 1B carcinogen	-	≥ 0,1%

Note: The concentration limits in the table above apply to solids and liquids (w/w units) as well as gases (v/v units).

Table 3.9

Generic concentration limits of ingredients of a mixture classified as reproduction toxicants or for effects on or via lactation that trigger classification of the mixture.

Ingredient classified as:	Generic concentration limits trigger classification of the formulation as:	
	Category 1A reproductive toxicant	Category 1B reproductive toxicant
Category 1A reproductive toxicant	≥ 0,3%	
Category 1B reproductive toxicant		≥ 0,3%

Table 3.10

Generic concentration limits of ingredients of a mixture classified as germ cell mutagens that trigger classification of the mixture.

Ingredient classified as:	Concentration limits triggering classification of the formulation as:	
	Category 1A mutagen	Category 1B mutagen
Category 1A mutagen	≥ 0,1%	–
Category 1B mutagen	–	≥ 0,1%

Note: The concentration limits in the table above apply to solids and liquids (w/w units) as well as gases (v/v units).

3.4 Derivation of endpoints and reference values for human risk assessment

3.4.1 Introduction

The submitted dossier should contain the full study reports of each study, and a summary. The endpoint per aspect (such as e.g. mutagenicity, carcinogenicity, reproduction toxicity etc.) are presented by the applicant in the application form.
The toxicological endpoints that are derived from the submitted studies and indicated by the applicant in the application form, are the basis for derivation of various reference values (ADI, AOEL and ARfD). Subsequently, these reference values are the basis of the risk assessment for the consumer, operator and worker.

3.4.2 NOAEL

For each study, if possible, the No Observed Adverse Effect Level (NOAEL) is derived. The NOAEL is the highest dose at which the most relevant critical effect (the adverse health effect that occurs first) is not yet observed. The Lowest Observed Adverse Effect Level (LOAEL) is the lowest dose at which there was an observed toxic or adverse effect.

Sometimes the terms No Observed Effect Level (NOEL) and Lowest Observed Effect Level (LOEL) may also be found in the literature. NOELs and LOELs do not necessarily imply toxic or harmful effects and may be used to describe beneficial effects of chemicals as well.

For most end-points it is generally recognized that there is a dose or concentration below which adverse effects do not occur; for these, an NOAEL and/or LOAEL can be identified. For genotoxicity and carcinogenicity mediated by genotoxic mechanisms, dose–response is considered to be linear, meaning that risk cannot be excluded at any exposure level. A pesticide containing such an active ingredient can therefore not be authorized.

The lowest relevant NOAEL/LOAEL value should normally be used for risk characterization and the setting of acceptable exposure levels.

If the critical NOAEL/LOAEL is derived from an animal study, a default Uncertainty Factor (UF) of 10 is usually recommended to account for interspecies differences (WHO, 1994; WHO, 1999). In addition a default UF of 10 is used to account for interindividual differences in the general population (WHO, 1994; WHO, 1999). Contributors to the overall UF are normally multiplied because they are considered to be independent factors; the most commonly used default UF for the setting of reference values for the general population is therefore 10 x 10 = 100 (WHO, 1994; WHO, 1999).
In some cases, the use of additional UFs is justified. Situations in which additional UFs should be considered include the following:

- When LOAEL is used instead of NOAEL, an additional UF (e.g. 3 or 10) is usually incorporated,
- When an NOAEL from a sub-chronic study (in the absence of chronic study) is used to derive a reference value for long-term exposure, an additional UF (often 10) is usually incorporated to take account of the attendant uncertainties,
- If the critical NOAEL relates to serious, irreversible toxicity, such as developmental abnormalities or cancer induced by a non-genotoxic mechanism (WHO, 1999),
- When there are exposed subgroups, which may be extra-sensitive to the effects of the compound (e.g. neonates because of the incompletely developed metabolism),
- If the database is limited.

WHO (1994). Environmental Health Criteria no. 170. Assessing Human Health Risks of Chemicals: Derivation of Guidance values for Health-Based Exposure Limits.

WHO (1999). Principles for Assessment of Risk to Human Health from Exposure to Chemicals. Environmental Health Criteria no. 210. World Health Organization, Geneva.

3.4.3 ADI

Consumers may be exposed to residues of plant protection products via food, throughout their life. The corresponding reference value (Acceptable daily intake, ADI) must therefore represent the dose that can be ingested over a lifetime via food without adverse health effects. The JECFA (Joint FAO/WHO Expert Committee on Food Additives) has defined the ADI as follows: 'the estimated amount of active substance, expressed per kg body weight, that can be consumed daily over a lifetime without appreciable health risks'.
Note that the US EPA refers to the chronic reference dose (chronic RfD or RfD) instead of ADI.

The ADI is usually derived from laboratory animal research in which the effect of prolonged exposure to the test substance has been studied, i.e. chronic toxicity research.

The following formula is used to set the ADI:

ADI (human dose) = NO(A)EL(experimental dose) / 100 (default uncertainty factor)

The ADI is based on the most sensitive, or most critical effect. 'Effect' is defined as: an effect that is considered adverse. Usually, data on several species are available (rat and mouse and sometimes also dog). The data of the most relevant animal species for the most critical effect form the basis for derivation of the ADI. The relevance of the observed effect for man is also important.

3.4.4 ARfD

Consumers may be exposed to residues of plant protection products via food, throughout their life. If a substance has acute toxic properties, an ARfD (Acute Reference Dose) is derived from the available toxicological studies.
The ARfD is defined as 'an estimate of the amount of a substance in food or drinking water, normally expressed on a body weight basis, that can be ingested in a period of 24 h or less without appreciable health risks to the consumer on the basis of all known facts at the time of the evaluation' (JMPR, 2002).

The following formula is used:

ARfD (human dose) = NO(A)EL (experimental dose) / 100 (default uncertainty factor)

There is a Guidance Document of the European Commission and a JMPR Guidance on setting of acute reference dose for pesticides. These documents provide a guideline on how the ARfD should be derived, which studies can be used as a starting point, and which effects are relevant for acute exposure.
http://ec.europa.eu/food/plant/protection/resources/7199_vi_99.pdf .
http://www.who.int/entity/foodsafety/chem/jmpr/arfd_guidance.pdf

Some substances have specific acute toxic properties or may after a short-term (single) (high) exposure induce prolonged effects. In such a situation it is possible that exceeding the ADI for a short period of time entails a health risk.

An ARfD is always derived unless the toxicological profile of the substance meets all following conditions:
- The substance induces no effects (including behaviour, clinical symptoms, or pathology) in an acute oral study at a dose level of 2000 mg/kg bw or higher.
- No embryonic, fetotoxic, or developmental effects were found at dose levels that are not maternally toxic.
- There are no indications or triggers from repeated dose studies which indicate toxic effects after acute exposure (e.g. acute neurological behaviour effects or effects on the gastrointestinal, cardiovascular or respiratory system).
- The substance shows no acute neurotoxicity or this is not expected on the basis of the available toxicological information.
- No other toxicological alerts such as hormonal or biochemical changes have been found in repeated dose studies which may also occur after a single dose.

As a general rule, the ARfD should be based on the most sensitive acute toxicological endpoint of human relevance, derived from the most suitable study in the most suitable (animal) species. Selection of the most relevant effect should be based on the full set of available toxicity research.

Knowledge about the mode of action of a substance may be very valuable when selecting the most relevant endpoint for acute exposure. The fact that the current database is not yet geared to the derivation of an ARfD makes it difficult to identify the correct endpoint and the most suitable study. Sound justification of the derivation of an ARfD is therefore important.
Some relevant effects for which an ARfD can be derived are: certain clinical effects (tremors, mucus formation/salivation), acetyl cholinesterase inhibition, delayed neuropathy, neurotoxicity, methemoglobin formation, disturbance of oxygen transport or dissociation in mitochondria, embryonic or foetotoxic effects, developmental effects, developmental neurotoxicity, direct effects on gastrointestinal tract, pharmacological effects.
When no ARfD is derived, this should also be justified in the evaluation.

An uncertainty factor of 100 is usually applied for extrapolation of the NOAEL from laboratory animal studies to the ARfD. This factor is based on a factor of 10 for differences between animal species (interspecies) and a factor of 10 for variation within the population (intraspecies). This latter factor compensates for the wider variation in sensitivity in the population of exposed workers in comparison with the relatively small (and relatively homogeneous) group of exposed laboratory animals. Additional uncertainty factors may be used, as indicated for the ADI.

3.4.5 AOEL

Operator exposure considered acceptable from a health point of view is in the EU referred to as AOEL (Acceptable Operator Exposure Level). The AOEL is defined as the maximum amount of a substance to which the operator (including workers in treated crops or treated spaces) can be exposed at which no adverse effects on health are expected.

The following formula is used:

AOELsystemic [mg/kg bw/day] = (NOAEL x Absorption) / 100

Absorption is given as the fraction of the substance absorbed by the body after oral administration, e.g. if the absorption is 60%, then the numerical factor Absorption = 0.6).

In Europe there is a Guidance Document on the setting of the AOEL.
http://ec.europa.eu/food/plant/protection/resources/7531_rev_10.pdf

Where relevant, different AOELs can be established for acute, short-term (semi-chronic) or long-term (chronic) exposure. The AOEL is expressed in mg/kg bw/day.

Systemic AOEL/AEL
In principle, a systemic AOEL is derived. Systemic effects of active substances are caused by the amount of active substance actually absorbed into the body. In practice, exposure to these substances occurs mainly via the dermal and –to a lesser extent- via the respiratory route. For most active substances in plant protection products that are to be evaluated, however, only suitable studies with repeated exposure via the oral route are available. In practice, an AOEL is therefore usually derived on the basis of an oral study. The choice of the systemic AOEL used in the risk assessment should be justified in the decision making.

Choice of data for calculation of the systemic AOEL/AEL
The suitable studies with repeated exposure to the substance are selected from the toxicological dossier for calculation of the systemic AOEL. In addition, the kinetic data on the substance are used to establish the systemic availability (via the oral, dermal or inhalatory route) of the substance.

In principle it is assumed that the period during which exposure takes place is shorter than or equal to 3 months per year. This means that the AOEL calculation is preferably based on a short-term, i.e., semi-chronic toxicity study.
If exposure during a period longer than 3 months per year cannot be excluded based on the application scenario, a chronic toxicity study is preferred.

Besides duration and frequency of exposure, the choice of the most relevant study can also be determined by the excretion rate of the active substance and its metabolites, and by the rate at which the effects that may be caused by exposure to a substance are reversible.

The most relevant studies are selected from the dossier on the basis of these considerations. The selection must be justified in the decision making.

The study with the most relevant NOAEL, obtained with the most relevant test animal, is selected. This does not necessarily always have to be the lowest NOAEL found in the most sensitive test animal. The choice of the NOAEL as starting point depends on the total package of available toxicity studies and the mutual relationships in dose regimes. The most suitable NOAEL on which the AOEL is based should be selected on a case-by-case basis, for which expert judgement is required.

Safety factor for calculation of the AOEL/AEL
A systemic AOEL is derived from the selected NOAEL by applying an uncertainty factor.
In accordance with the ADI principle the uncertainty factor applied is usually 100. The basis for this approach is a factor of 10 for differences within the animal species (intraspecies differences) and a factor of 10 for differences between animal species (interspecies differences). This latter factor compensates for the wider variation in sensitivity in the population of exposed workers in comparison with the relatively small (and relatively homogeneous) group of exposed laboratory animals.
Additional uncertainty factors may be used, as indicated for the ADI.

Absorption after oral exposure
Determination of the level of the systemic AOEL after oral exposure requires insight into the extent to which a substance is absorbed by the body after oral administration.
The value for absorption after oral exposure to a relevant amount of substance is the sum of the amounts of substance and metabolites that are subsequently excreted in the urine and that remain in tissues and carcass. If the absorbed dose is significantly lower (<80%) than the administered dose, this is adjusted by a correction factor equal to the percentage absorption. Because absorption may be dose-dependent, absorption data are required of a dose in the range of the NOAEL.

3.4.6 How to derive the reference values

Quick way:
Use the ADI, ARfD and AOEL that the applicant has indicated in the application form.

More detailed evaluation:
1. Quality check of submitted application forms
   - are all data requirements fulfilled?
   - are standard test protocol used?
   - are studies performed according to GLP?
   - Is there a proposal for reference values?
2. Check international AOEL, ADI, ARfD (see Table given below).
3. Compare the dossier with the international values
   - Is the submitted dossier in line with international reference values?

If the applicant's values are the lowest, chose these for risk assessment. Otherwise the JMPR reference values for ADI and ARfD are preferred, and the EU AOEL.

The values indicated by the applicant can be quickly scanned, if considered necessary. The applicant should have indicated all the available NO(A)ELs from the dossier in the application form.
For the ADI and ARfD, the lowest NO(A)EL in a relevant study should be 100 times the reference value. For the ARfD the relevant studies are usually acute neurotoxicity studies, 14-28 day oral studies, and developmental studies. For the ADI all studies should be considered relevant.
For the AOEL, the lowest NO(A)EL in a relevant study should be higher than the reference value by a factor of (100 / oral absorption). E.g. if the oral absorption is 60%, the NOAEL of the relevant study is 100 / 0.60 = 167 times higher than the AOEL. The AOEL is usually set for semichronic exposure, in which case the following studies are relevant: acute neurotoxicity studies, short-term studies (up to 90-days), 1-year dog studies, and developmental studies.

Table 3.11

Internet sources for reference values.

EU Pesticide database	EU database on all active substances notified as active substance in plant protection products. (in the box right to 'find substance' type (part of) the active substance name, then click 'find substance'. Click on the right name, and then click 'show details' In the next screen either just a pdf (review report) is indicated, or the pdf (review report) and a link to the EFSA risk assessment. The complete list of endpoints in included in the EFSA risk assessment. When no EFSA conclusion is available, the list of endpoints will be included in the pdf (review report) http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection&a=1 This database will include the reference values from JMPR and EPA when available.
JMPR	7

3.5 Occupational risk assessment

In this chapter, the occupational risk assessment will be described in detail. After a general introduction on hazard, exposure and risk the different models to estimate operator exposure during pesticide mixing, loading and application are described. Thereafter it is explained how the exposure of the worker, e.g. during harvesting the crops, can be estimated. Comparing the (estimated) exposure with the AOEL (hazard reference value) will result in the risk assessment.

3.5.1 Introduction

Pesticide Registration and Control Regulation

Legal basis for assessing operator exposure

Schedule II – Article 1.1.2

(The Ministry… shall evaluate…) operator's exposure to the pesticide, or to relevant metabolites, degradation or reaction products, likely to occur following the intended uses and under locally relevant conditions of use.

a. The pesticide will not be registered if, based on risk assessment for realistic worst case conditions, the extent of operator exposure in handling and use of the pesticide for the intended uses exceeds the Acceptable Operator Exposure Level (AOEL).
    a. Where the intended use of the pesticide requires the use of personal protective equipment (PPE), the pesticide will not be registered unless:
    i. that PPE is effective in reducing exposure to below the AOEL and is readily obtainable by the user; and
    ii. it is feasible to use the PPE under the conditions of use of the pesticide, taking into account climatic conditions in particular.

Legal basis for assessing worker exposure

Schedule II – Article 1.1.3

(The Ministry… shall evaluate…) the potential exposure of other humans (bystanders, workers or flagmen exposed after the application of the plant protection product) or animals to the pesticide, or to relevant metabolites, degradation or reaction products, following the intended uses and under locally relevant conditions of use, and shall verify that:

a. Waiting and re-entry safety periods or other precautions be such that the exposure of bystanders, workers or flagmen exposed after the application of the pesticide under realistic worst case conditions does not exceed the AOEL nor any limit values established for those compounds by the appropriate organ.

b. Waiting and re-entry safety periods or other precautions be established in such a way that no adverse impact on animals occurs.

c. Waiting and re-entry safety periods or other precautions mentioned under this sub-Article be realistic and adapted to the locally relevant conditions of use.

Applicants for registration of pesticides should provide a Table of Intended Uses (see Annex 16).

To assess whether the application of a plant protection product has no adverse consequences for operator and worker, the endpoints from the toxicological dossier and the corresponding reference value (e.g. AOEL) must be compared with the expected exposure.

RISK = HAZARD x EXPOSURE

Calculation of the systemic exposure
For operators and workers the dermal and inhalation routes are the most important routes of exposure. Since Good Agricultural Practice is that operators and workers should not be eating during handling the plant protection product or treated crops, the oral route is not considered a relevant route of exposure for these two groups.

The exposure models used will estimate the exposure on the outside of the human body, the external exposure. To compare this exposure to the AOEL, it is adjusted for route-specific absorption to calculate systemic, internal, exposure.

Uptake after dermal exposure
Insight in the extent to which the skin absorbs a substance and/or formulation after exposure to a relevant level is important for calculation of systemic exposure. There is an OECD Guidance note on dermal absorption (2011)
http://www.oecd.org/chemicalsafety/testingofchemicals/48532204.pdf
and a WHO report on dermal absorption (EHC no 235, 2006)
http://www.inchem.org/documents/ehc/ehc/ehc235.pdf

See also section 3.3.3.1 (dermal absorption) of this manual.

Usually the dermal absorption of a formulation is presented as a value for the concentrated formulation (used for mixing and loading) and a value for the diluted formulation (spray dilution used for application). Usually the lowest value is for the concentrated product, and the higher value is for the spray dilution.

Uptake after inhalation exposure
The level of systemic exposure requires insight in the extent to which a substance and/or formulation is taken up in the body via inhalation after exposure to a relevant level.
A default value of 100% is applied where no suitable data on respiratory absorption at the respiratory NOAEL are available.

National default values
Ethiopian operators and workers are considered to weigh 60 kg. The duration of a working day is assumed to be 8 hours.

3.5.2 Operator exposure

Operator exposure is defined as the exposure of the person who applies plant protection products. It is preferably assessed on the basis of exposure studies, carried out in accordance with the current guidelines. As usually such studies are missing, first an exposure estimation is prepared with generic or more specific models.
Supplementary data on actual exposure can be requested if necessary, based on this risk assessment.

There are several models available for estimation of the exposure to plant protection products. For practical reasons (availability and experience) only the German (DE) and the Dutch (NL) greenhouse model will be used in Ethiopia. The UK POEM model for outdoor uses will for the time being not be used in Ethiopia, and information is provided only for future reference.

Thus, the German (DE) model is generally used for estimation of exposure resulting from outdoor uses. The Dutch (NL) greenhouse model is specifically developed for estimation of exposure for various activities in greenhouses. Also, modules available in the DE model (manual upward spraying) can be used for applications in greenhouses, even though they were not specifically developed for greenhouses.

The abovementioned models are not suitable for a number of applications, such as dusting of crops before storage, seed treatment, spraying via airplane, spreading of granules, fumigation of greenhouses. While awaiting further research, a qualitative exposure estimation based on expert judgement is made for these applications.

WHO peer-reviewed, generic models of assessment of certain public health pesticides are available from WHOPES. These models refer only to public health, and consider only exposure resulting from impregnating mosquito nets. There are no occupational exposure models for plant protection products mentioned by the WHO.
http://www.who.int/whopes/guidelines/en/

Exposure is first estimated for the unprotected operator in normal working clothes.
Where necessary, the effect of protective measures is taken into account in a later phase of the risk evaluation based on expert judgement with regard to the applicability of using Personal Protective Equipment (PPE) in that situation. In general, for Ethiopia it seems probable that workers and small scale farmers will usually not be able to use proper PPE, and therefore these protective measures to reduce the exposure will not be considered in the risk assessment for these groups.

Models for operator exposure
There are several models available for estimation of the operator exposure during the handling of a plant protection product. The choice of model or of the module within a model depends on the type of application:
- Indoors vs outdoors.
- Manual (knapsack) vs mechanical (tractor).
- Upwards vs downwards.

For the exposure assessment, the following models will be used for standard spraying operations (note that the UK POEM model is not intended for use in Ethiopia, its details are given only for future reference):

Table 3.12
Overview of models used in exposure assessment.

Operators		PPE possible
Small scale – field	UK POEM + German model	no
Large scale – field	UK POEM + German model	yes
Large scale – greenhouse	NL greenhouse model	yes
Aircraft – field	No model for Ethiopia yet	-
Workers		
Field / greenhouse	EUROPOEM II	no
Bystanders/flag men	No model for Ethiopia yet	-
Residents	No model for Ethiopia yet	-

Operator: Involved in mixing/loading and application of PPP during an entire working day
Worker: Handles (e.g. harvesting) crop previously treated

Table 3.13

Overview of exposure scenarios used for crops.

Crop	Field[1)]		Greenhouse
	Tractor	Hand	
Tomato (=vegetable, fruiting)	Down	Down	Yes
Onion (=vegetable, bulb)	Down	Down	Yes
Cabbage (=vegetable, leafy)	Down	Down	Yes
Potato	Down	Down	No
Teff[2]	-	Down	No
Wheat	Down	Down	No
Maize	Down	Down	No
Barley	Down	Down	No
Faba bean (=pulses)[2]	-	Down	No
Green beans	Down	Down	No
Sweet potato[2]	-	Down	No
Cotton	Down	Down	No
Mango	Up	Up	No
Sugarcane	Down/up	Down/up	No
Banana	Up	Up	No
Citrus (lemon)	Up	Up	No
Coffee	Up	Up	No
Pome/stone fruit	Up	Up	No
Chat (chata edulis)[2]	-	Down/up	No
Flowers (greenhouses)[2]	-	Down	Yes

1) Indicates whether the crop is treated at large scale farms (tractor) or small scale (hand), and whether the application is considered upward- or downward spraying. Up- or downward depends also on the type of pesticide (herbicides are always applied by downward spraying), and on the growth stage of the crop at the time of treatment.

2) According to the information obtained from various experts, these crops are not sprayed by tractor in Ethiopia.

For practical reasons (commonly used in de EU, available on internet, easy to use), the following models will be used to estimate the operator exposure for the authorisation of plant protection products in Ethiopia:

1. German BBA model.
2. Dutch greenhouse model.

The Dutch greenhouse model has been incorporated into PRIMET-Registration_Ethiopia, while the German BBA model will be delivered with the software as well, but will be accessible as a stand-alone module.

German model

- Is developed by German industry and regulatory authority
- Applies to uses of wettable powder (WP), wettable granules (WG) and liquids
- Exposure scenarios:
  - Vehicle equipment: downwards and upwards
  - Handheld equipment: upwards only
  - Home and garden use
- Uses the geometric mean of data available in the database
- Underlying database is relatively small for mixing/loading of WP and WG and for downward spraying with tractor-mounted equipment
- No PPE = moderately dressed with shoes and socks; half of upper arms, forearms, thighs and lower legs are assumed uncovered and hence unprotected.

Model:

http://www.bfr.bund.de/cm/343/anwendersicherheit_deutsches_modell_v1.xls

Please note that for Ethiopia it was decided that the protection factors for PPE/RPE used in the German model have been changed to more realistic (and more worst case) protection factors. These more realistic factors are in line with the ones used in the UK POEM and NL greenhouse model.

The requirements for PPE vary considerably. Most countries start with a minimum requirement and then add to the requirement if extra protection is needed based on the outcome of the risk assessment.

Table 3.14

Reduction factors for personal protective equipment (PPE) to be used in Ethiopia when using the German model operator exposure calculations. Factors for UK POEM model are given for future reference only.

Personal protective equipment:	to lower[1]:	Original German model		UK POEM model		Proposal for Ethiopia[2]	
		Reduction Of exposure	Protection factor	Reduction Of exposure	Protection factor	Reduction Of exposure	Protection factor
Particle filtering half mask (m/l)	I	92%	0.08	90-95%	0.1-0.05	90%	0.1
Half mask with combined filter (m/l)	I	98%	0.02	n.a.	n.a.	90%	0.1
Particle filtering half mask (appl.)	I	92%	0.08	90-95%	0.1-0.05	90%	0.1
	D	20%	0.8	n.a.	n.a.	n.a.	n.a.
Half mask with combined filter (appl.)	I	98%	0.02	n.a.	n.a.	90%	0.1
	D	20%	0.8	n.a.	n.a.	n.a.	n.a.
Protective gloves (m/l)	D	99%	0.01	99%	0.01	90%	0.1
Protective gloves (appl.)	D	99%	0.01	90%	0.1	90%	0.1
Protective garment + sturdy footwear (appl.)	D	95%	0.05	n.a.	n.a.	90%	0.1
Broad-brimmed headgear (appl.)	D	50%	0.5	n.a.	n.a.	n.a.	n.a.
Hood and visor (appl.)	D	95%	0.05	n.a.	n.a.	n.a.	n.a.

1) Route for which the PPE can reduce the exposure: I=inhalation, D=dermal

2) Reduction values to be used in Ethiopia when using the German model to calculate operator exposure.

Background information on the German authority site:
http://www.bvl.bund.de/EN/04_PlantProtectionProducts/11_Applicants/02_AuthorisationProcedure/06_Toxicology/PlantProtectionProducts_toxicol_node.html

The following instructions on how to use the model itself are included. Important points to keep in mind when using the German model:

- Fill in the parameters, using the correct units,
- Dermal absorption = dermal penetration. Often the lowest value is for the concentrated product, used for mixing and loading, and the higher value is for the spray dilution, used for application,
- Change body weight from 70 kg to 60 kg for Ethiopia,
- First check if it is safe without any PPE. If not safe then start with:
  - 1st protective gloves during mixing and loading
  - 2nd protective garment and sturdy footwear during application
  - 3rd any other appropriate PPE.

How to find the result in the output generated by the German model:
In the table with results the dermal exposure and inhalation exposure are presented. The left side of the table is without PPE, the right side is with PPE. The exposure is first given as external exposure, and also as a systemic (internal) exposure by using the dermal or inhalation absorption value.

Dermal exposure consists of dermal exposure during mixing and loading, and dermal exposure during application, divided over exposure to hands, body and head. Inhalation exposure consists of exposure during mixing and loading and during application. The total systemic exposure consists of the sum of these dermal and inhalation exposures.

UK POEM

- Is developed by UK industry and regulatory authorities
- Is currently not used in Ethiopian registration, details are given for future reference only
- Applies to wettable powder (WP), wettable granules (WG), water soluble bags (WB) and liquid formulations
- Exposure scenarios:
  - Vehicle equipment: downwards and upwards
  - Handheld equipment: downwards and upwards
  - Home garden low level spraying
- Uses 75th percentile of data in the database (or maximum values for small databases) for exposure estimates
- Updated with data from other operator models (EUROPOEM and PHED)
- No PPE = a single layer of work clothing (long sleeved shirts, trousers with long legs) is assumed during professional use, T-shirt and shorts are assumed during home garden use.

Model:
http://www.pesticides.gov.uk/guidance/industries/pesticides/topics/pesticide-approvals/pesticides-registration/applicant-guide/updates/updates-to-the-uk-poem-operator-exposure-model

The UK POEM model is not included in the software package delivered to Ethiopia; information is given for future reference only.

Background information on the UK authority site:
http://www.pesticides.gov.uk/guidance/industries/pesticides/topics/pesticide-approvals/pesticides-registration/data-requirements-handbook/toxicity-working-documents

The following instructions on how to use the model itself are included. Important points to keep in mind when using UK POEM:

- Tractor downward: the use of tractor-mounted/trailed boom sprayer, with hydraulic nozzles is assumed,
- Tractor upward: use tractor-mounted/trailed broadcast air-assisted sprayer, and choose either 500 l/ha, 100 l/ha or 50 l/ha depending on the amount of water used per ha,
- Fill in the parameters, using the correct units,
- Dose: fill in the amount of formulation per ha (*i.e.* not the amount of active substance per ha),
- Application volume: fill in the amount of water used per ha,
- Body weight is already based on 60 kg
- First check if it is safe without any PPE. If not safe then choose an appropriate PPE.

How to find the result in the output generated by UK POEM:
UK POEM will present the results either without PPE or with PPE.
In the table with results the dermal exposure and inhalation exposure are presented. The exposure is in first instance given as external exposure, and is then expressed as a systemic (internal) exposure by using the dermal or inhalation absorption value.
Dermal exposure consists of dermal exposure during mixing and loading, and dermal exposure during application, divided over exposure to hands, trunk and legs. Inhalation exposure consists of exposure during mixing and loading (solids only) and during application. The total absorbed dose consists of the sum of dermal and inhalation exposures.

NL greenhouse
- Developed by Dutch authorities
- Exposure scenarios for the:
  - - Indoor (glasshouse) use of handheld equipment
- No distinction is made between up- and downwards spraying
- Uses 90th percentile of data available in the database for exposure estimates
- No distinction is made between exposure during mixing/loading and applications.

Model:
- www.ctgb.nl click on 'full text and Guidance documents' under 'Regulation placing of ppp on the market'

The following instructions on how to use the model itself are included. It is added only for information as the model has been included in PRIMET-Registration_Ethiopia, hence does not have to be used as a standalone version.

Important points to keep in mind when using the Dutch greenhouse model:
- Fill in the yellow fields, using the correct units,
- The area treated can be changed if necessary. In the EU, 1 ha is used as the maximum area that can be treated manually in one day,
- Fill in the AOEL in mg/person/day, based on a 60 kg person,
- First check if it is safe without any PPE. If not safe then start with:
  - 1st dermal PPE
  - 2nd any other appropriate PPE.

How to find the result in the output generated by the Dutch greenhouse model:
At the end of the spreadsheet, the results for the dermal exposure and inhalation exposure are presented as internal exposures. There is no distinction between exposure occurring during mixing and loading, and during application.

3.5.3 Worker exposure

Worker exposure is defined as the exposure of the person who enters an area or handles crop previously treated with a plant protection product. Worker exposure is preferably assessed on the basis of exposure studies, carried out in accordance with the current guidelines. As usually such studies are missing, a first exposure estimation is prepared using generic or more specific models. Supplementary data on actual exposure can be requested if necessary, based on this risk assessment.

There are several models available for estimation of the worker exposure to plant protection products. For practical reasons (availability and experience) the EUROPOEM model, which is commonly used in Europe, is chosen as a first tier model for use in Ethiopia.

Exposure is estimated for the unprotected worker in normal working clothes.

Model for worker exposure
For practical reasons (commonly used in de EU, available on internet, easy to use), the following model will be used to estimate the worker exposure for the authorisation of plant protection products in Ethiopia:

EUROPOEM II
- Developed in Europe by representatives of industry, regulatory authorities and research institutes.
- Estimates dermal exposure for worker in a crop previously treated with PPP.
- Scenarios: re-entry in field crops and greenhouse.
- Can be used as a conservative, first tier approach.
- Step 1: Residue decline is not taken into account.

Model: www.ctgb.nl click on 'full text and Guidance documents' under 'Regulation placing of ppp on the market'.

The following instructions on how to use the model itself are included. It is added just for information as the model has been included in PRIMET-Registration_Ethiopia, hence does not have to be used as a standalone version. Important points to keep in mind when using EUROPOEM:

- Fill in the yellow fields, using the correct units.
- Fill in the AOEL in mg/person/day, based on a 60 kg person.
- First check if it is safe without any PPE. If not safe then start with:
  – 1st dermal PPE, if appropriate.

How to find the results in the output generated by EUROPOEM:
At the end of the spreadsheet, the results for dermal exposure (field and greenhouse) and inhalation exposure (greenhouse only) are presented as internal exposures.

A 'Transfer Coefficient' (TC) is a theoretical estimate of the amount of contact (*i.e.* area of foliage) that occurs with a pesticide-treated crop during the conduct of a specific work activity. The following indicative TC values are proposed in EUROPOEM II for four different scenarios in which harvesting with bare hands is assumed:

(field) Vegetables:	0.25 m2/hour, assuming much contact with hands and not so much on forearms or body.
Fruit (from trees):	0.45 m2/hour, assuming much contact with hands and forearms, and also body.
(straw)Berries:	0.3 m2/hour, assuming much contact with hands, some with forearms, and not so much for body.
Ornamentals:	0.5 m2/hour, assuming much contact with hands and forearms and body.

The indicated crops are considered to be representative for a group of crops with respect to size of fruit/vegetable and foliar area to be touched during re-entry. For harvesting fruiting vegetables like tomatoes and cucumbers in greenhouses, the Netherlands use a TC value of 0.45 m2/hour, as these crops are growing upwards, and significant foliar contact during harvesting is likely.

Table 3.15

Transfer coefficients for some harvesting practices and some other cultivation practices of crops featuring in the surface water scenarios.

Crops	Practices for harvest and other cultivation activities		TC (m2/hour)
Tomato (=vegetable, fruiting)	Tomatoes are picked by hand, 1st time, 2nd time 5-7 d later, sometimes 3rd time. Plant remainings left in the field (no cattle grazing)	Can also be grown in greenhouse	0.25 (grown vertical) 0.45 (grown horizontal)
Onion (=vegetable, bulb)	Whole plant is taken out, bulb is taken, remainder left on the field, no cattle grazing	Can also be grown in greenhouse	0.25
Cabbage (=vegetable, leafy)	Leafy cabbage, stick is remaining in the field; head cabbage: only head is removed, remainder left in the field. After harvest cattle come in for grazing	Can also be grown in greenhouse	0.25
Potato	Tubers and plants are taken out, but plant remainings are left on the field until ploughing at first rains. No cattle grazing.		0.25
Teff	Cut by hand with aid sickle, gathered in bunches on the arm and next laid down on field with remaining stubbles. Cattle come in to graze stubbles. Ploughing at first rains		0.5
Wheat	See teff		0.5
Maize	Immediately after harvesting the cobs, the entire stick is taken (roots remain in soil)		0.5
Barley	See teff		0.5
Faba bean (=pulses)	Crop is 80 cm to 1-1.5 m high. Beans picked by hand, crop remainder left in the field, but can be collected: for cattle (threshed pods) or for firewood (sticks). Some remainders are left in the field until ploughing at first rains		0.3-0.45*
Sweet potato	Tubers and plants are taken out. Leafy parts are collected and fed to cattle. Soon after harvest the field is fallow		0.25
Cotton	Picked several times by hand. Thereafter plant remainders left in the field. For ploughing: first remainder removed, then real ploughing.		0.3-0.45*
Mango	(Large) tree with fruits. Peak harvest: April-June. After harvest older leaves drop during the dry season. At first rains new shoots and leaves are formed		0.45
Sugarcane	Crop up to 2 m high. Cut by hand		0.5
Banana	Bunch with bananas cut when nearly ripe		0.45
Citrus (lemon)	Fruits picked by hand		0.45
Coffee	Berries picked by hand		0.3-0.45*
Pome/stone fruit			0.45
Chat (chata edulis)	Permanent crop, fresh sprouts (to chew) during rainy season. Not picked after pesticide spraying		0.25
Flowers (greenhouses)	Picked by hand, bundles gathered on arms worker		0.5

* The lower TC value should be used for low crops and less crop contact, the higher TC value for rather intensive crop contact (higher scrubs, or fruits/berries difficult to pick without crop contact).

3.5.4 Risk assessment for operator and worker

In the models, the **total systemic exposure** and% **of AOEL** is given. By combining the exposure estimations with the reference value (AOEL), the risk assessment is performed.

RISK = HAZARD x EXPOSURE.

In the first tier the risk assessment is performed by assuming that no PPE is used. Note that in the risk assessment procedure for operators in Ethiopia the EXPOSURE for field applications is calculated using the German (DE) model, and that for practical reasons (availability and experience) the UK POEM model will for the time being not be used in Ethiopia.

No adverse effects on humans expected (**safe use**) if:
Total systemic exposure is $\leq$ 100% of AOEL.

Adverse effects on humans cannot be excluded (**no safe use**) if:
Total systemic exposure >100% of AOEL,

If adverse effects on humans cannot be excluded (no safe use without PPE), a refinement of the risk assessment should be considered with risk reduction measures:

1. by using PPE, if appropriate (large scale operators only).
2. Increasing the pre-harvest interval, leading to lower dislodgeable foliar residues at the time of re-entry.
3. other refinements, such as lowering of the application rate (but it still has to be effective), using better dermal absorption data (if default values are used). Both options can only be done in collaboration with the applicant.
4. exposure studies, in which the actual exposure is measured for that particular use.

It should be noted that this risk assessment contains a margin of safety.

1. The AOEL is based on a NOAEL in animals, the dose at which no adverse effects are observed. The next higher dose (the LOAEL) is the dose at which adverse effects are observed in the animals. Usually this LOAEL is a 3-10 times higher dose than the NOAEL.
2. The AOEL includes an uncertainty factor of 100, assuming that a sensitive person, e.g. a child or elderly person, is 100 times more susceptible than the test animals in the study.
3. The exposure estimations are based on models, which usually will overestimate the actual exposure.

A margin of safety is necessary to make sure that operators will not experience adverse effects if (incidentally) the product is not used entirely according to the GAP. In considering the need for a pesticide, the responsible authority should weigh the benefits against the risks the pesticide would pose if it were to be used under local conditions.

3.6 Consumer risk

People can be exposed to plant protection products by consuming treated food and drinking water that has been contaminated with (residues of) pesticides. In this chapter the assessment of residues in consumable crops and the assessment of consumer risk will be described in detail.

Consumer exposure is assessed by establishing which consumers will be exposed and, subsequently, comparing the magnitude of exposure to a toxicological reference value.

Pesticide Registration and Control Regulation

Legal basis for assessing consumer exposure through food

Schedule II – Article 1.1.4

(The Ministry ... shall evaluate ...) the exposure of consumers and animals through their diet following the intended uses and under locally relevant conditions of use, and:

a. The pesticide shall not be registered if its intended use will lead to residue levels at harvest, slaughter or after storage or processing, as appropriate, which exceed the nationally established maximum residue limit (MRL) or a provisional MRL.

b. In the absence of a nationally established MRL or provisional MRL, Codex Alimentarius MRLs shall apply, if established for the commodity and pesticide under review.

c. Taking into account all registered uses of the pesticide, the intended use shall not be authorized if the estimated total dietary exposure exceeds the Acceptable Daily Intake (ADI) or the Acute Reference Dose (ARfD). Where treated plants or plant products are intended to be fed to animals, the residues of the pesticide shall not have an adverse effect on animal health or on the food safety of products from animal origin.

To assess whether the residues resulting from the application of a plant protection product have no adverse consequences for the health of consumers, the endpoints from the toxicological dossier and the corresponding reference value (ADI and ARfD) must be compared with the expected exposure.

RISK = HAZARD x EXPOSURE

The expected exposure is calculated using the expected residue levels in the treated crops and contaminated water, consumption patterns, bodyweight of consumers and a number of other parameters. Expected residue levels and the MRL (legal value, Maximum Residue Level) are obtained from studies with the active substance. Furthermore, MRLs are needed for crop export to assess whether the instructions for use were adhered to during cultivation of the crop.

Annex 5 presents a flowchart with the routing of residue and consumer assessment. The general principle of assessing a residue profile is presented in Sections 3.6.1 to 3.6.5. Before the exposure can be assessed, the residues relevant for consumer exposure should be identified by means of metabolism studies, since the applied parent compound may be partly or completely degraded to metabolites.

When the residues relevant for consumer exposure have been established, supervised residue trials are performed in accordance with the intended use(s), analyzing the relevant residues. These residue trials are the basis for deriving the levels of exposure of the consumer, since levels found in these studies are used for the derivation of the magnitude of residues. For assessment of consumer risk, the outcomes of supervised residue trials are used in dietary assessment models, comparing the results against toxicological reference values.

Guidance for the PHRD on the assessment of consumer exposure and MRLs for export of crops are discussed in Section 3.6.6.

3.6.1 Plant metabolism and residue definition

Crops

To assess the fate of residues of active substances, metabolism studies need to be performed in plants representative of crops in which use of the active is intended, under conditions corresponding to the intended GAP, using a radiolabelled form of the active substance. For metabolism studies, a distinction is made between five different crop groups:

- Leafy crop.
- Root/tuber crop.
- Fruit.
- Cereal.
- Pulses/oilseeds.

For the classification of crops, reference is made to OECD guideline 501, Annex 1.
The method of application, e.g. foliar spray, soil or seed treatment, should be representative of the intended use. If the metabolism of the active substance is similar in three different plant groups investigated, metabolism is assumed similar in all crop groups and further study is not required.

A residue definition for plant products is derived from the data from plant metabolism studies, performed with an appropriate crop group and according to a GAP similar as applied for, using radiolabelled pesticide. The residue definition is established by taking the following principal points into account:

- the residue definition (for enforcement/ monitoring) must be suitable for routine monitoring, and should preferably be as reliable and as simple as possible in order not to hinder robust monitoring (*i.e.* the use of multi residue methods).
- the residue definition (for risk assessment) should include the toxicologically relevant metabolite(s) and/or the active substance and the components that constitute the largest part of the residue.

In principle all residues >0.05 mg/kg and/or >10% of total residue (TRR, total radioactive residue) will be included in the residue definition for risk assessment unless proven toxicologically irrelevant. The dose rate applied in the metabolism study should not be too low, as this could result in too small fractions to identify the metabolites. Applying too high dose rates can alter metabolic pathways due to saturation of enzymatic processes, and may therefore cause results which are not representative for the intended use.

Whether a metabolite needs to be included in the residue definition, depends on its toxicity. When a metabolite is formed in the rat during metabolism of the active substance, the toxicity of the metabolite is considered to be covered by the ADI and ARfD of the parent compound. When the metabolite is not formed in the rat, additional toxicity data should be requested to assess whether the metabolite is less or more toxic than the parent. The additional toxicity data are:

- Acute oral toxicity study, in order to assess the LD50.
- 90-day oral study in the rat.
- Genotoxicity testing.

When the studies indicate the metabolite is less toxic than the parent, the ADI and the ARfD of the parent can be used in the risk assessment, by using conversion factors (see below).
When the studies indicate that the metabolite is more toxic than the parent, a separate ADI and ARfD need to be derived for the metabolite to perform a risk assessment for the metabolite.

The residue definition for monitoring may differ from the definition established for risk assessment, *i.e.* the monitoring definition may consider less compounds than the risk assessment definition. This is the case if a suitable (routine) analytical method for a toxicologically relevant component of the residue is not available. A conversion factor is used to convert the analysed marker residue into the residue components that are relevant from a health point of view. These conversion factors may differ per product.
Metabolism studies can be used for derivation of conversion factors, but supervised residue trials are preferred. Example:

After application of compound 'parent A', residues are analysed. Relevant residues are parent A and metabolites M1 and M2, hence, the residue definition for risk assessment is parent A + Metabolite M1 + Metabolite M2.
The ratio (w/w) of these compounds in the total residue is parent A: 40%, metabolite M1: 40%, Metabolite M2: 20%
The residue definition for monitoring is parent A.

To use the residue levels found during monitoring, a conversion factor (CF) needs to be applied to perform the risk assessment.
The percentage of residues of parent, being the residue definition for monitoring, is equal to 40% and is set at 1. The percentages of the other relevant residues are derived using this factor of 1. Since the percentages of metabolite M1 is also 40%, its factor is also equal to 1. Since the percentage of metabolite M2 is 20%, its factor is 0.5 (20% being the half of 40%). The total CF in this example is 2,5, as the residue levels of parent is seen as 1 + 1 + 0.5 for parent + metabolite M1 + metabolite M2.

For already established conversion factors, existing references can be checked.

3.6.2 Supervised residue trials

To determine the amount of residues expected after the use of a plant protection product, trials are performed that should represent the commercial and agricultural use of the plant protect product. The trials should be performed in accordance with the proposed worst-case use on the label.

The worst-case use can be determined by taking the prescribed highest dose rate, maximum number of applications, the shortest spray interval and the shortest pre-harvest interval. The trials are not performed with radiolabelled material, but with a formulated product.

The crop residue trials that serve for derivation of MRLs in plant products must be carried out in accordance with the requested directions for use, in accordance with the most critical use where several directions for use are concerned (see also data requirements in section 3.3.3 and 3.3.4) and under GLP. It is also required that the relevant residue components are analysed at the time of harvest, *i.e.* the residues in the residue definition for risk assessment. Where the products contain residues above the limit of quantification, consisting of an edible and a non-edible part, these must be analysed separately to be able to derive a processing factor, which can be used for refinement of the consumer risk assessment, e.g. citrus analysis in both peel and pulp, stone fruits in both stone and flesh.
A quick scan can be performed on the supervised residue trials by taking into account the following check points:

- Application rates, interval and PHI (pre-harvest interval, time between (last) application and harvest) in accordance with the critical use;
- Weather details – large amounts of precipitation on the day of application can negatively influence residue levels;
- Indoor/outdoor – is the use applied for indoor or outdoor and are the trials performed accordingly;
- Varieties used – using different varieties of a crop can result in different results;
- Sample size – is the sample size taken large enough to represent a reliable sample? This varies per crop. A very detailed list of sample sizes is presented in EU guideline 7029/VI/95 rev.5 of July 22nd, 1997, appendix B: General recommendations for the design, preparation and realization of residue trials;
- Storage of samples – were the samples taken stored frozen shortly after sampling, during transport and at testing facility. Not freezing samples can result in underestimated levels due to degradation of residues after sampling;
- Analytical method used – is the method used acceptable for the pesticide concerned and are recovery rates acceptable in accordance with guidelines.

For crops intended for consumption the acreage per scenario zone (2 agro-ecologically different zones in Ethiopia) and the average diet intake per day determine whether a crop is a 'major crop' or 'minor crop'. This classification determines the number of trials to be submitted per crop.
For new active substances, five trials performed in Ethiopia are required, supported by available data from acceptable locations other than within Ethiopia.
For existing compounds, three trials from efficacy testing combined with residue testing, supported by available data from acceptable locations other than within Ethiopia, are required.
When trials result in residues below LOQ, 2 trials are required for minor crops, whereas 4 trials are required for major crops, as was agreed in the workshop on residues and consumer health of May 2013 (Debre Zeit).

A list of major crops for Ethiopia is given below. All crops not mentioned are considered minor crops:

Table 3.16

Overview of major crops grown in Ethiopia.

Vegetables
Kale
Onion
Garlic
Potato
Carrot
Cabbage
Tomato
Eggplant
Fruits:
Orange
Banana
Papaya
Mango
Avocado
Coffee
Cereals
Teff
Maize
Wheat
Barley
Sorghum
Legume vegetables/Pulses
Beans (fava beans, haricots, etc)
Green peas/chickpeas
Lentils
Oilseeds
Niger seed
Sesame
Linseed
Safflower
Sunflower
Cottonseed
Rapeseed

Where the requested use concerns a group of comparable products, determination of the residues in one or more representatives of the group is sometimes sufficient and results may then be extrapolated to related crops. Below, extrapolation possibilities are given for a number of crops[1]:

- Vegetables:
  - Tomato → eggplant.
  - Sweet pepper ↔ chilli pepper.
  - Onion → shallot, garlic.
  - Open leaf lettuce ↔ kale, spinach, herbs.
  - Cauliflower → broccoli.
  - Cucumber → squash, zucchini, melon.
  - Potato → Sweet potato/taro/yam/carrot.
- Cereals:
  - Teff ↔ Wheat, rye.
  - Barley → oats.
  - Maize/corn → Millet, Sorghum.
- Coffee.
- Oilseeds:
  - Rapeseed, Sesame.
    - Niger seed, Flax seed, Safflower, Sunflower, Cotton seed.
- Fruits:
  - Lemons → other citrus.

[1] → one way extrapolation, ↔ two way extrapolation

Storage stability

Samples taken from metabolism studies and from supervised residue trials will deteriorate in quality and residues can decline when samples are not stored appropriately.
Hence, directly after sampling, samples need to be stored frozen and remain frozen during transport and until analysis.
When these frozen samples are analysed within 30 days after sampling, studies to assess the stability of the residues during storage are not required.
When analysis is performed more than 30 days after sampling, storage stability studies are required. Samples of the product need to be fortified with the relevant residues (*i.e.* parent and/or metabolites) and the duration of the storage stability study must cover the duration of storage during the metabolism studies and supervised residue trials.

Crops are classified according to their matrix:

- High oil.
- High water.
- High starch.
- High acid.
- High protein.
- Special matrices.

For further instructions and examples of crops belonging to the above matrices, see OECD 506.
Recoveries of the fortification need to be in the range of 70-110%, recoveries below 70% indicate that the residue is not stable over the corresponding storage duration.

Example

Blank samples are fortified/spiked with an active substance and are stored in a freezer at -18°C for several periods. At each sampling period, the recovery of the active substance is analysed and presented as a percentage of the originally added amount of active substance. In this example two substances are studied for storage stability.

Table 3.17
Example of storage stability results.

Storage duration (months)	Recovery (%)	
	Active A	**Active B**
0	107	88
1	97	101
2	72	93
3	89	93
6	83	87
9	91	53
12	67	97
18	52	109
24	63	83

The conclusion can be drawn that for active A, the residues are stable during frozen storage for a maximum of 9 months. After this period, the residues deteriorate and the concentration decreases, resulting in an underestimation of the residue level. For Active B, the conclusion is drawn that the residues are stable for at least 24 months. The low recovery at 9 months is considered an anomaly/outlier.

3.6.3 Maximum Residue Levels

3.6.3.1 Definition and legislation

Maximum Residue Levels or Maximum Residue Limits (MRLs) are the legal limits for pesticide residues in food commodities. For the derivation of MRLs, see Section 3.6.3.3 MRLs are established world wide, with different legislation for countries/regions.
Europe, US and Japan for example all have their own legislation and consequently, their own limits. There is also a global forum that established MRLs: CODEX Alimentarius Commission. The Codex Alimentarius Commission was established by FAO and WHO in 1963. It develops harmonised international food standards, guidelines and codes of practice to protect the health of the consumers and ensure fair practices in the food trade.
One organisation (EU) and 185 countries, including Ethiopia, are members of CODEX.

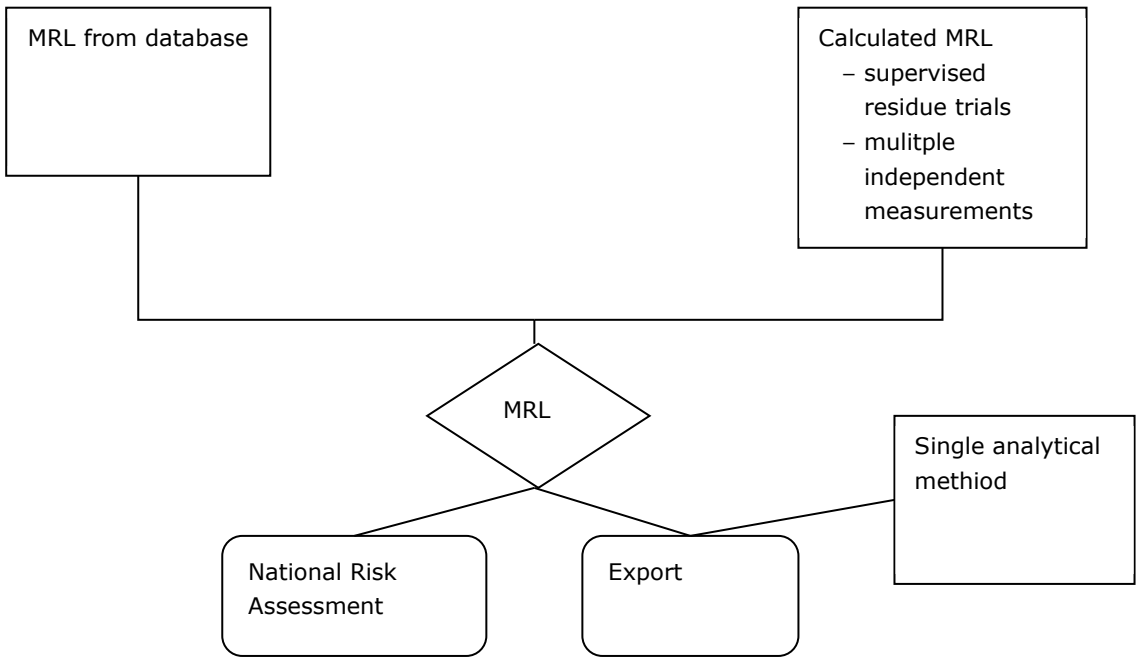
As Ethiopia is a member of CODEX Alimentarius, the CODEX MRLs (CXLs) are used as a basis for risk assessment. Where CODEX MRLs do not cover the use of a plant protection product in Ethiopia, no national MRL will be set as appropriate national Ethiopian legislation is currently not in place. Where the Ethiopian intended use results in an MRL that exceeds the CODEX MRL, Ethiopia should report this to CODEX, supported by data from the supervised residue trials where available.

3.6.3.2 MRL databases

MRLs can either be obtained from databases or they can be calculated using results from supervised residue trials or analytical measurements.

The MRL can subsequently be used for a national risk assessment or to compare analysed residue levels with the MRLs set in the country to which Ethiopian crops are exported. A single analytical measurement cannot be used to establish an MRL since multiple results are needed to form a dataset, but it can be used to check whether a batch of a crop complies with the MRL in the importing country. For more information on residue levels and export, see Section 3.6.4.

The situation is depicted below:



The most relevant databases for MRLs are listed below.

Worldwide MRLs can be found from:
http://www.mrldatabase.com/ by EPA (only for pesticides for which a permanently established EPA tolerance is available).

European MRLs can be obtained from Pesticide Web:
http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=substance.selection
for pesticides reported to the European Commission.

MRLs set for WHO and FAO member states (including Ethiopia) are set in the framework of CODEX Alimentarius, and can be found at:
http://www.codexalimentarius.net/pestres/data/pesticides/search.html.

3.6.3.3 Derivation of endpoints and reference values for consumer risk: MRL, STMR and HR for plant products

Three mathematical values can be derived from supervised residue trials which are needed for consumer risk assessment.

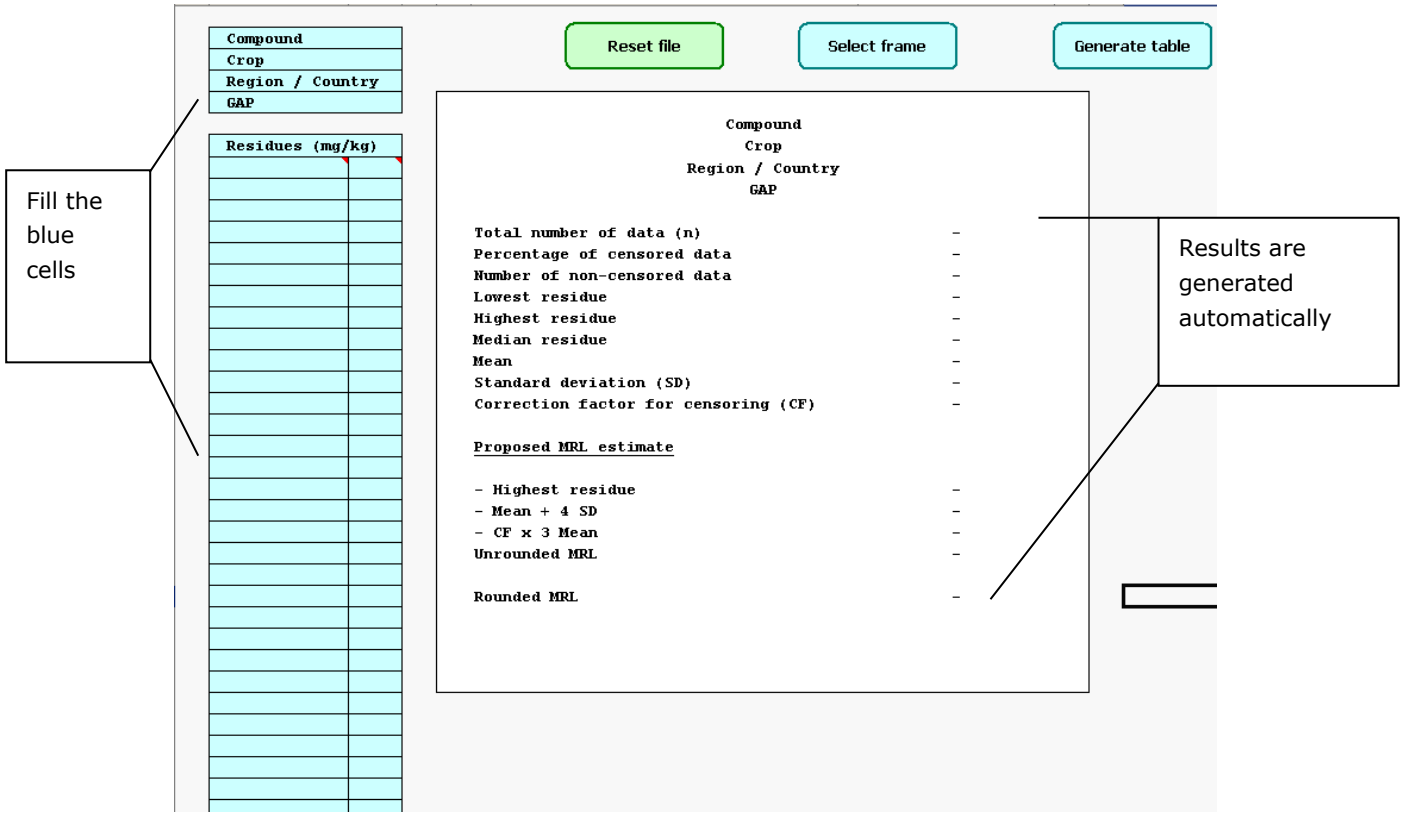
- STMR (Supervised Trial Median Residue) is the median residue value from the residue trials, which can be used for refined chronic and acute intake calculations and feeding studies;
- HR (Highest Residue) value is the highest value measured in a residue trial and can be used for acute intake calculations;
- MRL (Maximal Residue Level) is the maximum concentration of residue, calculated by using a statistical formula and results from supervised residue trials, which can be used for chronic and acute diet calculations for man, as a first tier. Derivation of the MRL is described below.

MRL calculation has been harmonised by the use of the OECD calculator, developed in 2011. As input parameters the results of the acceptable supervised residue trials at the prescribed pre-harvest intervals are used:

- For the calculation of an MRL, two values are used
  1) mean (of all input values) + 4 x SD (standard deviation)
  2) CF (correction factor) multiplied by 3 times the mean of all input values. A correction factor CF is added because it was observed that the mean of a dataset is overestimated for censored datasets. The correction factor CF is equal to 1 – 2/3 * fraction censored data (residues below the Limit of Quantification) in the dataset.
- These values are rounded on a case by case basis (upward or downwards).

The spreadsheet and a guide can be found at:
http://www.oecd.org/env/chemicalsafetyandbiosafety/agriculturalpesticidesandbiocides/oecdmaximumresiduelimitcalculator.htm

A screenshot of the single data set calculator is given below:



See also: http://www.who.int/ipcs/methods/harmonization/en/index.html

Where no residues at all are found above the LOQ (Limit of Quantification), the STMR (Supervised Trial Mean Residue), HR (Highest Residue) and MRL are based on the LOQ. Where there are indications that residue levels are really zero (because the residue levels in the overdosed trials are also < LOQ) the STMR and HR are set at 0 and the MRL at the LOQ.

3.6.4 Principles of consumer exposure assessment

Risk assessment concerning consumer exposure needs to be performed to exclude a risk for consumers. Consumer risk is assessed for chronic (lifelong) as well as acute exposure.

The endpoints from the toxicological dossier and the corresponding limit values (ADI, ARfD) (see section 3.4) must be compared with the expected exposure to assess whether the application of a plant protection product has no adverse consequences for public health. Exposure estimation is based on data from the residue dossier.

Consumer risk assessment uses a tiered approach. The first tier is based on a worst-case situation with regard to the estimated exposure. If the first-tier criteria are not met, supplementary data can be provided and a refined risk assessment should be carried out (higher tier).

In the assessment of risk to consumers, both chronic intake and acute intake are calculated. For each product a Supervised Trial Median Residue level (STMR), a Highest Residue (HR) and a Maximum Residue Limit (MRL) are derived from the residue trials, as explained in section 3.6.3.3. Consumer exposure to residues of plant protection products is determined on the basis of the residue data provided, in combination with diet data.

The intake calculations indicate how much residue is ingested by consumers as a result of the use of a certain active substance under Good Agricultural Practice (GAP). This intake may not exceed the value of the ADI (life-long exposure) and ARfD (single exposure).

Chronic risk assessment for consumers

A 'worst case scenario' is tested as a first tier. It is assumed that all crops from which the consumed products were derived have been treated, and residues will be present at the level of the MRL. All products are assumed to be consumed raw, not taking into account any possible decline in residues by processing.
This worst case scenario is also called the International Theoretical Maximum Daily Intake (ITMDI) calculation:

$ITMDI = \sum (MRL_i \times F_i)$
MRL_i = Maximum Residue Level of a certain product (mg/kg)
F_i = corresponding national consumption of the product in question per person (kg/day)

When the ITMDI is found to exceed the ADI of cluster A, which represents Ethiopia, a second tier calculation is performed: an IEDI (International Estimated Daily Intake) calculation, in which processing data are included and the STMR (median residue level) is applied as residue level instead of the MRL.

$IEDI = \sum (STMR_i \times E_i \times P_i \times F_i)$
STMR = Supervised trial median residue level of a certain product (mg/kg)
E = factor for the edible part of the particular product
P = processing factor of the particular product
F = corresponding national consumption of the particular product per person (kg/day)

Acute risk assessment for consumers

The internationally developed methodology (WHO, JMPR) for point estimation is used; acute risk assessments are based on the assumption that someone consumes a large portion ('Large Portion' = LP) of a crop and that one of the units consumed coincidentally contains a higher residue level than would have been determined based on composite sampling in residue trials. (expressed by the variability factor = v).

Currently, four different cases are distinguished for the calculation of the International Estimated Short-Term Intake (IESTI), each with a specific mathematical method, for which the following parameters are used:

U =	unit weight (g) of a commodity, calculated allowing for the edible fraction
LP =	highest available 'large portion' (97.5 percentile from consumption data) (kg/day)
v =	variability factor, representing the ratio of the 97.5th percentile residue to the mean residue in single units. Default factors for various commodities apply.
HR =	highest residue level in composite samples of the edible portion, found in the residue trials (mg/kg)
HR-P =	highest residue level, where processing of the crop (mg/kg) is taken into account
STMR =	Supervised Trial Median Residue (mg/kg)
STMR-P =	Supervised Trial Median Residue, where processing of the crop (mg/kg) is taken into account
bw =	body weight (kg) provided by the country for which the large portion (LP) was used.

Note, that as a first tier, the MRL is used in the calculations, even though the MRL is not mentioned in the cases given below. In the cases below, where HR(-P) or STMR(-P) are used in the equations, the MRL should be used as the input value for the first tier and the HR(-P) or STMR(-P) for second tier calculations. Only when the calculations result in >100% of the ARfD, a refinement (second tier) needs to be performed by using the appropriate STMR and HR values.

Case 1:
The residue concentration in composite (combined) samples from residue trials (raw or processed) more or less corresponds with the residue in a portion (meal size) of the product; a portion consists of several units (unit weight is < 25 g):

IESTI = [LP × (HR or HR-P)] / bw

Cases 2a and 2b:
The portion (meal size), e.g. a piece of fruit or vegetable, may contain a higher residue than composite samples from residue trials (unit weight > 25 g).
A variability factor is therefore introduced (a standard factor or, alternatively, based on available residue data in separate pieces of fruit or vegetable).
Depending on the properties of a product, the following standard variability factors are applied:

Table 3.18
Variability factors used by 2002 JMPR.

Product property	V
Unit weight of head lettuce	3
Unit weight of the whole portion > 250 g	5
Unit weight of the whole portion ≤ 250 g	7
Unit weight of the whole portion ≤ 250 g, ànd the pesticide is granule for soil treatment	10
Leafy vegetables where the unit weight of the whole portion ≤ 250 g	10

Specific for case 2a:
This concerns the unit weights that are smaller than the large portion (LP):

IESTI =[{U × (HR or HR-P) × v} + {(LP-U) × (HR or HR-P)}]/bw

The Case 2a equation is based on the assumption that the first unit contains residues at the HRxv level and the next ones contain residues at the HR level, which represents the residue in the composite from the same lot as the first one.

Specific for case 2b:
Concerns unit weights larger than the large portion:

IESTI = LP × (HR or HR-P) × v/bw

Where sufficient residue data in separate units are available to derive a HR for separate units, this value should be entered into the equation, without variability factor.

Case 3:
Concerns processed products that have been combined or mixed; the STMR-P value represents the highest residue concentration:

IESTI = LP × STMR-P/bw

The mentioned variability factors (v) are standard factors. Generally, these are conservative values, i.e., they are overestimates. Variability can therefore also be calculated from field measurements of a large number of samples taken of the crop in question which has been treated with the pesticide in accordance with GAP. The mathematical procedure for calculating the variability factor is still under debate but a draft proposal has been made by the IUPAC Advisory Committee on Crop Protection Chemistry.

Relevant references
http://www.who.int/foodsafety/publications/chem/en/pesticide_en.pdf
http://www.who.int/foodsafety/chem/Global_GEMS_02112010.PNG

3.6.5 Guidance specifically for Ethiopia

Since residue data will not be generated in Ethiopia in the near future, the focus of the national assessment is currently on consumer risk assessment and export only.

National risk assessment for food products

All of the cases presented in Section 3.6.4 are included in the PRIMET-Registration_Ethiopia tool. Hence, the formulas are also included in the model. The only input parameters needed for PRIMET-Registration_Ethiopia are the ADI, ARfD, MRL and STMR, and if available, HR and processing data. In Annex 4 of this Handbook, general instructions on the use of the spreadsheet as it can be found on the WHO website are given.

Chronic risk assessment for consumers
As currently no diet information is present for the Ethiopian people, a model designed to fit the Ethiopian people is not available. The EHNRI is currently processing consumption data for Ethiopian mothers (ages 15-49) and their children from both urban and rural areas, and a small group of men.

Until that time the revision 14 of the WHO-GEMS using the GEMS/Food Consumption Cluster Diets from August 2006 is used, with WHO-GEMS cluster diet A considered as the most appropriate.

The model can be downloaded from the WHO website:
http://www.who.int/foodsafety/chem/acute_data/en/index1.html

As teff is not mentioned in the model, another commodity in the model with similar amount of intake per day will be used to extrapolate to teff, see PRIMET-Registration_Ethiopia.

Acute risk assessment for consumers
Since models specifically designed for use in Ethiopia are unavailable, the WHO-GEMS model is used. However, the data from the WHO-GEMS diets are from statistical information on crop production and trade and therefore do not contain specific information on large portions (which is the maximum amount of a certain product consumed on a day). Such data should be derived from food consumption surveys.

In the models, the results of the acute and chronic calculations are expressed as a **percentage of the ARfD and ADI**, respectively.

In the first tier, the risk assessment is performed by using the established CODEX Alimentarius MRLs and/or MRLs calculated using the OECD MRL calculator and the submitted studies.

No adverse effects on consumers are expected (**safe use**):
Total dietary exposure (ITMDI) is $\leq$ 100% of ADI
Acute dietary exposure (IESTI) is $\leq$ 100% of ARfD.

Adverse effects on consumers cannot be excluded (**no safe use**):
Total dietary exposure (ITMDI) >100% of ADI
Acute dietary exposure is (IESTI) > 100% of ARfD.

If adverse effects on consumers cannot be excluded (no safe use when MRLs are used), a refinement of the risk assessment should be considered by performing a second tier:

1. By using STMR and HR instead of the MRL
2. when an STMR is not available, e.g. because original study data are not available, the general rule of thumb can be applied that the STMR is one third of the MRL. For the HR, such a rule cannot be applied.
3. Include processing data, such as peel-pulp distribution, boiling etc in the intake calculations. The processing factor needs to be multiplied with the MRL or HR and STMR.
4. For acute intake calculation, apply a specific variability factor, derived from studies with the same crop/pesticide combination.

After refinement, the same conclusion can be drawn as after the first tier:

No adverse effects on consumers are expected (**safe use**):
Total dietary exposure (IEDI) is $\leq$ 100% of ADI
Acute dietary exposure (IESTI) is $\leq$ 100% of ARfD.

Adverse effects on consumers cannot be excluded (**no safe use**):
Total dietary exposure (IEDI) >100% of ADI
Acute dietary exposure is (IESTI) > 100% of ARfD.

Assessing residue levels for crop export

In view of export of crops grown and treated in Ethiopia, there is a need to assess whether the residue levels in products are in accordance with international (CODEX) MRLs.

Crops are grown for export in Ethiopia. Countries have their own MRLs with which the residues on the Ethiopian products should comply. Various sources for obtaining MRLs are given in Section 3.6.3.2.

To assess whether the residues on Ethiopian products will comply with the MRLs for the importing countries, the results of analytical measurements of treated crops can be used. Alternatively, results from Ethiopian residue trials, if available, may be used to calculate a 'virtual MRL'. The term 'virtual MRL' is used, since no risk assessment needs to be performed and no MRL will be set. The 'virtual MRL' is calculated using the OECD calculator. If the 'virtual MRL' is lower or at the level of the MRL of the importing country, there is no objection against exporting the product. When the 'virtual MRL' is higher than the MRL set in the importing country, export will be hindered, as the country can refuse the product. If the latter is the case, an import tolerance (an MRL based on residue data in an exporting country) can be set. This procedure is different for different countries, and therefore no description is given here.

4 Drinking water risk assessment

4.1 Introduction

This chapter is intended to give guidance on how to assess the risk of pesticides to humans resulting from the use of groundwater and surface water as a source for drinking water. Many of the toxicological terms and abbreviations used are explained in more detail in section 3.4.

This chapter is divided into the following sections:

4.2 Detailed protection goals
4.3 Exposure analysis
4.4 Effect assessment
4.5 Risk assessment and risk classification
4.6 Environmental risk management suggestions.

Pesticide Registration and Control Regulation

Legal basis for assessing consumer exposure through drinking water

Schedule II – Article 2.1.2

(The Ministry… shall evaluate…) the contamination of groundwater and surface water, and the risk of using these as sources of drinking water, following the intended uses and under locally relevant conditions of use.

a. *The pesticide will not be registered if the expected concentrations of the pesticide, or of relevant metabolites, degradation or reaction products, in groundwater or in surface water exceed the nationally established drinking water standard under realistic worst case conditions.*

b. *In the absence of a nationally established drinking water standard, the WHO drinking water guidance value shall apply.*

4.2 Detailed protection goals

This section describes the assessment of risk for humans resulting from the consumption of groundwater and surface water used as a source for drinking water. All groundwater and surface water should be sufficiently protected to enable their use as a source for drinking water. The health of people should be ensured for a life-long time window. Moreover, the occurrence of acute risk as a result of the consumption of water should be ruled out. Since risk as a result of the consumption of drinking water is considered unacceptable, the calculations of exposure concentrations aim to generate sufficiently protective estimates and were designed to generate 99-percentile concentrations both for surface water and for groundwater. For groundwater long-term effects are considered, whereas for surface water both short-term and long-term risks in relation to the consumption of water are considered.

Short-term risks in relation to the consumption of drinking water generated from groundwater seem less relevant in view of the relatively long time between the application of a pesticide and its occurrence at locations from which groundwater is collected (wells etc.), which are usually located at some distance from the location of application.

The long-term risk assessment for surface water is rather conservative, because of the use of a maximum concentration instead of an average concentration. A more realistic assessment may be performed by using a time-weighted average concentration, but this is beyond the scope of the present long-term assessment for surface water.

Summarizing: The detailed protection goal for consumer exposure through drinking water is defined as follows:

i. What should be protected?
   → All consumers of drinking water originating from non-purified groundwater or surface water.
ii. Where should this be protected?
   → Throughout Ethiopia. This is represented by 3 vulnerable scenarios in the following scenario locations (see also Chapter 4.3):
   Surface water:
   - Small streams > 1500 m: grid 191, west of Lake Tana,
   - Ponds between 1500 and 2000 m: grid 217, southeast of Bure,
   - Ponds below 1500 m elevation but with more than 500 mm rain: grid 373, west of Arba Minch.

   Groundwater:
   - Alluvial aquifers along small rivers and volcanic aquifers with shallow wells, both above 1500 m elevation: grid 219 close to Bichena in the Amhara region Alluvial aquifers in the Rift Valley margins and lowlands in areas below 1500 m: grid 346around 100 km southwest of Jimma (SNNP), including both the Kolla and Woina Dega agro-ecological zones,
   - Alluvial aquifers in the Rift Valley margins in areas between 1500-2000 m: grid 323close to Abala Kuliti (SNNP), west of Lake Ziway and Lake Kolla.
iii. How strict should it be protected?
   → No acute effects on the health of the consumer, *i.e.* no exceedance of the Acute Reference Dose (ADI) after drinking a large portion of surface water, for 99th percentile pesticide concentration in surface water.
   → No chronic effects on the health of the consumer, *i.e.* no exceedance of the Acceptable Daily Intake (ADI), for 99th percentile pesticide concentration in groundwater or surface water.

4.3 Exposure analysis

For Ethiopia, the data requirements for active ingredients are indicated in the active ingredient index section of the application form ('List I'), and a guideline on how to fill in this application form is provided. An overview of the specific requirements is given in Annex 8, both for fate in surface water and groundwater.

4.3.1 Scenario zones and locations

To be able to select 'realistic worst-case' scenarios the area which they represent should be selected. It is possible to consider the entire country as one area for which a 'realistic worst-case' should be selected (often operationalised by a 99th or 90th percentile probability of occurrence in time and space over this area) or to divide the country into more areas, called scenario zones, *i.e.* zones which are represented by the scenario. Utilization of more than a single scenario zone caters for the large variation in relevant properties (temperature, rainfall, soil properties etc.) within the country. Although

more difficult to uphold a registration system employing more scenario zones, it has the benefit of increased flexibility. For Ethiopia the choice was made to use two scenario zones.

The zones were chosen in line with the considerations for efficacy testing, *i.e.* distinguishing between two zones on the basis of elevation: one zone below 1500 m elevation and one zone above 1500 m elevation. This seems a 'natural' distinction, coinciding with the delimitation between the traditional 'Kolla' and 'Woina Dega' agro – ecological zones.

Surface water

The scenarios with the highest vulnerability for contamination by pesticides were identified to be small streams/rivers with an upstream catchment on the one hand, and shrinking ponds on the other hand. In terms of association with population and agricultural area these are the most widely distributed scenarios.

The selection of scenario locations is described in general terms in Teklu et al. (2014) and technical details are given by Adriaanse et al. (2014). Locations for small streams are considered only above 1500 m, since they hardly occur below 1500 m elevation. Retreating ponds occur both below 1500 m (but with more than 500 mm annual rainfall) and above 1500 m (predominantly between 1500 – 2000 m) elevation.

Preliminary calculations demonstrated that surface runoff in the surplus of rainfall was the main driving factor for the target variable concentration in surface waters in Ethiopia. Since daily precipitation amounts > 20mm per day are a good indication for the occurrence of runoff events (Blenkinsop et al., 2008), the meteorological data was taken from the ERA Interim dataset (Dee *et al.*, 2011) which is a reanalysis of all available observations from different sources (satellite, ground observations, etc.) made by the European Centre for Medium-Range Weather Forecasts (ECMWF) to create an analysis field on a regular grid. The ERA Interim dataset from 1979 up to and including 2011 was used. Selection of grids considered the number of days per year with rainfall exceeding 20 mm per day over the available 33 years. Some additional criteria like the presence of surface water within the selected (80 * 80 km^2) location (grid), the presence of crops with high use of pesticides and the presence of a populace were also included in the selection procedure. After a first screening 27 locations were identified as meeting the above criteria. Candidate locations were further filtered in order to obtain the three grids representing realistic worst case conditions. The grid with the highest percentile judged to be suitable according to PHRD experts was selected. The selected location for protection goal 1 (small streams above 1500 m) was grid cell 191, west of Lake Tana. For protection goal 2 (ponds below 1500 m) grid cell 373 was chosen, which is located west of Arba Minch, whereas for protection goal 3 (ponds located between 1500 and 2000 m) grid cell 217, southeast of Bure was chosen.

PECs (Predicted Environmental Concentrations) were estimated using the PRZM model for the stream scenario, including a TOXSWA meta model, while PRZM was coupled to TOXSWA to calculate the PECs for the two pond scenarios (see sections 4.3.2 and 4.3.3 for details). For each of the stream and pond scenarios, the 33 annual maximum concentrations were determined, for the entire period (1979 - 2011) covered in the simulation. From the ranked list of annual maximum concentrations, the second highest concentration was used as the exposure concentration for the assessment of risk associated with the consumption of surface water, whereas the sixth highest annual maximum concentration was used as the exposure concentration in the aquatic risk assessment (see Chapter 5). The second and sixth highest concentrations correspond to the 95.5 and 83.3 - temporal percentile concentrations which, combined with the spatial percentiles, approach the desired 99^{th} and 90^{th} overall probability of occurrence as close as possible. The 95.5-temporal percentile concentrations in the selected grids are used in the assessment of risk resulting from the consumption of surface water, whereas the 83.3-percentile concentrations in the same grids are used in the environmental risk assessment. The percentiles used reflect the protection levels defined as desirable during workshops with Ethiopian experts of the Animal and Plant Health Regulatory Directorate (PHRD), Addis Ababa University (AAU) and the Ethiopian Institute of Agricultural Research (EIAR) (www.prrp-ethiopia.org).

Groundwater
In rural areas 90% of the population get their drinking water from ground water, whereas in major towns this applies to approx. 40% of the population. Obviously, ground water is an important source of drinking water.

The most vulnerable scenarios when using ground water for consumption were identified to be alluvial aquifers along small rivers, volcanic aquifers with shallow wells and alluvial aquifers at the Rift margins and lowlands.

The first scenario (alluvial aquifers along small rivers above 1500 m) occurs in regions with high rainfall, in the absence of perennial streams and/or springs, and only if slopes are not too steep. Steep slopes in such areas result in the second scenario (volcanic aquifers with shallow wells), and these 2 types of wells may therefore occur in close vicinity of each other. This may result in a single location being suitable as a scenario location for both of the scenarios. Since both scenarios only occur above 1500 m elevation, only locations with elevations above 1500 m were included in the selection of scenario locations for these 2 scenarios.

The third scenario (alluvial aquifers at the Rift margins and lowlands) occurs in (late) tertiary and younger soils, and only locations with this soil type were included in the selection of locations for this scenario, making a distinction between locations located below and above 1500 m elevation.

Using the EuroPEARL meta-model to calculate the geographical distribution of leaching for some compounds over all of Ethiopia, a map of candidate locations for the ground water scenarios was prepared.

The selected locations for scenarios 1 and 2 (alluvial aquifers along small rivers and volcanic aquifers with shallow wells, both above 1500 m elevation) were located very close together, and it was therefore decided to use the same scenario location for both. From the possible candidates, grid cell 219 was selected because relevant and pesticide treated crops are grown there. This grid cell is located close to Bichena in the Amhara region.

For protection goal 3a (alluvial aquifers in the Rift Valley margins and lowlands in areas below 1500 m), grid point 346 is used, which is located approx. 100 km southwest of Jimma (SNNP).

For protection goal 3b (alluvial aquifers in the Rift Valley margins in areas between 1500 - 2000 m) grid cell 323 is considered sufficiently vulnerable and is used as the location for this scenario. It is located close to Abala Kulito (SNNP).

Parameterization of surface water and groundwater scenario locations
Locations are parameterized and implemented in the PRIMET-Registration_Ethiopia software in such a way that location specific parameter values for soil properties, meteorological data etc. cannot be altered by the user. An overview of the compound specific parameter values that the user has to provide is given in the PRIMET-Registration_Ethiopia manual (Wipfler et al., 2014).

4.3.2 Surface water models

The PRIMET-Registration_Ethiopia software tool used in the Ethiopian registration procedure uses a combination of PRZM (Carsel et al., 1998), the TOXSWA (Adriaanse, 1996) model and TOXSWA meta model for calculation of the concentrations in surface water.

To calculate runoff fluxes into Ethiopian surface water (be it small streams, or temporary ponds) the PRZM model (Pesticide Root Zone Model) was selected. The FOCUS PRZM version used for Ethiopia is the same as used in the EU for simulation of runoff and erosion. It was downloaded from the EU FOCUS surface water website (http://viso.ei.jrc.it/focus/sw/): FOCUS_PRZM_SW_3.1.1 – 4 June 2012.

In view of the limited resources, standard PRZM input of the EU FOCUS surface water R4 scenario (the worst case scenario in the EU) was used, but using Ethiopian weather data (daily rainfall, pan evaporation, temperature, wind speed and solar radiation) and Ethiopian crop data for the selected scenario sites.

Exposure in surface water is calculated differently for the different protection goals. Concentrations in small streams > 1500 m are calculated using runoff as the only source of input of pesticides, whereas the concentrations in temporary ponds assume that apart from runoff, also spray drift constitutes a relevant input of pesticides. Table 4.1 gives an overview of spray drift percentages used for tractor mounted spraying equipment, whereas Table 4.2 gives drift percentages used in the calculations for situations where knapsack sprayers are used, associating the crops with the deposition based upon the EU_FOCUS data (based upon crop stage averaged deposition).

The maximum concentrations in small streams are calculated with the aid of a meta model for TOXSWA, in which the stream flow is composed of a constant base flow, a small subsurface drainage flow and the runoff water flux, all originating from a 100 ha catchment area. 20 ha of the 100 ha are assumed to be treated with pesticide. The main entry of pesticides and water into the streams occurs during runoff events and thus the maximum concentrations in the stream are approximately 5 times lower than the maximum concentrations in the runoff, as calculated by PRZM. This approach of the TOXSWA meta model (instead of running TOXSWA for 33 years for streams) was used in order to reduce calculation time in the PRIMET-Registration_Ethiopia tool. It is acceptable since during runoff the residence times in the streams are very short (< 1 day).

For small ponds, the influx of water is much smaller and residence times are consequently longer. Therefore, the course of pesticide concentration over time in ponds is calculated with the aid of TOXSWA, accounting for decline of concentration through degradation, evaporation and sorption processes. In view of the limited resources, the parameterisation of the EU FOCUS R1 pond scenario (FOCUS, 2001) was used for TOXSWA calculations. However, it was recognized that for the Ethiopian pond scenarios the standard FOCUS sediment segmentation used results in an overestimation of the exposure concentrations calculated by TOXSWA for substances with Kom values in sediment of 3500 L/kg and higher (Adriaanse et al., 2014). A higher tier option for these cases is to run TOXSWA stand alone for the Ethiopian scenarios, using the FOCUS ‘highKoc’ sediment segmentation (Beltman et al., 2014).

Table 4.1

Spray drift deposition in% of application rate for the Ethiopian pond scenarios calculated with the aid of the EU-FOCUS Drift Calculator. Where the Ethiopian crop does not correspond to one of the FOCUS crops, it is associated with a FOCUS crop with closely similar characteristics. The 70-percentile probability of occurrence values are assumed to correspond to Large Scale Farming practices in Ethiopia (Adriaanse et al, 2014).

Crop	FOCUS-crop	70-percentile deposition
		% of appln rate
Tomato#	Vegetables, fruiting	0.1270
Onion#	Vegetables, bulb	0.1270
Cabbage#	Vegetables, leafy	0.1270
Potato#	Potato	0.1229
Teff	Cereals, spring	0.1270
Wheat	Cereals, spring	0.1270
Maize	Maize	0.1229
Barley	Cereals, spring	0.1270
Faba bean	Field beans	0.1229
Sweet potato	Potato	0.1229
Cotton	Cotton	0.1229
Mango (pome/stone representative)	Pome,stone fruits, late applications	1.0459
Sugarcane	Maize	0.1229
Banana	Tobacco	0.1204
Citrus (lemon)	Citrus	1.0459
Coffee	Citrus	1.0459
Appln, hand, crop < 50 cm	Arable, veg<50 cm	0.1270
Appln, hand, crop > 50 cm	Vines, late	0.4722

Cultivated twice: once in the rainy season Kremt and once with irrigation in Bega

Table 4.2

Association between Ethiopian crops and spray drift deposition for knapsack spraying (70 – percentile probability of occurrence) (Adriaanse et al, 2014).

Crop	FOCUS-crop	Deposition by knapsack spraying	No knapsack spraying possible
		% of appln rate	
Tomato#	Vegetables, fruiting	0.1270	
Onion#	Vegetables, bulb	0.1270	
Cabbage#	Vegetables, leafy	0.1270	
Potato#	Potato	0.1270	
Teff	Cereals, spring	0.1270	
Wheat	Cereals, spring	0.1270	
Maize	Maize	0.1270	
Barley	Cereals, spring	0.1270	
Faba bean	Field beans	0.1270	
Sweet potato	Potato	0.1270	
Cotton	Cotton	0.1270	
Mango (pome/stone representative)	Pome,stone fruits, late applications	-	No knapsack
Sugarcane	Maize	0.1270	
Banana	Tobacco	0.1270	
Citrus (lemon)	Citrus	-	No knapsack
Coffee	Citrus	-	No knapsack

Cultivated twice: once in the rainy season Kremt and once with irrigation in Bega

For the small stream surface water scenario (grid 191) the maximum of hourly concentrations in the runoff water flowing out of the catchment of the small stream is used to derive an estimate of the exposure concentration. As water flow in the ponds is less dynamic than in the streams, the pond scenarios (grids 373 and 217) use the maximum daily concentrations in the pond water. For each of the scenarios, the basic hourly or daily maximum concentrations are used to derive a yearly maximum concentration.

Since meteorological data covering 1979 – 2011 are used in the simulations, this results in 33 yearly maximum concentrations. These 33 yearly maximum concentrations are ranked and the desired temporal percentiles are selected, resulting as close as possible to the desired 99 and 90 overall percentiles of occurrence of the concentrations. The 99-percentile exposure concentration is used as an estimate of the exposure concentration in drinking water derived from surface water, whereas the 90-percentile concentration is used as the exposure concentration in environmental risk assessment (Chapter 5).

Multiple crop cycles

Some crops are cultivated during the dry season with the aid of irrigation. The most common crops to which this applies are tomatoes, onions, cabbage and (Irish) potatoes. These four crops are often cultivated twice during a single year: one crop cycle where water is supplied through rainfall, and one crop cycle where water is supplied through irrigation. The distinction between the different crop cycles is taken into account for the environmental protection goals: 'Aquatic ecosystem' and 'Surface water for drinking water' only. Although it might be relevant for other protection goals as well (e.g. leaching to groundwater), this has not been considered. For the two protection goals mentioned above, simulations are done using, among others, the PRZM model. A technical constraint of the PRZM model is that it can only simulate one crop cycle per year. For crops with two crop cycles per year, PRZM simulations are done separately for the first and second cycle, resulting in different exposure concentrations in surface water. For the crops tomatoes, onions, cabbage and (Irish) potato a first and second crop are defined in the crop table in PRIMET-Registration_Ethiopia. This applies to e.g. tomatoes, for which PRIMET-Registration_Ethiopia contains 'tomatoes, first crop cycle' and 'tomatoes, second crop cycle'. The first crop cycle represents crop cultivation during the rainy season (Kremt; no irrigation) and the second crop cycle represents crop cultivation during the dry season (Bega, irrigated).

In the registration process, the different 'crops' relating to either the first or the second crop cycle should be handled as follows:

1. If an authorisation is asked for applying a PPP in a specific season (rainy or dry) or under specific circumstances (irrigated, non-irrigated) the corresponding crop (e.g. either first or second crop cycle) should be used in the assessment.
2. If an authorisation is asked for applying a PPP in the crop in general, assessments should be done for both the first and second crop cycle, and the assessment resulting in the highest ETR should be used in the authorisation process. Note that only the results of the assessments of protection goals 'Aquatic ecosystem' and 'Surface water for drinking water' will result in different ETR values for the different crop cycles.

4.3.3 Groundwater models and scenarios

The PRIMET-Registration_Ethiopia software tool used in the Ethiopian registration procedure uses the EuroPEARL meta-model of Tiktak *et al.* (2006) for the calculation of leaching concentrations.

Tiktak *et al.* (2006) rewrote the original meta-model (see eqn. 6 in Tiktak et al., 2006) as a multiple linear regression model and fitted the leaching concentration in this regression model to the leaching concentration obtained by simulations with the spatially distributed EuroPEARL model. They determined the regression parameters for four major climate zones in the EU: i) temperate and dry, ii) temperate and wet, iii) warm and dry and iv) warm and wet. Out of these four, climate zone iv, warm and wet (annual average precipitation > 800 mm/yr and annual average temperature > 12.5°C), was found to be the one most representative for Ethiopia. Therefore the values of the Model III regression parameters for climate zone iv were used in this project (Table 1 in Tiktak et al., 2006), using the results for a spring application in maize. Note that the meta-model has been calibrated on the 80-percentile leaching concentration, because the EU – based procedures for assessment of leaching concentrations use the 80-percentile concentrations for comparison to a fixed standard concentration of 0.1 µg/L. Although this is plausible for the identification of compounds with high leaching potential, the 80-percentile leaching concentration is considered to offer insufficient protection for use in human risk assessment. Since toxicological effects at human level should be ruled out, the 99-percentile of leaching concentrations was used. Adriaanse et al. (2014) have shown that the results of the meta-model can be transformed into more worst-case situations, e.g. estimating 95- or 99-percentile leaching concentrations through multiplication by a constant correction factor. For deriving 99-percentile leaching concentrations, the results of the original meta-model have to be corrected by multiplying by a correction factor equal to 3. This has been included in the PRIMET-Registration_Ethiopia model calculations.

4.3.4 Acute exposure: surface water

Although the low concentrations in water are generally not expected to evoke acute toxicity in humans, it is not possible to decide whether a risk assessment is necessary until after it has been performed. If it shows unacceptable risk, then it was needed, but if it does not, the acute risk assessment did not add value. In this sense, and in accordance with US regulatory practice, an acute toxicity assessment is always needed (Travis et al., 2004).

To assess short term (acute) risks, caused by drinking a large volume (or Large Portion) of contaminated water during 1 day, the amount taken up through drinking during 1 day (the Daily_Intake_Acute) is compared to a dose that does not cause effects, calculated from ARfD values, *i.e.* Acute Reference Dose values. If for a pesticide no ARfD value is available, this indicates that acute effects are highly unlikely, and acute risk resulting from the consumption of surface water is classified as low. The acceptable dose taken in during a day is referred to as the Daily_Acceptable_Intake_Acute.

The Large Portion (LP) intake, representing the amount of surface water used as drinking water, is set to 6 L per day for Ethiopia. This is higher than the 2 L per day usually assumed for adults, and was chosen to account for increased fluid intake at elevated temperatures (above 25^{o}C). More detailed information on daily consumption of drinking water in Ethiopia, or Large Portion drinking water intake at elevated temperatures in general, were not found in the WHO Guidelines for Drinking Water Quality (4th ed., 2011).

Daily_Intake_Acute = LP_dw * PECsw

in which

Daily_Intake_Acute	= Intake by drinking water from surface waters (µg/day)
LP_dw	= Large Portion of drinking water (6 L/day)
PECsw	= 99-percentile concentration in the selected surface water (µg/L)

The Daily_Acceptable_Intake_Acute is derived from the ARfD:

Daily_Acceptable_Intake_Acute = 1000 * ARfD * BW

Daily_Acceptable_Intake_Acute = Acceptable intake by drinking surface water (µg/day)

ARfD	= Acute Reference Dose (mg/(kg .day))
BW	= Body Weight (60 kg)
1000	= Factor to convert mg into µg.

4.3.5 Chronic exposure: surface and groundwater

To assess long term (chronic) risks, caused by drinking a volume of contaminated water during 1 day, the amount taken up through drinking during 1 day (the Daily_Intake_Chronic) is compared to a dose that does not cause effects when taken up daily during an entire life, which is calculated from ADI values. The acceptable dose taken in every day during the entire life span is referred to as the Daily_Acceptable_Intake_Chronic.

The amount of surface water used as drinking water is set to 2 L per day for Ethiopia, a value typicalla assumed for adults (WHO Guidelines for Drinking Water Quality, 4th ed., 2011).

The Acceptable Daily Intake (ADI) values for active substances and the relevant metabolites should be obtained from the conclusion of the toxicological assessment. However, for existing pesticides the Acceptable Daily Intake values in the database and/or public literature can also be used for the assessment of groundwater as source for drinking water.
Hence, no additional data are required.

Daily_Intake_Chronic_SW = ConsWater * PECsw

Daily_Intake_Chronic_GW = ConsWater * PECgw

in which

Daily_Intake_Chronic_SW	= Intake by drinking water from surface water (µg/day)
Daily_Intake_Chronic_GW	= Intake by drinking water from groundwater (µg/day)
ConsWater	= daily drinking water consumption (2 L/day for adults)
PECsw	= 99 – percentile concentration in the surface water (µg/L)
PECgw	= 99 – percentile concentration in the groundwater (µg/L)

The Daily_Acceptable_Intake_Chronic is derived from the ADI:

Daily_Acceptable_Intake_Chronic = 1000 * P * ADI x BW

In which

ADI	= Acceptable Daily Intake (mg/(kg .day))
BW	= Body Weight (60 kg)
P	= Fraction of the ADI allocated to drinking water (0.1)
1000	= Factor to convert mg into µg.

Note that by introducing P, the fraction of the ADI allocated to drinking water, chronic risks with respect to drinking water are assessed independently from the risk for consumers with respect to food commodities. The risks for humans of drinking water and of the food commodities are not combined into one overall risk for humans in the PRIMET-Registration_Ethiopia tool.

4.4 Effect assessment

Acute risks resulting from the consumption of surface water are assessed by comparing acute intake through drinking water to an acceptable acute intake, calculated using the Acute Reference Dose (ARfD). Similarly, chronic risks are assessed by comparing chronic intake to acceptable chronic intake, calculated using the Acceptable Daily Intake (ADI).

Hence, the acceptable intake is derived from a human toxicity standard, either the Acute Reference Dose (ARfD) for acute toxicity assessment, or the Acceptable Daily Intake (ADI) for chronic toxicity assessment. Both for surface water and groundwater, risks are assessed on the basis of the overall (temporal and spatial) 99-percentile concentration for each of the scenario locations.

4.5 Risk assessment and risk classification

4.5.1 Acute risk assessment: surface water

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach is used, comparing daily uptake to acute toxic dose. The acute toxic dose (acute reference dose, or ARfD) is expressed in µg pesticide per kg body weight (BW) per day. The body weight assumed in the risk assessment is set at 60 kg for Ethiopia.

Acute human risk from the consumption of drinking water is calculated as:

$$ETR_{sw\text{-}dw\text{-}acute} = \frac{Daily\_Intake\_Acute}{Daily\_Acceptable\_Intake\_Acute}$$

Daily_Intake_Acute = Intake by drinking water from surface waters (µg/day)
Daily_Acceptable_Intake_Acute = Acceptable intake by drinking surface water (µg/day)

For the risk classification an exceedance factor has to be defined. Although a high safety factor is used to derive the ARfD (factor 100) an exceedance factor of 1 is still considered necessary since human risk is considered to be unacceptable. The risk classification is presented below.

Acceptable risk: if $ETR_{sw\text{-}dw} \leq 1$
Unacceptable risk: if $ETR_{sw\text{-}dw} > 1$

The risk assessment in surface water is performed using the freely dissolved concentration of the compound, *i.e.* the part of a compound sorbed to suspensed solids present in the surface water is disregarded. For highly hydrophobic compounds, having a tendency to sorb to suspended solids, this may result in an underestimation of risk. For less hydrophobic compounds, and for water that has been filtered or where solids have been allowed to settle before consumption of the water, the freely dissolved concentration is the best estimate of exposure concentration.

4.5.2 Chronic risk assessment: surface water and groundwater

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach is used, comparing the uptake from the 95.5-percentile concentration in surface water (PECsw) or the 99-percentile concentration in groundwater (PECgw) to the chronic toxicity standard, the Acceptable Daily Intake (ADI). For surface water this results in a rather conservative estimate of risk, since the maximum concentration in surface water is used instead of an average concentration. A more realistic assessment may be performed by using a time-weighted average concentration in surface water, but this is beyond the scope of the present assessment.

$$ETR_{sw\text{-}dw\text{-}chronic} = \frac{Daily\_Intake\_Chronic\_SW}{Daily\_Acceptable\_Intake\_Chronic}$$

$$ETR_{gw\text{-}dw\text{-}chronic} = \frac{Daily\_Uptake\_Chronic\_GW}{Daily\_Acceptable\_Intake\_Chronic}$$

Daily_Intake_Chronic_SW = Intake by drinking water from surface water (µg/day)
Daily_Intake_Chronic_GW = Intake by drinking water from groundwater (µg/day)
Daily_Acceptable_Intake_Chronic = Acceptable life-long intake from drinking water (µg/day)

For the risk classification an exceedance factor has to be defined. Although a high safety factor is used to derive the ADI (factor 100) an exceedance factor of 1 is still considered necessary since human risk is considered to be unacceptable. Hence, a factor of 1 is considered appropriate for the risk classification. The risk classification is presented below.

Surface water:

Acceptable risk: if ETRsw-dw-chronic ≤ 1
Unacceptable risk: if ETRsw-dw-chronic > 1

Similarly, for groundwater:

Acceptable risk: if ETRgw-dw-chronic ≤ 1
Unacceptable risk: if ETRgw-dw-chronic > 1

The risk assessment in surface water is performed using the freely dissolved concentration of the compound, *i.e.* the part of a compound sorbed to suspensed solids present in the surface water is disregarded. For highly hydrophobic compounds, having a tendency to sorb to suspended solids, this may result in an underestimation of risk. For less hydrophobic compounds, and for water that has been filtered or where solids have been allowed to settle before consumption of the water, the freely dissolved concentration is the best estimate of exposure concentration.

4.6 Environmental risk management suggestions

Proposals for restriction sentences:

- To protect groundwater do not apply this or any other product containing (identify active substance or class of substances, as appropriate) more than (time period or frequency to be specified),
- To protect groundwater do not apply to (*soil type or situation to be specified*) soils,
- To protect surface water respect an unsprayed buffer zone of (*distance to be specified)* to surface water bodies,
- To protect surface water install vegetated buffer zones of (*distance to be specified*) to surface water bodies.

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5 Environmental risk assessment

5.1 Introduction

5.1.1 The concept of Environmental Risk Assessment (ERA)

The Environmental Risk Assessment (ERA) approach outlined in this section attempts to address the concern for the potential impact of pesticides on the environment by examining both exposures resulting from pesticide emissions and the effects of such emissions on the structure and function of the ecosystem.

The ERA approach is based on three basic assessment processes:

- -Exposure analysis,
- -Effect assessment,
- -Risk characterization.

The risk should be characterized in a quantitative fashion, based on the comparison between the exposure parameters and the effect parameters. For those cases where a quantitative assessment of the exposure and/or effects is not possible a qualitative assessment can be performed.

Figure 5.1 gives an overview of the approach of the Environmental Risk Assessment adopted in this handbook.

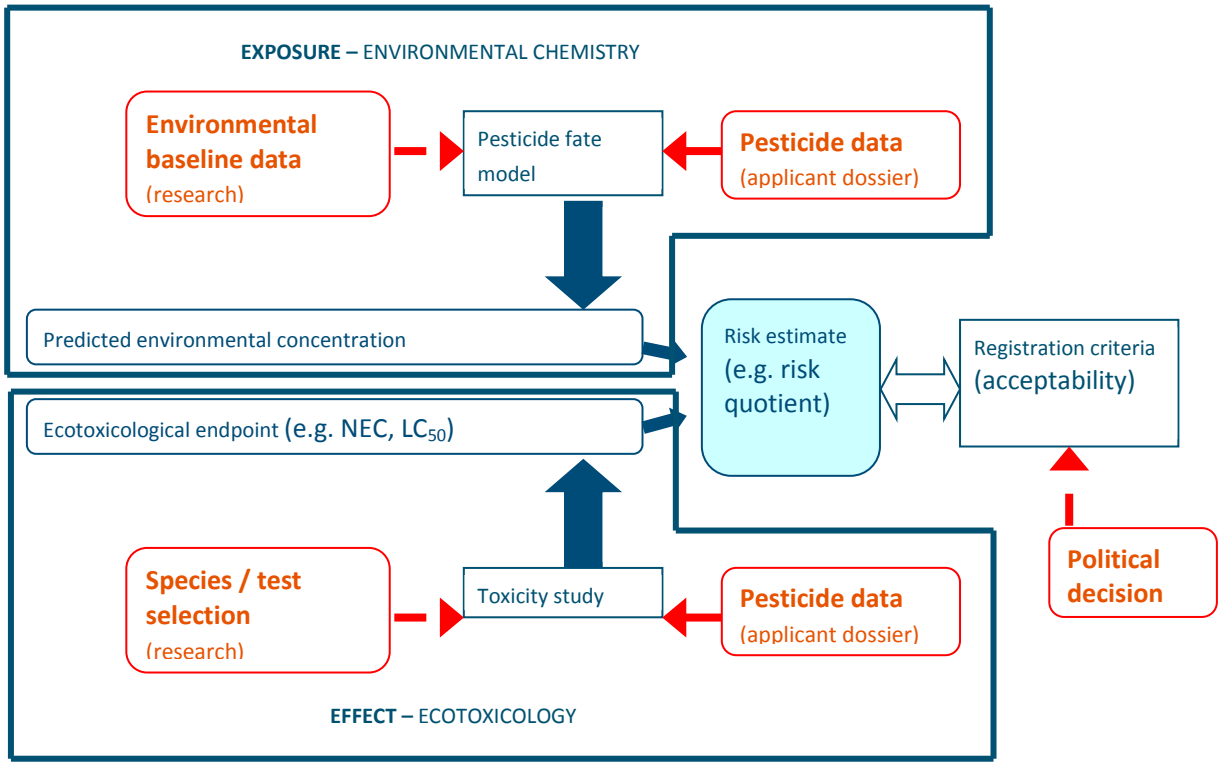


Figure 5.1: Flowchart for the Environmental Risk Assessment approach adopted in this manual.

Notes:

1. Environmental baseline data: the data used for establishing pesticide environmental fate model and scenario, including geographic data, meteorological information, crop category etc.
2. Pesticide data: the data submitted in accordance with the data requirements for Ethiopia for environmental fate and ecotoxicology.
3. Pesticide fate model: the tools (*i.e.* computer program) used in exposure analysis for estimating the Predicted Environmental Concentration (PEC). It should be noted that for several protection goals (e.g. birds, bees, soil organisms), the exposure analysis may be performed with methods other than pesticide fate models.
4. Risk estimate: the ratio between the predicted environmental concentration and the ecotoxicological endpoint such as e.g. LC50, EC50, NOEC.
5. Registration criteria (or acceptability criteria): These are mostly safety factors or uncertainty factors and are in principle established by political decisions. In this Manual the safety factors chosen by the EU are taken into account.

Exposure analysis

The information on fate and behaviour of pesticides in the environment is crucial to the assessment of impact on non-target species. For each environmental compartment an exposure analysis shall be carried out in order to predict the concentration of the active ingredient (a.i.) of the formulated product in the various compartments. This concentration is known as the Predicted Environmental Concentration (PEC).

A PEC only needs to be determined for the environmental compartments to which emissions, discharges or distributions, including any relevant contribution from material (e.g. crop, etc.) treated with formulated products, are known or are reasonably foreseeable. The PEC shall be determined taking into account, in particular, and if appropriate:

- Adequately measured exposure data.
- The form in which the formulated product is marketed.
- The type of the formulated product.
- The application method and application rate.
- The physical-chemical properties of the pesticide.
- The relevant metabolites.
- Likely pathways to environmental compartments and potential for degradation and adsorption/desorption.
- The frequency and duration of exposure.

Where adequately measured and representative exposure data are available, special consideration shall be given to them when conducting the exposure assessment. Where calculation methods are used for the estimation of exposure levels, adequate models shall be applied.

Effect assessment

The effect assessment shall be based on the data from the ecotoxicological studies submitted in accordance with the dossier requirements. Usually results from single species laboratory tests are available, e.g. LD50 (median lethal dose), LC50 (median lethal concentration), EC50 (median effect concentration), or NOEL/NOEC (no-observed-effect level, no-observed-effect concentration resp.). The Predicted No Effect Concentration (PNEC) is extrapolated from the lowest toxicity data resulting from tests on organisms by applying a proper uncertainty factor or safety factor.

An uncertainty factor is an expression of the degree of uncertainty in extrapolation from single-species laboratory data to the multi-species ecosystem. In general, more extensive data and longer test duration result in less uncertainty and smaller uncertainty factors. The following aspects should be taken into account, if appropriate, when choosing the appropriate uncertainty factor:

- Intra- and inter-laboratory variation of toxicity data.
- Intra- and inter-species variation of toxicity data.
- Short-term to long-term/chronic toxicity extrapolation.
- Extrapolation of mono-species laboratory data to field impact on ecosystems.

For Ethiopia the uncertainty factors (or safety factors) as applied in the European Union will be used. Quite extensive experience has been gathered using these factors and they are considered sufficiently protective, without being overprotective.

Risk assessment and risk classification
A risk assessment will be performed for those environmental compartments that are exposed to the formulated product. The risk characterization will be expressed as an Exposure-Toxicity-Ratio (ETR) which is defined as the exposure concentration (PEC) divided by the Predicted No Effect Concentration (PNEC). PNEC is equal to the Toxicity value divided by a safety factor. If the ETR is smaller than 1, *i.e.* the exposure is lower than the safe concentration, the risk is acceptable. If the ETR is higher than 1, *i.e.* the exposure is higher than the safe concentration, there is a chance of unacceptable risk.

An ETR above 1 would usually result in a higher tier risk assessment, but due to the limited capacity on risk evaluations and the complexity of higher tier risk assessments, the risk assessment in Ethiopia will for the time being be based on a first tier risk assessment only. For that reason the level of the risk will be classified in low risk, possible risk and high risk:

Low risk: the ETR is lower than 1: the risk is acceptable,

Possible risk: the ETR is higher than 1 but lower than a certain exceedance factor: the risk is uncertain. If risk reduction measures are possible, they should be applied. Also risk assessments from other countries could be taken into account (e.g. EFSA conclusions),

High risk: the ETR is higher than the exceedance factor: the risk is not acceptable and authorization in principle not possible, unless risk mitigation measures are available which reduce the risk to an acceptable level. Depending on the exceedance factors, some uses of the pesticide may be authorized, whereas other uses cannot be authorized.

The level of the exceedance factor will be different for different protection goals, and may depend on the type of organism. Vertebrates (fish, birds) have a higher protection level than non-vertebrates (dead birds and fish are not desired). Organisms which can reproduce fast have a higher ability of recovery after suffering from effects.

The exceedance factor may also depend on how conservative the first tier assessment is (e.g. a safety factor of 100 for invertebrates is quite strict; the exposure calculation may be conservative). The risk classification is based on the considerations mentioned above, *i.e.* on the ecotoxicological and exposure-related aspects.

The economic consequences will also play a role (which percentage of pesticides will have a high risk and may possibly have to be banned). This aspect has not been taken into account within the risk classification.

A further analysis of the impact of the choice of acceptable exceedance factors on the classification of pesticides (how many of the pesticides will be considered high risk compounds) is desirable.

5.1.2 Data requirements

Environmental risk assessment for pesticide registration is normally carried out on the basis of dossiers which are submitted by the applicants in line with the provisions of Dossier Requirements for Pesticide Registration.

From a scientific point of view, the dossiers submitted must be sufficient to permit an assessment of the impact on every protection goal which is likely to be at risk from exposure to the active ingredient, its metabolites, degradation and reaction products, where they are of toxicological significance.

Impact can result from a single, a prolonged or a repeated exposure and can be reversible or irreversible. In particular, the dossiers submitted should be sufficient to:

- specify appropriate conditions or restrictions to be associated with any registration.
- permit an evaluation of risks for the protection goal in question.
- classify the pesticide product / active ingredient as to hazard.
- specify the precautions necessary for the protection of selected protection goals, to be mentioned on packaging (containers).

5.1.3 Protection goals

The following environmental protection goals are considered to be most relevant for the situation in Ethiopia:
- Aquatic ecosystems.
- Birds.
- Bees.
- Non-target arthropods.
- Soil organisms.
- Soil microorganisms.
- Non-target terrestrial plants.

The following sections will give a uniform description of each of the protection goals.

5.2 Aquatic ecosystems

5.2.1 Introduction

This section is intended to give guidance on how to assess the risk of pesticides to aquatic ecosystems, resulting from their agricultural use. The assessment process described in this chapter follows the same methodology and concept of ERA as laid out in the general introductory chapter, section 5.1. This section is divided into the following paragraphs:

5.2.2 Detailed protection goals
5.2.3 Exposure analysis
5.2.4 Effect assessment
5.2.5 Risk assessment and risk classification
5.2.6 Environmental risk management suggestions.

Pesticide Registration and Control Regulation

Legal basis for assessing risks to aquatic ecosystems

Schedule II – Article 2.1.3

(The Ministry… shall evaluate…) the expected exposure of aquatic organisms to the pesticide, or to relevant metabolites, degradation or reaction products, in aquatic ecosystems relevant to the intended uses of that pesticide and under realistic worst case conditions, considering that.

a. Where there is a possibility that aquatic organisms be exposed, the pesticide shall not be registered if:
i. the exposure/toxicity ratio for fish or aquatic invertebrates is greater than or equal to 0.01 for acute exposure, or to 0.1 for long-term exposure; or
ii. the exposure/toxicity ratio for algae or macrophytes is greater than or equal to 0.1,
unless it can be clearly shown through risk assessment that under field conditions no unacceptable effects on aquatic organisms will occur following the intended use of the pesticide.

[Note: The apparent inconsistency between the exposure/toxicity ratio (ETR) in the Regulation and in the Manual text below is due to the fact that the ETR in the Regulation does not include the safety factor while in the Manual it does.]

5.2.2 Detailed protection goals

'Aquatic ecosystems' is identified as one of the protection goals in this handbook. Details of the protection goal are addressed by answering the following 3 questions:

Question 1: What do we want to protect?

Answer: Ecosystems existing in surface water.

Question 2: Where do we want to protect?

Answer: All natural or semi natural water bodies, which can be streams, rivers, ponds, (temporary) lakes, marshland. For Ethiopia this has been operationalized by selecting two types of most vulnerable small surface waters, *i.e.* small streams only existing in the highlands of Ethiopia (> 1500 m) and temporary ponds existing between 1500-2000 m and below 1500 m, but with at least 500 mm of rain.

Question 3: How strict do we want to protect?

Answer: The sustainability of the aquatic ecosystem should be ensured. Therefore, survival and reproduction of the most sensitive aquatic organisms should not, or only briefly, be affected.

5.2.3 Exposure analysis

When the exposure of aquatic ecosystems cannot be excluded, the exposure level in the aquatic ecosystem should be estimated. The exposure of aquatic ecosystems to pesticides depends on the loading to the surface water. In this handbook, the Predicted Environmental Concentrations (PECs) of a.i. in the surface water are calculated for short-term time-windows under the relevant exposure scenarios by using certain models. The exposure scenarios for Ethiopia resulted from discussions on the detailed protection goals and the vulnerability concept. These exposure scenarios and models are used to estimate the exposure concentration in surface water.

The physical and chemical properties, environmental fate data of the active ingredients and use patterns of the formulated products are of particular importance to the calculation of the PECs. Moreover, attention should be given to the question which time window is considered relevant in the risk assessment.

Data requirements for the active ingredients fate in surface water are given in Annex 8.
Surface water models used for establishing 90-percentile PEC, which are used both for the acute and chronic aquatic risk assessment, are already discussed in Chapter 4. The considerations with regard to crops with multiple crop cycles in Chapter 4 also apply to the risk assessment for aquatic organisms in this Chapter. If application for registration pertains to a single crop cycle, use the exposure concentration applicable to that crop cycle. But if the application for registration includes a crop which has multiple crop cycles, use the highest exposure concentration among crop cycles to evaluate whether exposure results in acceptable risk for aquatic organisms (see Section 4.3.2 for details).

5.2.4 Effect assessment

For Ethiopia, the data requirements are indicated in the application form, and a guideline on the required information is provided.
The applicant has to provide the full study reports and a summary.

An overview of the required data on aquatic organisms is given in Annex 9.

5.2.5 Risk assessment and risk classification

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach is used.
An acute risk assessment is performed for fish, aquatic invertebrates and algae. For herbicides a risk assessment for aquatic plants is included.
A chronic risk assessment is performed for fish and aquatic invertebrates.
For the acute risk assessment the maximum PEC (PECmax) is taken as the relevant exposure concentration in surface water. The chronic risk assessment is also based on the maximum PEC, since a short term exposure to the active substance can result in chronic effects. Moreover, chronic exposure concentrations are not determined in the exposure calculations for pragmatic reasons. In cases where chronic effects are not caused by short term exposure this simplified approach results in conservative risk estimates.

5.2.5.1 Acute risk assessment for fish

For the acute risk assessment one or more LC50 values for fish are available. The lowest LC50 value is chosen. The EU safety factor of 100 is applied to the toxicity value to account for uncertainty.

The ETR for the acute risk assessment of fish is calculated as follows:

$$ETR = \frac{PECmax}{LC50\ (fish)/100}$$

For the risk classification an exceedance factor has to be defined. Because fish belong to the group of vertebrates a somewhat higher protection level is needed than for non-vertebrates. A factor of 10 is considered appropriate for the acute risk classification. The risk classification is presented below.

Low risk:if $ETR < 1$
Possible risk:if $1 \leq ETR \leq 10$
High risk:if $ETR > 10$

5.2.5.2 Chronic risk assessment for fish

For the chronic risk assessment one or more NOEC values for fish are available. If several NOEC values are available, the lowest value is used for risk assessment. The EU safety factor of 10 is applied to the toxicity value to account for uncertainty.

The ETR for the chronic risk assessment of fish is calculated as follows:

$$ETR = \frac{PECmax}{NOEC\ (fish)/10}$$

A factor of 10 for the exceedance factor is considered appropriate, because the exposure is calculated in a conservative way for a chronic risk assessment. The risk classification is presented below.

Low risk:if $ETR < 1$
Possible risk:if $1 \leq ETR \leq 10$
High risk:if $ETR > 10$

5.2.5.3 Acute risk assessment for invertebrates

For the acute risk assessment for invertebrates one or more EC50 values are available. If more than one value is available, the lowest will be chosen for risk assessment.
The EU safety factor of 100 is applied to the toxicity value to account for uncertainty.

The ETR for the acute risk assessment of invertebrates is calculated as follows:

$$ETR = \frac{PECmax}{EC50\ (invertebrates)/100}$$

Because invertebrates normally reproduce faster than vertebrates and faster recovery is therefore expected, a higher exceedance factor is considered appropriate. A factor of 100 is chosen to define a possible risk. Hence, the risk classification is as follows:

Low risk:if ETR < 1
Possible risk:if 1 ≤ ETR ≤ 100
High risk:if ETR > 100

5.2.5.4 Chronic risk assessment for invertebrates

For the chronic risk assessment one or more NOEC values for invertebrates are available. If several NOEC values are available, the lowest value is used for risk assessment. The EU safety factor of 10 is applied to the toxicity value to account for uncertainty.

The ETR for the chronic risk assessment of invertebrates is calculated as follows:

$$ETR = \frac{PECmax}{NOEC\ (invertebrates)/10}$$

A factor of 100 is considered appropriate, because of the usually fast recovery of invertebrates and the fact that the exposure is calculated in a conservative way for a chronic risk assessment. The risk classification is presented below.

Low risk:if ETR < 1
Possible risk:if 1 ≤ ETR ≤ 100
High risk:if ETR > 100

5.2.5.5 Risk assessment for algae

For algae no distinction is made between acute and chronic risk assessment. The appropriate toxicity value is an EC50 value based on growth rate. If EC50 values are available for different algae species the lowest value will be taken for risk assessment. The EU safety factor used to account for the uncertainty in the toxicity estimate is 10, since the life cycle of such species is comparably quite short and the toxicity endpoint is based on growth inhibition instead of immobilization (as is the case for invertebrates) or lethal effect (in the case of fish).

The ETR for the risk assessment of algae is calculated as follows:

$$ETR = \frac{PECmax}{EC50\ (algae)/10}$$

The life cycle of algae is relatively short and the endpoint is based on growth inhibition. Therefore a factor of 100 is considered appropriate to define a possible risk. Hence, the risk classification is as follows:

Low risk:if ETR < 1
Possible risk:if 1 ≤ ETR ≤ 100
High risk:if ETR > 100

5.2.5.6 Risk assessment for aquatic plants

For aquatic plants no distinction is made between acute and chronic risk assessment. The appropriate toxicity value is an EC50 value based on growth rate. If EC50 values are available for different aquatic plant species the lowest value will be taken for risk assessment. The EU safety factor used to account for uncertainty in the toxicity estimate is 10, since the endpoint is based on growth inhibition and not lethality.

The ETR for the risk assessment of aquatic plants is calculated as follows:

$$ETR = \frac{PECmax}{EC50\ (aquatic\ plants)/10}$$

Because aquatic plants have a longer life cycle and will not reproduce very fast, a lower value for the exceedance factor is allowed in comparison with algae. A factor of 10 is considered appropriate to define a possible risk. The risk classification is presented below.

Low risk:if ETR < 1
Possible risk:if 1 $\leq$ ETR $\leq$ 10
High risk:if ETR > 10

5.2.6 Environmental risk management suggestions

Proposals for restriction sentences:

- To protect aquatic organisms respect an unsprayed buffer zone of (*distance to be specified)* to surface water bodies.

5.3 Birds

5.3.1 Introduction

This chapter is intended to give guidance on how to assess the risk from the use of pesticides to birds. The assessment process described in this chapter follows the same methodology and concept of ERA as laid out in the general introductory chapter, section 5.1.

This chapter is divided into the following sections:
5.3.2 Detailed protection goals
5.3.3 Exposure analysis
5.3.4 Effect assessment
5.3.5 Risk assessment and risk classification
5.3.6 Environmental risk management suggestions.

Pesticide Registration and Control Regulation

Legal basis for assessing risks to birds

Schedule II – Article 2.1.7

(The Ministry… shall evaluate…) the expected exposure of birds and other non-target terrestrial vertebrates to the pesticide, or to relevant metabolites, degradation or reaction products, in (agro-) ecosystems relevant to the intended uses of that pesticide and under realistic worst case conditions.

a. Where there is a possibility that birds and other non-target terrestrial vertebrates are exposed, the pesticide shall not be registered if:
   i. the acute exposure/toxicity ratio for birds and other non-target terrestrial vertebrates is greater than or equal to 0.1; or
   ii. the chronic exposure/toxicity ratio for birds and other non-target terrestrial vertebrates is greater than or equal to 0.2; or
   iii. if consumption of one treated seed or pesticide granule leads to exposure which exceeds 1/10th of the acute LD_{50} of the pesticide to birds,

unless it can be clearly shown through risk assessment that under field conditions no unacceptable effects on birds and other non-target terrestrial vertebrates will occur following the intended use of the pesticide.

[Note: The apparent inconsistency between the exposure/toxicity ratio (ETR) in the Regulation and in the Manual text below is due to the fact that the ETR in the Regulation does not include the safety factor while in the Manual it does.]

5.3.2 Detailed protection goals

'Birds' are identified as one of the protection goals in this handbook. For this protection goal, the detailed protection goals are addressed by answering the following three questions:

Question 1: What do we want to protect?

Answer: Populations of non-target birds.

Question 2: Where do we want to protect?

Answer: Treated crop field or other treated locations.

Question 3: How strict do we want to protect?

Answer: No individual mortality or reproduction effects should occur in populations of non-target birds.

At present, use is made of EU indicator species, assuming that they are representative for the birds in Ethiopia.

For the time being spray applications of pesticides will be taken into account in the risk assessment; moreover seeds or granules treated with pesticides for compounds thought to be very toxic to birds will be considered (one seed/granule criterion).

5.3.3 Exposure analysis

There is an EU guidance document on Birds and Mammals (SANCO/4145/2000)[2] available. The risk assessment for birds in Ethiopia is based on this document and relevant parts from the guidance document are presented below.

5.3.3.1 Standard exposure scenarios for the first tier assessment

General approach and default values
In order to avoid bias due to different food intake rates between lab and field, the exposure should be expressed as daily dose for all time scales. Thus the equations for acute and long-term exposure estimates are similar, but the assumptions for the input parameters may be different.

Basically the estimated daily uptake of a compound is given by the following equation:

ETE = (FIR / bw) * C * AV * PT * PD (mg/kg bw/d)

ETE	Estimated Theoretical Exposure, defined as dose (mg/kg bw) or daily dose (mg/kg bw/d)
FIR	Food intake rate of indicator species (gram fresh weight per day)
bw	Body weight (g)
C	Concentration of compound in fresh diet (mg/kg)
AV	Avoidance factor (1 = no avoidance, 0 = complete avoidance)
PT	Fraction of diet obtained in treated area (number between 0 and 1)
PD	Fraction of food type in diet (number between 0 and 1; one type or more types).

In case of multiple applications and/or long-term considerations the concentration C may be expressed as

$C = C_0 * MAF * f_{twa}$

C_0	Initial concentration after a single application (mg/kg)
MAF	Multiple application factor (concentration immediately after the last application compared to a single application; see Table 5.3)
f_{twa}	Time-weighted-average factor (average concentration during a certain time interval, compared to the initial concentration after single resp. last application); $f_{twa} = (1-e^{-kt})/kt$ (-) kln2/DT50 (velocity constant; DT50 on vegetation) (day^{-1}) tAveraging time (days)

In the first tier it is assumed that
- The contaminated diet is not avoided.
- Animals satisfy their entire food demand in the treated area.
- Animals feed on a single food type.

Thus the factors av, pt and pd become 1 and can be omitted.

For food intake rate (FIR) and concentration default values are described below.

[2] Anonymous (2002): Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2000.

Food intake rate (FIR)
Data are derived from an extensive review by Crocker et al. (2002)[3]; the estimates of food intake are based on means of daily energy expenditure for free-ranging animals, energy content, moisture content and assimilation efficiencies.

Concentration (C)

a. Concentrations on vegetation following spray applications:
   Estimates are based on Fletcher et al. (1994)[4]; depending on the time scale either arithmetic means or 90th percentiles are used; the original figures were normalised to an application rate of 1 lb/acr; for the purpose here they are converted to 1 kg a.s./ha (residue per unit dose - RUD) and have to be multiplied by the actual application rate. The RUD values for the acute and long-term risk assessment are given in tables below.
   In the case of fungicides and insecticides applied in tall-growing crops such as orchards and vineyards it is assumed that a fraction of 60% of the applied amount reaches the ground which is the maximum value applying to stages without leaves (FOCUS 2000)[5]; in later stages the interception is higher and accordingly the deposition lower; for refinement the deposition values given in FOCUS (2000) may be used:
   – Vines: no leaves 60%, first leaves 50%, leaf development 40%, flowering 30%. ripening 15%,
   – Orchards like citrus and mango: full foliage 20%.

b. Concentrations on insects following spray application:
   In the current assessment, in line with the current EU assessment, improved residue data are used. The previously used residue estimates for small insects (SANCO guidance document on birds and mammals from 2002, SANCO/4145/2000) were considered unsatisfactory, and were replaced by the present, improved, data (EFSA Journal 2009; 7(12):1483: Risk Assessment for Birds and Mammals). The current 90th percentile RUD value on foliar dwelling insects is 54 mg/kg and the mean value is 21 (see also Tables 5.4 and 5.6 given below).

5.3.3.2 Establishment of scenarios

In the tier-1 assessment standardised realistic worst-case scenarios are considered. These involve generic indicator species representative for various groups of birds. In each crop category several indicator species with different feeding preferences may be relevant. For the tier-1 assessment, however, the number of scenarios has been restricted as far as possible.

Table 5.1 shows which of the indicator species are considered in the various crops.

[3] Crocker DR, Hart A, Gurney J and McCoy C (2002): Methods for estimating daily food intake of wild birds and mammals. Central Science Laboratory, Project PN0908. Final Report. http://www.pesticides.gov.uk/general/ResearchReports/index.htm.

[4] Fletcher JS, Nellessen JE and Pfleeger TG (1994): Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, in instrument for estimating pesticide residues on plants. Environ Toxicol Chem 9, 1383-1391.

[5] FOCUS (2000): FOCUS Groundwater Scenarios in the EU review of active substances. Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference Sanco/321/2000 rev 2, 202 pp.

- 'Grassland' includes pasture, lawn and turf; the vegetation in this group is represented by the category 'short grass' in the database of Fletcher et al. (1994),
- 'Cereals' are divided into early and late stages where 'early' refers to a stage when the crop itself is likely to be grazed; in that case the category 'short grass' is taken to estimate residues on the vegetation,
- 'Leafy crops' form the bulk of the remainder of major field crops. Tier-1 scenarios in this group of crops are based on insectivorous and herbivorous birds; however, many of these crops are not eaten by birds and mammals in late stages, so in cases where refinement becomes necessary the relevance of herbivores should be checked,
- For 'orchard/vine/hops' it is assumed that these cultures have a ground vegetation which is represented by the category 'short grass'. In case of insecticides and fungicides, but not for herbicides, it is assumed that 60% of the applied amount reaches the ground.

Table 5.1

Relevant indicator species according to crop and crop stage.

Crop	Crop stage	Indicator species	Example
Grassland		Large herbivorous bird - 3000 g	Goose
		Insectivorous bird - 10 g	Wren, tit
Cereals	Early	Large herbivorous bird - 3000 g	Goose
		Insectivorous bird - 10 g	Wren, tit
	Late	Insectivorous bird - 10 g	Wren, tit
Leafy crops	Early / late	Medium herbivorous bird - 300 g	Partridge, pigeon
		Insectivorous bird - 10 g	Wren, tit
Orchard / vine / hops	Early / late	Insectivorous bird - 10 g	Wren, tit

In the case of herbicides applied to bare soil (with regard to crops and weeds) residues in vegetation may be negligible, in which case the use of herbivores as indicator species may not be relevant.

For the short-term as well as the long-term time scale the same indicator species will be used. In order to estimate the ETE the food demand needs to be known. In Table 5.2 the Food Intake Rate (FIR) is given for each of the indicator species.

These scenarios are designed for a generalised assessment of a substance intended for major crops or a broad spectrum of crops on EU level, and are assumed to be applicable to Ethiopia.

Table 5.2

Food intake rate (FIR) for indicator species.

Indicator species	Example	Body weight (g)	DEE (Daily Energy Expenditure, kJ/d)		Food characteristic (App I Tab 3)			Assimil. efficiency		FIR (fresh material) (g/day)	FIR / bw
			Equation	DEE (kJ/d)	Food type	Energy (kJ/g dry wgt)	Moisture (%)	Food type	%		
Medium herbivorous bird	Partridge, pigeon	300	Other birds	389	Non-grass herbs	18	82.1	Herbage (Mean)	53	228	0.76
Large herbivorous bird	Goose	3000	Other birds	2302	Grasses, ceral shoots	18	76.4	Herbage (Ans)	41	1322	0.44
Insectivorous bird	Wren	10	Passerines	51	Arthropods	21.9	70.5	Animal (Pass)	76	10.4	1.04

5.3.3.3 Acute exposure

With regard to residues in vegetation and insects, 90th percentiles of the initial concentration are used. This percentile has been chosen to give, along with the other settings, a reasonable and realistic worst case exposure for the first tier assessment. Multiple applications may cause accumulation of residues and therefore need consideration. In the case of vegetation a simple model based on first-order decline is used to calculate multiple-application factors (MAF) which gives the ratio of the initial concentration after the last of n applications compared to the initial concentration after the first application. MAF is a function of the number of applications, interval, and DT50 on vegetation. In the first tier a default value of 10 days for DT50 on vegetation is used. However, ordinary MAF-values cannot be applied to upper percentiles because it is unlikely that each time the upper percentile is exceeded. Therefore special MAF factors have been calculated in order to predict the true 90th percentile of the peak after n applications based on the log distribution of the residue data (Table 5.3). Note that these MAF_{90FI} values contain specific variance information; they are only applicable on the 90th percentiles of these residue data, not on other data.

Table 5.3

Multiple Applications Factors (MAF_{90FI}) to be used in connection with 90th percentiles for residues on short grass and leafy crops.

	Number of applications					
Interval (d)	**2**	**3**	**4**	**5**	**6**	**8**
7	1.4	1.7	1.8	1.9	1.9	2.0
10	1.3	1.5	1.6	1.6	1.6	1.6
14	1.2	1.3	1.4	1.4	1.4	1.4

Table 5.4 shows the standard residues (normalised to an application rate of 1 kg/ha) for the various scenarios. Calculation of the Estimated Theoretical Exposure (ETE) in terms of daily dose (mg/kg bw) is as follows:

- Spray application: Multiply relative daily intake (column 4) by RUD (column 6) and application rate of the active substance (kg a.s./ha); when applicable multiply also by MAF which is taken from Table 3. Hence, the formula is: ETE = FIR/bw * RUD * application rate active substance * MAF.

Table 5.4

Standard scenarios for the acute exposure estimate.

1	2	3	4	5	6	7
Crop	**Crop stage**	**Indicator species**	**FIR / bw**	**Category**	**RUD (90%)**	**MAF**
Grassland	-	Large herbivorous bird	0.44	short grass	142	Table 3
		Insectivorous bird	1.04	small insects	54	Table 3
Cereals	Early	Large herbivorous bird	0.44	short grass	142	Table 3
		Insectivorous bird	1.04	small insects	54	Table 3
	Late	Insectivorous bird	1.04	small insects	54	Table 3
Leafy crops	Early / late	Medium herbivorous bird	0.76	leafy crops	87	Table 3
		Insectivorous bird	1.04	small insects	54	Table 3
Orchard / vine / hops	Early / late	Insectivorous bird	1.04	small insects	54	Table 3

5.3.3.4 Long-term exposure

The exposure estimate for long-term exposure is different from the acute assessment. Residue estimates are based on arithmetic means, for vegetation different multiple application factors are employed and in contrast to the acute assessment time-weighted average (twa) residues are used here as these better reflect long-term exposure. It is obvious that a constant exposure level (if above the response threshold) will have more serious long-term effects than a rapidly declining exposure level starting at the same level. This has to be considered when relating toxicity (constant exposure level) to field exposure. Also, when comparing exposure to a persistent and a non-persistent substance the degradation rate in some way should be reflected in the exposure estimate and the risk

indicator. An appropriate means to reduce such kind of bias is to average the exposure over a certain time interval. Unfortunately there is no sound scientific basis and no generally accepted rule on how long this interval should be; to simply take the study duration is disapproved of by most experts. For the time being a period of three weeks is proposed as a convention, unless there are good reasons to take shorter or longer times. For example, cases where the effects data used are derived from a study with a shorter exposure period, or where a short delay between the onset of exposure and the onset of effects is observed, or where effects are to be ascribed to the exposure during a brief sensitive period would call for a shorter averaging time. With regard to residues on vegetation a simple twa-factor is used in the first tier which is based on the following default values:

- time window (averaging time) = 3 weeks
- DT50 = 10 days

With these assumptions f_{twa} is 0.53; it means that over a period of three weeks the average concentration is about half the initial concentration. (Note: In case of repeated applications the maximum twa may be underestimated when the interval is shorter than the time window; with a time window of three weeks and a DT50 of 10 days the inaccuracy is small and the factor of 0.53 can be used uncorrected).

Many birds are extremely mobile and hence there is the possibility of concurrent and repeated exposure in adjacent fields which may be an issue, particularly in long-term assessments. In the standard procedure the risk from multi-field scenarios is addressed by the conservative assumption that birds obtain all of their food all of the time from a single treated area.

Table 5.5 shows the standard Muliple Application Factors (MAF) for residues in vegetation based on a DT50 of 10 days. When the interval and/or number of applications is different from the example calculations in the table, the equation in the upper row of the table can be used for calculation of the MAF.

Table 5.5

Standard Multiple Applications Factors (MAF) for residues in vegetation based on a DT50 of 10 days (equation and example calculations).

MAF = $(1-e^{-0.069 * n * i})/(1-e^{-0.069 * i})$ i = interval; n = number of applications						
	Number of applications					
Interval (d)	2	3	4	5	6	8
7	1.6	2.0	2.2	2.4	2.5	2.5
10	1.5	1.8	1.9	1.9	2.0	2.0
14	1.4	1.5	1.6	1.6	1.6	1.6

Table 5.6 shows the standard residues (normalised to an application rate of 1 kg/ha) for the various scenarios. Calculation of ETE in terms of daily dose (mg/kg bw) is as follows:

- Spray application: Multiply relative daily intake (4) by RUD (6), twa-factor (7) and application rate of the active substance (kg a.s./ha); when applicable multiply also by MAF (8) which is taken from Table 5. Hence, the formula is: ETE = FIR/bw * RUD * application rate active substance * MAF * f_{twa}.

Table 5.6
Standard scenarios for the long-term exposure estimate.

1	2	3	4	5	6	7	8
Crop	**Crop stage**	**Indicator species**	**FIR / bw**	**Category**	**RUD (mean)**	**f_{twa}**	**MAF**
Grassland	-	Large herbivorous bird	0.44	short grass	76	0.53	Table 5
		Insectivorous bird	1.04	small insects	21	0.53	Table 5
Cereals	Early	Large herbivorous bird	0.44	short grass	76	0.53	Table 5
		Insectivorous bird	1.04	small insects	21	0.53	Table 5
	Late	Insectivorous bird	1.04	small insects	21	0.53	Table 5
Leafy crops	Early / late	Medium herbivorous bird	0.76	leafy crops	40	0.53	Table 5
		Insectivorous bird	1.04	small insects	21	0.53	Table 5
Orchard / vine / hops	Early / late	Insectivorous bird	1.04	small insects	21	0.53	Table 5

5.3.4 Effect assessment

For Ethiopia, the data requirements are indicated in the application form and a guideline on the required information is provided. An overview of the data requirements related to birds is given in Annex 10, both for the active ingredient and for the formulated product.

The applicant has to provide the full study reports and a summary.

5.3.5 Risk assessment and risk classification

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach will be used.
An acute and a chronic risk assessment is performed for birds.

5.3.5.1 Acute risk assessment for birds

For the acute risk assessment an LD50 value for birds is available. The lowest LD50 value is chosen. The EU safety factor of 10 is applied to the toxicity value to account for uncertainty.

The ETR for the acute risk assessment of birds is calculated as follows:

$$ETR = \frac{ETEacute}{LD50\ (birds)/10}$$

For the risk classification an exceedance factor has to be defined. Because birds belong to the group of vertebrates a somewhat higher protection level is needed than for non-vertebrates. Based on expert judgement a factor of 5 is considered appropriate for the acute risk classification. It is estimated that not many birds will die at this level of exceedance of the safe level defined by the EU, because the ETEacute is calculated in a quite conservative way. The risk classification is presented below.

Low risk:	if ETR < 1
Possible risk:	if $1 \leq ETR \leq 5$
High risk:	if ETR > 5

5.3.5.2 Chronic risk assessment for birds

For the chronic risk assessment a NOEC value for birds from reproduction studies is available. If there are more NOEC values available, the lowest value is used for risk assessment. The EU safety factor of 5 is applied to the toxicity value to account for the uncertainty.

The ETR for the chronic risk assessment of fish is calculated as follows:

$$ETR = \frac{ETEchronic}{NOEC\ (birds)/5}$$

For the risk classification an exceedance factor has to be defined. Because birds belong to the group of vertebrates a somewhat higher protection level is needed than for non-vertebrates. Based on expert judgement a factor of 10 is considered appropriate for the chronic risk classification, because chronic risk assessment takes sublethal effects into account, from which birds may recover. Moreover, the exposure calculation is quite conservative (birds are considered to eat 100% of their diet from the treated field and also 100% of the same food item).The risk classification is presented below.

Low risk:if ETR < 1
Possible risk:if 1 $\leq$ ETR $\leq$ 10
High risk:if ETR > 10

Seeds/granules
Only the one seed/granule criterion is considered: if consumption of one seed/granule is already enough to exceed the LD50 divided by the EU safety factor (LD50/10), there is a very high risk for birds. As indicator species a bird of 25 gram is taken for risk assessment. The critical dose for this indicator species in mg is: LD50 * 0.025/10 (where the LD50 is given in mg/kg and 10 is the safety factor).

The quantity of an active ingredient in 1 seed or granule item must be calculated from the dosage given in the Table of Intended Uses. For formulations used in seed treatment, the dosage is given as X kg a.i./100000 seeds. The amount per seed then is A = 10 * X mg a.i./seed

If A / Critical Dose (indicator species) > 1 there is a high risk for birds, otherwise the risk is acceptable.

5.3.6 Environmental risk management suggestions

Proposals for restriction sentences:
- To protect birds the product must be entirely incorporated in the soil; ensure that the product is also fully incorporated at the end of rows,
- To protect birds remove spillages,
- Do not apply during the bird breeding period.

5.4 Bees

5.4.1 Introduction

This chapter is intended to give guidance on how to assess the risk from the use of pesticides to bees. The assessment process described in this chapter follows the same methodology and concept of ERA as laid out in the general introduction chapter.
This chapter is divided into the following sections:
5.4.2 Detailed protection goals
5.4.3 Exposure analysis
5.4.4 Effect assessment
5.4.5 Risk assessment and risk classification
5.4.6 Environmental risk management suggestions.

Pesticide Registration and Control Regulation

Legal basis for assessing risks to bees

Schedule II – Article 2.1.4

(The Ministry… shall evaluate…) the expected exposure of honey bees and wild bees to the pesticide, or to relevant metabolites, degradation or reaction products, in (agro-) ecosystems relevant to the intended uses of that pesticide and under realistic worst case conditions.

a. Where there is a possibility that bees are exposed, the pesticide shall not be registered if:
   i. the risk quotients for oral and contact exposure of honeybees to sprayed pesticides are greater than 50; or
   ii. the exposure/toxicity ratio for oral exposure of honeybees following soil or seed treatments is greater than or equal to 0.1; or
   iii. honeybee larvae or honeybee behaviour are adversely affected,

unless it can be clearly shown through risk assessment that under field conditions no unacceptable effects on colony development and survival will occur following the intended use of the pesticide.

5.4.2 Detailed protection goals

'Bees' are identified as one of the protection goals in this handbook. For this protection goal, the detailed protection goals are addressed by answering the following 3 questions:

Question 1: What do we want to protect?

Answer: Colonies of honeybees and populations of wild bees.

Question 2: Where do we want to protect?

Answer: Both inside and outside treated crops.

Question 3: How strict do we want to protect?

Answer: No long-term effects on colonies of honeybees should occur.

Only the risk to honeybees is assessed. The assumption is that the risk assessment for honeybees will sufficiently protect wild bees and other pollinators. Preliminary findings indicate that for the insecticide dimethoate the honeybee was not the most sensitive species among the pollinators tested, but that the use of the honeybee (*Apis mellifera*) as an indicator species did not significantly bias the risk assessment for pollinators (Roessink et al., 2011). However, extrapolation to bumble bees and other pollinator species has not yet been verified. The western honeybee (*Apis mellifera*) is taken as the indicator species for other bees and pollinators in general, because this is the standard species tested according to the existing guidelines.

For the time being only exposure resulting from spray applications is taken into account.

5.4.3 Exposure analysis

For the exposure the single dose rate is considered:
- Exposure in-crop: single dose rate (g as/ha).
- Exposure off-crop: single dose rate (g as/ha) x drift factor.

With regard to the drift factor, the drift figures from the EU are used for the exposure analysis, just because of pragmatic reasons. The drift factor is equal to the drift value in% as given in Table 5.7, divided by 100. The basic EU drift figures are given in the table below. More research should be done to assess whether these figures are appropriate for the Ethiopian situation.

5.4.4 Effect assessment

For Ethiopia, the data requirements are indicated in the application form and a guideline on the required information is provided. An overview of the specific data requirements related to risk assessment for bees is given in Annex 11.

The applicant has to provide the full study reports and a summary.

Table 5.7

Basic EU drift values for the off-crop exposure; values in grey are the default values assuming the standard buffer zone appropriate for that crop. Other drift values may be used for selection of an alternative buffer zone in situations of high risk.

Basic drift values Ground deposition in% of the application rate (90th percentiles)								
Distance	**Field crops**	**Fruit crops**		**Grapevine**		**Hops**	**Vegetables Ornamentals Small fruit**	
[m]		Early	Late	Early	Late		Height < 50 cm	Height > 50 cm
1	2.77						2.77	
3		29.20	15.73	2.70	8.02	19.33		8.02
5	0.57	19.89	8.41	1.18	3.62	11.57	0.57	3.62
10	0.29	11.81	3.60	0.39	1.23	5.77	0.29	1.23

5.4.5 Risk assessment and risk classification

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach will be used.
An in-crop and an off-crop risk assessment is performed for bees.

For the risk assessment an oral LD50 and a contact LD50 are available. The lowest value is chosen. The EU trigger value of 50 is used. This value is based on empirical research. An assessment of observed bee kills/colony effects for various pesticides and different application rates showed that for sprays a factor of the ETR below 50 is always safe (no field incidents at ETR < 50). Hence, no additional safety factor is used in this case.

The ETR for the in-crop and off-crop risk assessment for bees is calculated as follows:

$$ETR_{in\text{-}crop} = \frac{\text{dose rate (g as/ha)}}{\text{LD50 (ug/bee)}}$$

$$ETR_{off\text{-}crop} = \frac{\text{dose rate (g as/ha)} * \text{drift factor}}{\text{LD50 (ug/bee)}}$$

For the risk classification an exceedance factor has to be defined. From assessment of observed bee kills/colony effects for various pesticides and different application rates and from two studies with data from the United Kingdom (Mineau et al., 2008) it appeared that there is about 50% probability of hive mortality at a trigger value of 400 for the ETR. This value is taken as the upper limit of the risk classification. The risk classification (in-crop as well as off-crop) is presented below.

Low risk:if ETRin-/off-crop < 50
Possible risk:if 50 ≤ ETRin-/off-crop ≤ 400
High risk:if ETRin-/off-crop > 400

Unacceptable in-crop risks can often be handled using restriction measures related to how/when the pesticide is applied, whereas unacceptable off-crop risks usually have to be lowered through the use of a larger buffer zone (see section 5.4.6).

If the substance possibly acts as an insect growth regulator (IGR) the effects on bee brood must be assessed. Colonies of honeybees are fed the insect-growth regulating insecticide to be tested at the quantity of 1 litre per colony at the concentration recommended for field use. The IGR is presented as formulated product in sugar solution. The test provides a qualitative screening of plant protection products in such a way that products causing no harmful effects to bee brood in the test are classified as posing a low risk to bee brood, while products causing harmful effects to bee brood need further testing in the field in order to assess the actual risk.
However, for the time being no higher tier tests are required and evaluated in Ethiopia. In the situation that a risk is indicated from the bee brood test it is proposed to look at the outcome of higher tier risk assessments from other countries (e.g. the EU), to be able to make a decision about the risk. Also risk mitigation measures could be taken into account.

Roessink, I., J. van der Steen, M. Kasina, M. Gikungu, R. Nocelli (2011). Is the European honeybee (Apil mellifera mellifera) a good representative for other pollinator species? SETAC Europe 21st Annual Meeting Abstract Book (SETAC Europe Milan, 15 – 19 May 2011), p. 35; SETAC Europe, Brussels, Belgium.

5.4.6 Environmental risk management suggestions

Proposals for restriction sentences in-crop:
- Dangerous to bees/To protect bees and other pollinating insects do not apply to crop plants when in flower/Do not use where bees are actively for (*state time)* after treatment/Do not apply when flowering weeds are present/Remove weeds before foraging/Remove or cover beehives during application and flowering/Do not apply before (*state time*).
- Dangerous to bees. Use only after sunset.
- Notify beekeepers of the neighbouring areas before application of the pesticide.

Proposals for restriction sentences off-crop:
- To protect bees respect an unsprayed buffer zone of (*distance to be specified)* to non-agricultural land. Drift factors for alternative buffer zones can be found in Table 5.7, section 5.4.3.
- Dangerous to bees. Use only after sunset.
- Notify beekeepers of the neighbouring areas before application of the pesticide.

5.5 Non-target arthropods

5.5.1 Introduction

This chapter is intended to give guidance on how to assess the risk from the use of pesticides to non-target arthropods. The assessment process described in this chapter follows the same methodology and concept of ERA as laid out in the general introductory chapter.
This chapter is divided into the following sections:

5.5.2 Detailed protection goals
5.5.3 Exposure analysis
5.5.4 Effect assessment
5.5.5 Risk assessment and risk classification
5.5.6 Environmental risk management suggestions

Pesticide Registration and Control Regulation

Legal basis for assessing risks to non-target arthropods

Schedule II – Article 2.1.5

(The Ministry… shall evaluate…) the expected exposure of beneficial arthropods to the pesticide, or to relevant metabolites, degradation or reaction products, in (agro-) ecosystems relevant to the intended uses of that pesticide and under realistic worst case conditions.

a. Where there is a possibility that beneficial arthropods are exposed, the pesticide shall not be registered if:
   i. the exposure/toxicity ratio on artificial substrate for the indicator organisms (Aphidius rhopalosiphi and Typhlodromus pyri) is greater than or equal to 2; or
   ii. the exposure/toxicity ratio on natural substrate for relevant organisms is greater than or equal to 1,

   unless it can be clearly shown through risk assessment that under field conditions no unacceptable effects on beneficial arthropods will occur following the intended use of the pesticide.

b. Any claim for selectivity and proposals for use in integrated pest or vector management shall be substantiated by appropriate data ascertaining that the product will not affect beneficial arthropods adversely in the referred integrated pest or vector management system.

5.5.2 Detailed protection goals

'Non-target arthropods' are identified as one of the protection goals in this handbook. For this protection goal, the detailed protection goals are addressed by answering the following 3 questions:

Question 1: What do we want to protect?

Answer: Populations of non-target arthropods.

Question 2: Where do we want to protect?

Answer: In-crop as well as off-crop.

Question 3: How strict do we want to protect?

Answer: No long-term effects on populations of non-target arthropods should occur.

Non-target arthropods are very important in relation to Integrated Pest Management (IPM).

5.5.3 Exposure analysis

For the exposure the dose rate, the Multiple Application Factor (MAF) (in case of multiple applications per season) and the drift factor (in case of off-field exposure) are considered:
- exposure in-crop: single dose rate (g as/ha) x MAF.
- exposure off-crop: single dose rate (g as/ha) x MAF x drift factor.

With regard to the drift factor, the drift figures from the EU are used for the exposure analysis, just because of pragmatic reasons. The basic EU drift figures are given in Table 5.7, see section 5.4.3. The drift factor is equal to the drift value in% as given in Table 5.7, divided by 100. More research should be done to assess whether these figures are appropriate for the Ethiopian situation.

The MAF depends on the number of applications and is given in the table below. The grey shaded values are default values appropriate to use in the first tier assessment for non-target arthropods in situations where either DT50 or the application interval is unknown.

Table 5.8

Multiple application factor for various half-lifes (DT50) : spray interval ratios. Data taken from the ESCORT 2 proceedings (modified, Candolfi et al. 2000). The shaded/grey line indicates the values for a DT50 : spray interval ratio of 1:2.3, which is recommended by ESCORT 2 if no specific data on the DT50 value and the application interval are available.

DT_{50} : spray interval	MAF after n applications, where n =							
	1	2	3	4	5	6	7	8
1 : 8	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
1 : 4	1.0	1.1	1.1	1.1	1.1	1.1	1.1	1.1
1 : 2	1.0	1.3	1.3	1.3	1.3	1.3	1.3	1.3
1 : 1	1.0	1.5	1.8	1.9	1.9	2.0	2.0	2.0
2 : 1	1.0	1.7	2.2	2.6	2.8	3.0	3.1	3.2
2.3 : 1	1.0	1.7	2.3	2.7	3.0	3.2	3.4	3.5
4 : 1	1.0	1.8	2.5	3.1	3.6	4.1	4.4	4.7
6 : 1	1.0	1.9	2.7	3.4	4.0	4.6	5.1	5.5
8 : 1	1.0	1.9	2.8	3.5	4.2	4.9	5.5	6.0
16 : 1	1.0	2.0	2.9	3.8	4.6	5.4	6.2	6.9

5.5.4 Effect assessment

For Ethiopia, the data requirements are indicated in the application form and a guideline on the required information is provided. An overview of the required data is given in Annex 12.

The applicant has to provide the full study reports and a summary.

5.5.5 Risk assessment and risk classification

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach will be used.
An in-crop and an off-crop risk assessment is performed for non-target arthropods.

For the risk assessment LR50 values (g as/ha) are available for the two sensitive standard species: *Aphidius rhopalosiphi* and *Typhlodromus pyri* from laboratory tests on glass-plates.The EU trigger value of 2 is used for the ETR. This value is an empirical value and is based on an analysis of laboratory as well as (semi-)field data for a wide range of products with differing modes of action. Based on these data an ETR value below this trigger value appears to be safe. No additional safety factor is applied in this case.
Information from more extended laboratory tests performed on natural substrates may also be available. From these tests an alternative LR50 value (g as/ha) may be derived. In the case of extended laboratory tests the trigger value that will be used is 1, based on the criterion that more than 50% effect is acceptable. No additional safety factor is applied.

In-crop assessment
The ETR for the risk assessment of non-target arthropods is calculated as follows:

$$ETR = \frac{\text{dose rate (g as/ha) x MAF}}{\text{LR50 (g as/ha) (from lab or extended lab test)}}$$

For the risk classification an exceedance factor has to be defined to define a possible risk. Based on expert judgement a factor of 50 is considered appropriate for the risk classification. In-crop species are mostly fast reproducing species adapted to agricultural practices. The risk classification is presented below.

Risk classification in the case of glass-plate tests:
Low risk: if ETRnta-glass < 2
Possible risk:if 2 < ETRnta-glass < 100
High risk:if ETRnta-glass > 100

Risk classification in the case of extended laboratory tests:
Low risk: if ETRnta-ext < 1
Possible risk:if 1 < ETRnta-ext < 50
High risk:if ETRnta-ext > 50

Off-crop assessment
The ETR for the risk assessment of non-target arthropods is calculated as follows:

$$ETR = \frac{\text{dose rate (g as/ha) x MAF x drift factor}}{\text{LR50 (g as/ha) (from lab or extended lab)}}$$

For the risk classification an exceedance factor has to be defined. The protection level off-crop is more strict than in-crop, because severe in-crop effects should be compensated by recolonisation of organisms from the off-crop area. Moreover, species are less adapted to agricultural practices and slowly reproducing species may be present. For that reason a factor of 10 is considered appropriate for the risk classification. The risk classification is presented below.

Risk classification in the case of glass-plate tests:
Low risk: if ETRnta-glass < 2
Possible risk:if 2 < ETRnta-glass < 20
High risk:if ETRnta-glass > 20

Risk classification in the case of extended laboratory tests:
Low risk: if ETRnta-ext < 1
Possible risk:if 1 < ETRnta-ext < 10
High risk:if ETRnta-ext > 10

5.5.6 Environmental risk management suggestions

Restriction sentences:
- To protect non-target arthropods respect an unsprayed buffer zone of (*distance to be specified)* to non-agricultural land. Drift factors for alternative buffer zones can be found in Table 5.7, section 5.4.3.

5.6 Soil organisms

For the soil ecosystem the following organisms will be taken into account:
- earthworms (as indicator species for the soil macro-organisms).
- soil micro-organisms.

5.6.1 Soil macro-organisms

5.6.1.1 Introduction

This chapter is intended to give guidance on how to assess the risk from the use of pesticides to soil macro-organisms. Earthworms are taken as the indicator species for the group of soil macro-organisms.The assessment process described in this chapter follows the same methodology and concept of ERA as laid out in the general introductory chapter.

This chapter is divided into the following sections:
5.6.1.2 Detailed protection goals
5.6.1.3 Exposure analysis
5.6.1.4 Effect assessment
5.6.1.5 Risk assessment and risk classification
5.6.1.6 Environmental risk management suggestions.

Pesticide Registration and Control Regulation

Legal basis for assessing risks to soil macro-organisms

Schedule II – Article 2.1.6

(The Ministry… shall evaluate…) the expected exposure of earthworms to the pesticide, or to relevant metabolites, degradation or reaction products, in (agro-) ecosystems relevant to the intended uses of that pesticide and under realistic worst case conditions .

a. Where there is a possibility that earthworms are exposed, the pesticide shall not be registered if:
i. the acute exposure/toxicity ratio for earthworms is greater than or equal to 0.1; or
ii. the chronic exposure/toxicity ratio for earthworms is greater than or equal to 0.2,

unless it can be clearly shown through risk assessment that under field conditions no unacceptable effects on earthworms will occur following the intended use of the pesticide.

[Note: The apparent inconsistency between the exposure/toxicity ratio (ETR) in the Regulation and in the Manual text below is due to the fact that the ETR in the Regulation does not include the safety factor while in the Manual it does.]

5.6.1.2 Detailed protection goals

'Soil macro-organisms (earthworms)' are identified as one of the protection goals in this handbook. For this protection goal, the detailed protection goals are addressed by answering the following 3 questions:

Question 1: What do we want to protect?

Answer: Populations of earthworms.

Question 2: Where do we want to protect?

Answer: In-field.

Question 3: How strict do we want to protect?

Answer: No long-term effects on populations of earthworms should occur.

5.6.1.3 Exposure analysis

Exposure: The concentration for the within field soil compartment is calculated from the dose of the pesticide divided by the amount of soil (kg) in the upper part of the soil (default depth of upper part of the soil = 0.05 m). The following formula for the concentration in soil is used:

Csoil = 0.1 * M / DEPTH

Csoil = concentration in the upper part of the soil (mg pesticide / m3 soil)
0.1 = correction factor to convert from g/ha to mg/m^2
M = individual dose applied (g a.i./ha)
DEPTH = depth of the field (default value = 0.05 m)

This is converted to the PECsoil by the following procedure:

PECsoil = Csoil / (ρb * 1000)

PECsoil = concentration in the upper part of the soil from one application (in mg pesticide / kg soil)
Csoil = concentration in the upper part of the soil (in mg pesticide / m3 soil
ρb = dry bulk density of the soil (default value = 1.0 kg/dm3)
1/1000 = factor to convert from kg /m3 to kg/dm3

5.6.1.4 Effect assessment

For Ethiopia, the data requirements are indicated in the application form and a guideline on the required information is provided. An overview of the data requirements for the risk assessment of soil macro-organisms is given in Annex 13.

The applicant has to provide the full study reports and a summary.

5.6.1.5 Risk assessment and risk classification

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach will be used.
An acute and a chronic risk assessment is performed for earthworms.

5.6.1.5.1. Acute risk assessment for earthworms

For the acute risk assessment a LC50 value for earthworms is available. The EU safety factor of 10 is applied to the toxicity value to account for uncertainty.

The ETR for the acute risk assessment of earthworms is calculated as follows:

$$ETR = \frac{PECmax}{LC50\ (earthworms)/10}$$

For the risk classification an exceedance factor has to be defined. Based on expert judgement a factor of 5 is considered appropriate for the acute risk classification. It is estimated that not too many earthworms will die at this level of exceedance of the safe level for earthworms as defined by the EU. Furthemore, it appears from field tests with earthworms that populations of earthworms recover quite quickly when the compound is not too persistent. The risk classification is presented below.

Low risk:if ETRearth-ac < 1
Possible risk:if 1 ≤ ETRearth-ac ≤ 5
High risk:if ETRearth-ac > 5

5.6.1.5.2. Chronic risk assessment for earthworms
For the chronic risk assessment a NOEC value for earthworms is available. The EU safety factor of 5 is applied to the toxicity value to account for uncertainty.

The ETR for the acute risk assessment of earthworms is calculated as follows:

$$ETR = \frac{PECmax}{NOEC\ (earthworms)/5}$$

For the risk classification an exceedance factor has to be defined. Based on expert judgement a factor of 5 is considered appropriate for the chronic risk classification. The risk classification is presented below.

Low risk:if ETRearth-chr < 1
Possible risk:if 1 $\leq$ ETRearth-chr $\leq$ 5
High risk:if ETRearth-chr > 5

5.6.1.6 Environmental risk management suggestions
Proposal restriction sentence:
To protect soil organisms do not apply this or any other product containing (identify active substance or class of substances, as appropriate) more than (time period or frequency to be specified).

5.6.2 Soil micro-organisms

5.6.2.1 Introduction
This chapter is intended to give guidance on how to assess the risk from the use of pesticides to soil micro-organisms. The assessment process described in this chapter follows the same methodology and concept of ERA as laid out in the general introductory chapter.
This chapter is divided into the following sections:
5.6.2.2 Detailed protection goals
5.6.2.3 Exposure analysis
5.6.2.4 Effect assessment
5.6.2.5 Risk assessment and risk classification
5.6.2.6 Environmental risk management suggestions.

Pesticide Registration and Control Regulation

The assessment of pesticide effects on soil micro-organisms has not been included in the Regulation. European evaluation criteria are therefore applied in the meantime.

5.6.2.2 Detailed protection goals
'Soil micro-organisms' are identified as one of the protection goals in this handbook. For this protection goal, the detailed protection goals are addressed by answering the following 3 questions:

Question 1: What do we want to protect?

Answer: Soil processes influenced by soil micro-organisms (e.g. litter break down).

Question 2: Where do we want to protect?

Answer: In-field.

Question 3: How strict do we want to protect?

Answer: No long-term effects on soil processes influenced by soil micro-organisms should occur.

5.6.2.3 Exposure analysis

See section 5.6.1.3

5.6.2.4 Effect assessment

For Ethiopia, the data requirements are indicated in the application form and a guideline on the required information is provided. An overview of the data requirements for soil micro-organisms is given in Annex 14.

The applicant has to provide the full study reports and a summary.

5.6.2.5 Risk assessment and risk classification

No ETR approach is used, and the outcome of the soil micro-organism test is directly given in terms of the magnitude of effects that can be expected. The decisive parameter is the magnitude of effect compared to the untreated control (be it increase or decrease of activity), and the time-course of recovery. According to the EU criteria the critical level is $\pm$25% effect after 100 days. Larger deviations will require refinement of the assessment. Obviously, the concentrations used in the test must cover the maximum PEC.

Because exceedance of the critical level of $\pm$25% effect after 100 days is rare, no exceedance factor is introduced. If the effect in the laboratory tests is below the critical level, the risk is low. If the critical level is exceeded, the risk is high.

5.6.2.6 Environmental risk management suggestions

Proposal restriction sentence:

- To protect soil organisms do not apply this or any other product containing (identify active substance or class of substances, as appropriate) more than (time period or frequency to be specified).

5.7 Non-target terrestrial plants

5.7.1 Introduction

This chapter is intended to give guidance on how to assess the risk from the use of pesticides to non-target terrestrial plants. The assessment process described in this chapter follows the same methodology and concept of ERA as laid out in the general introductory chapter.
This chapter is divided into the following sections:
5.7.2 Detailed protection goals
5.7.3 Exposure analysis
5.7.4 Effect assessment
5.7.5 Risk assessment and risk classification
5.7.6 Environmental risk management suggestions.

Pesticide Registration and Control Regulation

Legal basis for assessing risks to non-target terrestrial plants

Schedule II – Article 2.1.5

(The Ministry… shall evaluate…) the expected exposure of non-target terrestrial plants to the pesticide, or to relevant metabolites, degradation or reaction products, in (agro-) ecosystems relevant to the intended use of that pesticide and under realistic worst case conditions.

a. Where there is a possibility that non-target terrestrial plants are exposed, the pesticide shall not be registered if:

i. the exposure/toxicity ratio for non-target terrestrial plants is greater than or equal to 0.2,

unless it can be clearly shown through risk assessment that under field conditions no unacceptable effects on non-target terrestrial plants will occur following the intended use of the pesticide.

[Note: The apparent inconsistency between the exposure/toxicity ratio (ETR) in the Regulation and in the Manual text below is due to the fact that the ETR in the Regulation does not include the safety factor while in the Manual it does.]

5.7.2 Detailed protection goals

'Non-target terrestrial plants' are identified as one of the protection goals in this handbook. For this protection goal, the detailed protection goals are addressed by answering the following 3 questions:

Question 1: What do we want to protect?

Answer: Populations of non-target terrestrial plants off-field

Question 2: Where do we want to protect?

Answer: Locations alongside agricultural fields.

Question 3: How strict do we want to protect?

Answer: No long-term effects on populations of non-target off-field terrestrial plants should occur.

5.7.3 Exposure analysis

For the exposure the dose rate, the Multiple Application Factor (MAF) (in case of multiple applications per season) and the drift factor are considered:
PEC (off-field): single dose rate (g as/ha) * MAF * drift factor

With regard to the drift factor, the drift figures from the EU are used for the exposure analysis, just because of pragmatic reasons. The basic EU drift values are given in Table 5.7 in section 5.4.3. The drift factor is equal to the drift value in% as given in Table 5.7, divided by 100. More research should be done to assess if these figures are appropriate for the Ethiopian situation.

The MAF depends on the number of applications; the same MAF values as used for non-target arthropods are used (see Table 5.8, section 5.5.3).

5.7.4 Effect assessment

For Ethiopia, the data requirements are indicated in the application form and a guideline on the required information is provided. An overview of data requirements for non-target terrestrial plants is given in Annex 15.

The applicant has to provide the full study reports and a summary.

5.7.5 Risk assessment and risk classification

For the risk assessment the ETR (Exposure-Toxicity Ratio) approach will be used.
An off-crop risk assessment is performed for non-target terrestrial plants.

For the risk assessment ER50 values for different species of terrestrial plants are available. The lowest ER50 value is used for risk assessment. The EU safety factor of 5 is applied to the toxicity value to account for uncertainty

The ETR for the risk assessment of non-target terrestrial plants is calculated as follows:

$$ETR = \frac{PEC(off\text{-}field)}{ER50/5}$$

For the risk classification an exceedance factor has to be defined. Based on expert judgment a factor of 10 is considered appropriate for the risk classification, because the risk assessment is quite conservative by taking the lowest ER50 value and a safety factor of 5. The risk classification is presented below.

Low risk:if $ETR < 1$
Possible risk:if $1 \leq ETR \leq 10$
High risk:if $ETR > 10$

5.7.6 Environmental risk management suggestions

Proposal restriction sentences:

- To protect non-target plants respect an unsprayed buffer zone of (*distance to be specified)* to non-agricultural land. Drift factors for alternative buffer zones can be found in Table 5.7, section 5.4.3.

Annex 1 Draft of the Directive on efficacy testing of pesticides

Draft version August 2014, not yet endorsed by the State Minister.

Whereas …{it is important to ascertain that pesticides that are used in Ethiopia are efficacious against the intended pests, (i.e. any organism, including diseases, insects or weeds, decreasing the quality or quantity of the agricultural product) while not adversely affecting the long-term sustainability of agricultural production or disease vector control…}

Whereas …{requirements for efficacy testing of pesticides should be clear to applicants of a registration and to research institutions conducting pesticide trials…}

Whereas …{etc.}

Therefore this Directive is issued in accordance with article 5 of the Proclamation No. 674/2010 to Provide for the Registration and Control of Pesticides, and with Articles 4, 5 and 8 of the Pesticides Registration and Control Council of Minister Regulation No. xxx/201y.

1. Designation
This Directive may be cited as 'Directive no. ZZZ' issued to determine the procedures on efficacy testing of pesticides

The Proclamation No. 674/2010 to Provide for the Registration and Control of Pesticides is hereafter referred to as 'the Proclamation'. The Pesticides Registration and Control Council of Minister Regulation No. xxx/201y is hereafter referred to as 'the Regulation'

The Ministry of Agriculture is hereafter referred to as 'the Ministry'

An applicant requesting the registration of a pesticide by the Ministry is hereafter referred to as 'the Applicant'

2. Definitions
The definitions provided in the Proclamation and in the Regulation apply to this Directive.

In addition, for the purpose of this Directive the following definitions apply:

Growing area. A zone within Ethiopia consisting of one or more agro-ecologies where the crop and pest are common.

Minor uses. Those uses of pesticides (defined in relation to crops/use and pests) in which either the crop/use is considered to be of low economic importance in Ethiopia (minor crop/use), or the pest (minor pest) is not important on a major crop. leading to a low total volume of the product being used in the country

Product (or **pesticide product**) means the formulated product (pesticide active ingredient(s) and co-formulants), in the form in which it is packaged and sold.

Reference product. A pesticide product which acts as a positive control, to check if the trial setup and execution succeeded and to relate the observed efficacy of the test product to that of a known previously recommended product. A reference product should have a registration for the tested use and has preferably the same characteristics as the test product with respect to active substance, formulation, application methods etc.

3. Scope

Pursuant to Article 5 of the Proclamation, the Ministry has to ascertain that the pesticide is effective for the purpose for which it is intended, before it can authorize the registration of that pesticide. The Regulation, in its Articles 4 and 8, requires that the Applicant generates biological efficacy data for any pesticide that it submits for registration.

Article 5 of the Regulation subsequently defines the overall procedure for generating efficacy data. Pursuant to Articles 4.1 and 8.5 of the Regulation, this Directive provides further details about the data that need to be generated by the Applicant, for the Ministry to be able to assess the efficacy of the pesticide submitted for registration. Furthermore, and pursuant to Article 5.4 of the Regulation, this Directive describes the general requirements for efficacy testing.

4. Procedure of efficacy evaluation

The evaluation of the efficacy of a pesticide for registration is conducted in accordance with the following steps: (Schedule A of this Directive).

1. Submission by the Applicant of efficacy data as part of the pre-evaluation dossier (pursuant to Article 4.2 of the Regulation).
2. Decision by the Ministry whether the Applicant should undertake local efficacy trials (pursuant to Article 4.5 of the Regulation), as well as the number and type of trials to be conducted and the protocol(s) to be followed (if relevant) (pursuant to Article 5.4 of the Regulation).
3. Designation by the Ministry of the institution(s) that will conduct the trial(s) (pursuant to Articles 4.5 and 4.6 of the Regulation).
4. Establishment of a contract between the Applicant and the designated institution(s), and payment of costs of the trial(s) by the Applicant to the institution(s) (pursuant to Article 5.2 of the Regulation).
5. Release of the import permit by the Ministry for the necessary pesticide samples (pursuant to Article 5.3 of the Regulation).
6. Execution of the efficacy trial(s) by the designated institution(s).
7. Submission by the designated institution(s) of the trial report(s) to the Ministry and to the Applicant (pursuant to Article 5.4 of the Regulation).
8. Submission by the Applicant of the trial report(s) and other relevant efficacy data to the Ministry, as part of the registration dossier (pursuant to Article 8 of the Regulation).
9. Verification of completeness of the efficacy information by the Ministry, as part of the completeness check of the registration dossier, and request for missing data to the Applicant (if required) (pursuant to Article 10 of the Regulation).
10. Evaluation by the Ministry of the efficacy information in the registration dossier and assessment whether the pesticide is effective for the purpose for which it is intended (pursuant to Article 11 and of Regulation, and taking into consideration the criteria for evaluation in Schedule II of the Regulation).

5. Pre-evaluation

Pursuant to Article 4.2d of the Regulation, and as stipulated in the *Directive on pre-evaluation of a pesticide proposed for registration*, the Applicant shall submit efficacy trial results from comparable climates for the intended uses, or for relevant similar uses, for pre-evaluation by the Ministry.

The Applicant shall submit relevant available efficacy trial reports which shall comprise, as a minimum, of the information listed in Schedule B of this Directive. In addition, the Applicant shall provide a table of intended uses, according to Schedule A of the *Directive on pre-evaluation of a pesticide proposed for registration*.

6. Stages of efficacy testing

The Ministry shall determine the number and types of efficacy trials to be conducted by the Applicant. Two stages of efficacy testing of pesticides are recognized in Ethiopia:

6.1 Pre-verification trials

Pre-verification trials generally are required for pesticide products that are new for Ethiopia or extension of use of an already registered pesticide product.

A pre-verification trial shall be conducted in three different growing areas during one growing season. In case that three different growing areas are not available, a pre-verification trial may be conducted in one growing area during two growing seasons. For testing herbicides the trials should in principle be conducted in at least four growing areas because of the higher risks involved with this type of products and generally a group of species is claimed (weeds, broadleaved or grass weeds).

A pre-verification trial shall include a treatments at the proposed dose rate and frequency of the pesticide product, as well as at least at one lower rate (i.e. 50% – and preferably also 75% – of the proposed rate). Each trial shall, in principle, include a reference product and an untreated control. If no appropriate reference product is available the comparison to the untreated control is sufficient. The treatments should be arranged in a statistically suitable design, with typically four treatment replications.

Pesticide applications shall be performed according to the proposed label claims and directions for use. Whenever possible, the pre-verification trial is conducted according to an established efficacy testing protocol. If no established testing protocol is available, it shall be elaborated for the crop-pest combination to be studied, according to the procedure described in Article 9.4 of this Directive, before commencement of the trials.

6.2 Verification trials

Verification trials follow the pre-verification stage if the pesticide is considered to be efficacious, or in case of major changes to the pesticide product or its proposed use.

In a verification trial, large-scale operational treatments of the pesticide product are conducted. A verification trials shall be carried out in at least three different growing areas. In case that three different growing areas are not available, the trial may be carried out in one growing area, but with at least three replications.

The verification trial shall be conducted at the recommended dose rate and frequency of the pesticide product. Each trial shall including a reference product and an untreated control. Statistics shall be performed, regarding the three growing areas as replicates.

Pesticide applications shall be performed according to the proposed label claims and directions for use. Whenever possible, the pre-verification trial is conducted according to an established efficacy testing protocol. If no established testing protocol is available, it shall be elaborated for the crop-pest combination to be studied, according to the procedure described in Article 9.4 of this Directive, before commencement of the trials.

7. Number and type of efficacy trials

7.1 New product

When a new product is submitted for registration, for each relevant crop-pest combination there shall be two stages of testing. First, pre-verification trials are conducted, according to section 6.1 of this Directive. Following the pre-verification stage, verification trials shall be performed according to Section 6.2 of this Directive.

7.2 Formulation change

Major formulation changes (e.g. emulsifiable concentrate to wettable powder) will be tested for comparability in the verification stage by including the new and old formulation.

No efficacy trials are required in case of minor formulation changes, as defined in the *Directive on data requirements for pesticide registration*. Attempting significantly to change a formulation, by making a series of 'minor' changes that would not in themselves require efficacy data, is not acceptable.

7.3 Equivalent products
A new pesticide product that contains the same active ingredient – in the same concentration and in the same or a similar formulation – as an already registered pesticide product may be evaluated for equivalence. If the two products are considered equivalent by the Ministry, and registration is requested for the same crop/pest combination, only verification trials need to be performed according to Section 6.2 of this Directive, comparing the two equivalent products.

If a pesticide product cannot be considered equivalent to an already registered product, efficacy testing shall be conducted as for a new product.

7.4 Extension of use
An application for extension of use – additional uses for an already registered pesticide product (i.e. new crops or target pests) shall be regarded as a new use, and both pre-verification and verification trials shall be required.

Pre-verification and/or verification trials may be waived by the Ministry if the applicant can substantiate the recommended dose rate and treatment frequency by means of extrapolation.

7.5 Minor uses
For some uses of pesticides (defined in relation to crops and pests) either the crop is considered to be of low economic importance in Ethiopia (minor crop/use), or the pest is not important on a major crop (minor pest). In such cases, an applicant can request registration as a 'minor use', which does not require any additional efficacy data.

For a claim as 'minor use' to be taken into consideration by the Ministry, the claimed pest must be specific to the claimed crop and may not also occur in other similar crops. Furthermore, it should be reasonable to assume efficacy of the product against claimed target pest. The product shall be registered for the use against the target pest on another crop or for the control of similar organisms on the same crop.

A minor use has to be indicated on the product label and accompanied by a warning that no effectiveness and crop safety data have been generated for that specific use.

A detailed justification of the claim as 'minor use' shall be provided by the applicant. The Ministry shall decide if the claim is acceptable and shall notify the applicant whether efficacy trials can be waived.

8. Zoning

8.1 Climate zones for efficacy testing in Ethiopia
Pesticide efficacy data for uncovered crops shall be generated in the climate zone(s) in Ethiopia where the target crop(s) and pest(s)/disease(s)/weed(s) occur for which registration is sought. For the purpose of this Directive, two climate zones are distinguished in Ethiopia, determined by elevation level:
- Lowlands, below approximately 1500 m.
- Mid-/highlands, above approximately 1500 m.

Efficacy trials shall be conducted in one of the two or both of the zones, depending on the crop and as specified in Schedule D of this Directive.

For covered crops no division is made into climate zones.

8.2 Comparable climate zones in East Africa
Pesticide efficacy data generated from comparable climate zones in East Africa may be accepted by the Ministry to complement or replace data to be generated in Ethiopia.

In the north, the area of comparable climate zones is bordered by the semi-desert climate that initiates halfway across the Sudan. The west boundary is marked by the wet tropical climate which is found in the Central African Republic and the Democratic Republic of Congo. In the south, the area covers the entire Great Lakes Region which includes Uganda, Rwanda, Burundi, Kenya and the United Republic of Tanzania; the coastal forests of Kenya and Tanzania are excluded. The dry low-altitude desert area of Somalia, Djibouti and Eritrea are of minor importance with respect to agricultural potential (see Schedule C for indicative map boundaries).

Within this area the same climate division, based on elevation levels, is applied as in Ethiopia (Section 8.1 of this Directive). For covered crops no division is made into climate zones.

When efficacy trial locations are within a zone of assumed comparable climate, and the target crop(s) and pest(s)/disease(s)/weed(s) are the same as for which registration is sought in Ethiopia,then the applicant may submit relevant trial reports and request a waiver of local efficacy trials based on climate comparability. Efficacy data originating the zone comparable climates described in this Directive will, in principle, be accepted without the necessity of additional substantiation.

Pesticide efficacy data originating from other climate zones may also be submitted as part of the registration dossier, but their applicability for Ethiopian conditions should be motivated in detail by the applicant. Such data may be accepted by the Ministry, for example, when the climate zone represents more harsh circumstances with respect to pesticide performance or crop safety.

Efficacy trials performed outside of Ethiopia shall be conducted and reported in accordance to the requirements of this Directive.

9. Testing procedures

9.1 Location
Field efficacy trials shall be located in the area where the pest/disease/weed is most prevalent in order to find sufficient pest pressure. In other locations (warehouses, greenhouses, etc.) pest pressure should be sufficient. Whenever possible, crop varieties are chosen which are susceptible to the pest/disease/weed concerned and conditions are chosen or created which favour its development.

9.2 Untreated control and reference product
The efficacy of the pesticide (effectiveness and crop safety) shall be compared to an untreated control and one or more reference products. An untreated control shall be included in each trial to quantify the level of control and to verify the pest pressure at the location of the trial.

The reference product shall act as a positive control, to check whether no problems occurred in the trial design and execution, and to relate the observed efficacy of the test product to that of a product with known efficacy. A reference product shall be registered in Ethiopia for the intended use and shall preferably have the same characteristics as the test product with respect to mode of action, formulation and application method. If no appropriate reference product is available the comparison to the untreated control is sufficient. In cases where it is not possible to identify an appropriate reference product, the applicant shall provide a justification.

9.3 More active ingredients in one product
When a pesticide product contains more than one active ingredient the benefit of that combination should be justified by the applicant. When one of the active ingredients is already registered by itself for the same crop-pest combination in the same formulation, that registered product should be included in the efficacy trials and applied at the recommended dose rate.

9.4 Protocols
The Ministry is responsible for the approval of the efficacy testing protocols for the crop-pest combinations most widely present in Ethiopia. The applicant shall use these protocols as a basis for the efficacy trials. Any modifications made to adopted efficacy testing protocols shall be motivated in the report of the trial.

In cases where no efficacy testing protocols have been adopted by the Ministry, the applicant shall request the Ethiopian Institute of Agricultural Research (EIAR) to review the protocol before commencing the trial. The EIAR will provide its review to the Applicant within three months of submission by the Applicant. The protocol, accompanied by the review of EIAR, shall subsequently be submitted by the applicant to the Ministry for its approval.

9.5 Safety procedures
For all efficacy trials, the EIAR Internal Directives on the Use of Pesticides (IAR Technical Manual No.2.) should be followed to ensure that occupational and environmental risks are minimized.

10. Effectiveness of the pesticide product
For the effectiveness claim of the pesticide product two terms are distinguished: control or reduction. The trial results shall correspond to the respective claim. For a product that suppresses the development of a target pest/disease/weed, and is to be applied as an element of IPM, where other pest management methods are applied simultaneously, 'control' of that target pest shall not be claimed. Alternatively, whenever 'control' is claimed, the applicant shall show that the treatment with the pesticide product keeps or kills the target pest/disease/weed below the damage threshold level.

In principle, the pesticide product tested in the efficacy trail shall demonstrate effectiveness, at least equal to that of the reference product. However, it may be justified to accept a lower level of control (or reduction) when the test product, when compared to the reference product:
- results in less, or no, adverse effects;
- has a broader spectrum of activity;
- allows for a broader period of application;
- reduces the risk of resistance development;
- can be better used in IPM.

The Ministry will evaluate the effectiveness of the product and decide whether it is sufficient for the indicated conditions of use.

11. Adverse or unintended side-effects
The applicant shall justify, in the efficacy section of the registration dossier, the reasons for not conducting any of the assessments listed below.

11. 1 Phytotoxicity
An assessment of possible phytotoxicity caused by the pesticide product shall be made in all trials and preferably on different cultivars. Occurrence, or absence, of phytotoxicity shall be recorded and reported.

11.2 Effects on yield

Quality
An assessments of visible residues shall be made when relevant (*e.g.* for flowers, fruit crops). Occurrence, or absence, of visible residues shall be recorded and reported.

Data on the possible effects of the pesticide on the quality of the yield (*e.g.* taint, odour, sugar content) are required when there are indications of an increased risk. Studies on taint may be accepted from other countries when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence.

Processing procedures
Data on the possible effects of the pesticide on processing procedures (*e.g.* fermentation, baking, brewing) are required when there are indications of an increased risk. Studies on processing procedures may be accepted from other countries when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence.

Quantity
The efficacy evaluation shall provide sufficient information to ascertain that yield reduction does not occur.

11.3 Development of resistance
The applicant shall provide sufficient data to allow an analysis of the risk of resistance development to the pesticide. A resistance risk analysis and, where applicable, a resistance risk management strategy shall be suggested by the Applicant.

11.4 Succeeding crops
Data on possible adverse effects of the pesticide product on succeeding crops (*i.e.* to be sown during the following cropping season) or replacement crops (*i.e.* to be re-sowed following a failed crop) are required when there are indications of an increased risk. Testing of effects on succeeding crops is in principle mandatory for herbicides, unless the applicant can argue satisfactorily that this is not necessary. Studies from other countries may be accepted when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence.

11.5 Adjacent crops
Data on possible adverse effects of the pesticide product on adjacent crops is required when there are indications of an increased risk. Studies from other countries may be accepted when it can be argued that these represent a worse case situation or that climatic conditions have negligible influence.

11.6 Propagation purposes
Data on possible adverse effects of the pesticide product on plants or plant products to be used for propagation purposes are required when there are indications of an increased risk. Adverse effects on plants or plant products that are to be used for propagation purposes are not accepted since in Ethiopia many farmers use the harvested seeds for sowing in the following cropping season.

11.7 Beneficials
Any adverse effects on beneficial arthropods (*e.g.* honeybees) shall be reported when observed in the efficacy trials.

12. Experimental sample
The sample of the pesticide product to be tested shall be properly packaged with a manufacturer's label indicating 'TO BE USED FOR EXPERIMENTAL USE ONLY'.

The label of the experimental sample shall contain, as a minimum, the following information:
- product name of pesticide
- common name of active ingredient
- hazard statement and hazard symbol according to the GHS
- date of manufacture and shelf-life

13. Reporting
Efficacy trial reports shall be written in English. They shall be concise, clear and complete. All trial reports shall contain at least the information listed in Schedule B of this Directive, irrespective whether the trial was conducted in Ethiopia or elsewhere.

14. Fees
Fees to be paid by the Applicant to the EIAR for the evaluation of an efficacy testing protocol are set by Directive of the Ministry.

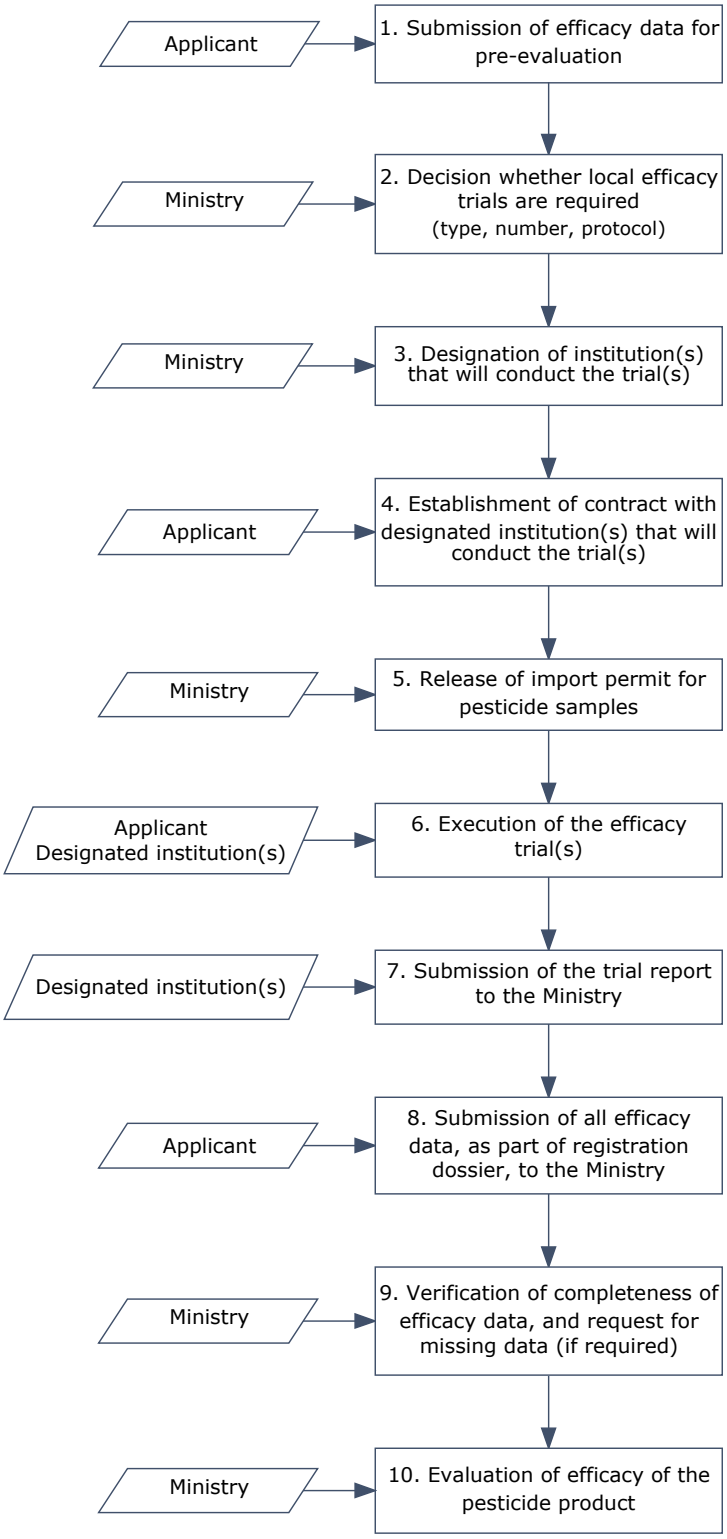
Fees for the conduct of an efficacy trial to be paid by the Applicant to the designated Research Institution are agreed between the Applicant and the Research Institution. The height of the fees will depend on the size and complexity of the trial, and shall be based on the principle of cost recovery by the Research Institution.

Effective date
This Directive shall enter into force as of the … day of 20..

Done at Addis Ababa, this … day of

The Minister of Agriculture

Schedule A – Schematic representation of the procedure for evaluation of the efficacy of a pesticide for registration in Ethiopia



Schedule B – Contents of an efficacy trial report

The report of the efficacy trial shall include, at least, the following information:

1. Title of the experiment
2. Introduction
   - Brief introduction of the importance of the pest, of the pesticides tested and the purpose of the study
3. Materials and Methods
   - Including location(s) of the trial(s), crop and variety, crop stage when pesticide is applied, target pest (common and scientific name), pesticide (common and product name) and reference product (if relevant), formulation type and concentration of the active ingredient(s), dosage and application frequency, application technique, duration of the trial, meteorological data and, if indicated in the efficacy testing protocol, edaphic data.
4. Results
   - Including a summary description of the results of the trial, as well as tables and/or graphs and a statistical analysis, and any unacceptable effects
5. Conclusions
   - Including the explicit evaluation of the researcher of the performance of the pesticide, its appropriateness for the conditions of use in Ethiopia, any specific directions for use and/or use restrictions, and whether the control objectives of the pest, disease or weed have been achieved.
6. References
7. Person(s) responsible for the trial and person(s) reporting
8. Signature and date
9. Raw data

Schedule C – Area within which the climatic conditions may be considered comparable to those employed in Ethiopia for the evaluation of pesticide efficacy.

Schedule D – Requirements on the distribution of uncovered efficacy trials

Cereals		Fruits	
barley	H	avocado	H+L
maize	H+L	apple	H
sorghum	L	banana	H+L
teff	H	citrus	L
wheat	H+L	grape	H+L
		papaya	H/L
Pulses		peach	H
chickpea	H	pineapple	L
faba bean	H	plum	H
field pea	H	mango	H+L
haricot bean	H+L		
lentil	H	Stimulants	
		chat	L
Vegetables, roots and tubers		coffee	H/L
beet	H/L		
cabbage	H/L	Industrial crops	
carrot	H/L	cotton	L
enset	H/L	sugar cane	H+L
onion	H/L	tobacco	H+L
pepper	H/L		
potato	H/L	Oilseeds	
sweet potato	H/L	gomenzer	H
tomato	H/L	groundnut	L
yam	H/L	linseed	H
		noug	H
		sesame	L
		sunflower	H+L

H: highland only
L: lowland only
H+L: high- and lowland
H/L: high- or lowland

Annex 2 Draft test protocols for efficacy testing

Draft versions August 2014, not yet endorsed by the State Minister.

Pre-verification Protocol 1: Red tefworm on tef

Red tefworm on tef
Date: 29 August 2011
Trial stage: Pre-verification
Test organism: Red tefworm, *Mentaxya ignicollis* (Walker)
Test crop: Tef
Experimental units:

Gross: 3m x 5m, superimposed in tef fields
Net: 0.5m x 0.5m quadrates
Inter plot spacing: 3m (teff covered)

Design:
RCBD with 5 over site replications
Included treatments: standard check (Fenithrothion EC formulation) and untreated check
NB. Each replication to be put in a farm as it is often difficult to get big plots that could accommodate such replicated trials
Specific treatments:

three rates of the test pesticide, producers recommended dose (R), R-0.25R and R+0.25R,

Application timing:

Crop: any stage
Pest: 1 larva per 0.25 m^2 quadrate

Efficacy assessments
type: Number of larvae, damaged and undamaged panicles per 0.25 m^2 quadrate on five randomly taken quadrates per plot, grain yield per 1 m^2 quadrate on five randomly taken quadrates per plot
time: pre spray count of larvae to be recorded at dusk
post spray count of larvae to be recorded at dusk on the following day
panicle damage at pre spray, 7 and 14 days latter
Phytotoxicity assessments:

scoring for leaf scorching on a scale of 0-4, where 0=no, 1= top leaves 2=entire panicle, 3=top leaves and entire panicle, 4=entire plant scorched

Symptom(s) description:

chewed leaf edges
panicles lacking growing seed

Recommendations:

the pest is a problem in deeply cracking heavy black clay soils and infestation to varying degrees occurs every year in limited yet major tef growing areas in the country that include Becho Plane and Bechena areas

Extrapolation:
pests: none

crops: none

Pre-verification Protocol 2: Shootflies on tef

Shootflies on tef

Date: 29 August 2011
Trial stage: Pre-verification
Test organism: shootflies (*Atherigonia hyalinipennis* Em and *Delia aramburgi* (Seguy)
Test crop: Tef grown in moisture deficit seasons and in seasons of terminal drought
Experimental units:
Gross: 2m x 3m
Net: 0.5m x 0.5m quadrates
Inter row spacing: Not applicable (Broadcast)
Inter plot spacing: 1.5m
Design:
RCBD with 3 replications
Included a standard insecticide and untreated control
Specific treatments:
three rates of the test pesticide, recommended dose (R), R-0.25R and R+0.25R
Application timing:
Crop: any stage
Pest: 10% seedling damage per 0.25 m^2 quadrate or 2% damaged panicles per 1 m^2 quadrate
Efficacy assessments
type: damaged and undamaged seedlings per 0.25 m^2 quadrate per plot in ten randomly taken quadrates
damaged and undamaged panicles per 1 m^2 quadrate in ten randomly taken quadrates per plot
grain yield per 1 m^2 quadrate on five randomly taken quadrates per plot
time:
if damage starts at seedling stage:
pre spray count of damaged and undamaged seedlings
post spray count of damaged and undamaged seedlings after 1 week and carrying out second spray, if required
post spray count of damaged and undamaged seedlings after 1 and 2 weeks from the 2^{nd} spray
if damage starts on panicles:
pre spray count of damaged and undamaged panicles
post spray count of damaged and undamaged panicles after 1 week and carrying out second spray, if required
post spray count of damaged and undamaged panicles after 1 and 2 weeks from the 2^{nd} spray
Phytotoxicity assessments:
scoring for leaf scorch on a scale of 0-4, where 0=no, 1= top leaves 2=entire panicle, 3=top leaves and entire panicle, 4=entire plant scorched
Symptom(s) description:
dead seedlings, which can be clearly seen by the number of seedlings turned yellow and are stacked to the soil.
damaged panicles, which can be confirmed by trying to pull panicles of tef plants contained in the sample quadrates. When the damage is severe, shootfly damaged tef panicles die out and turn white and remain in an upright position. Such panicles when threshed by hand are often found being without seeds or may contain prematurely aborted seeds.
Recommendations:
the pest is a major problem in areas where there is shortage of moisture and infestation to varying degrees occurs every year and in other places in seasons of rainfall shortage as well as in times of terminal drought.
Extrapolation:
pests: none
crops: barley and wheat

Pre-verification Protocol 3: Tef Epilachna on tef

Tef Epilachna on tef
Date: 29 August 2011
Trial stage: Pre-verification
Test organism: Tef epilachna, *Epilachna simillis*
Test crop: Tef
Experimental units:
Gross: 2m x 3m
Net: 0.5 x 0.5 m quadrates
Inter row spacing: Not applicable (broadcast)
Inter plot spacing: 1.5m
Design:
RCBD with 3 replications
Included standard (Carbaryl) and untreated checks)
Specific treatments:
Three rates of the test pesticide, recommended dose (R), R- 0.25 and R+0.25R,
Application timing:
Crop: any stage
Pest: 5 larvae and/or adults per 1 m^2 quadrate
Efficacy assessments
type: larvae and adults per 0.25 m^2 quadrate on five randomly taken quadrates per plot
skeletonized leaves per plant on fifteen randomly selected plants per plot
damaged and undamaged plants per 0.25 m^2 quadrate on five randomly taken quadrates per plot
grain yield per 0.25 m^2 quadrate on five randomly taken quadrates per plot
time: pre spray count of larvae and adults;
post spray count of larvae and adults after 24 hours;
at pre spray, 7 and 14 days latter count of number of skeletonized leaves per plant;
damaged and undamaged plants at pre spray, 7 and 14 days latter
Phytotoxicity assessments:
scoring for leaf scorch on a scale of 0-4, where 0=no, 1= top leaves 2=entire panicle, 3=top leaves and entire panicle, 4=entire plant scorched
Symptom(s) description:
skeletonized leaves
Recommendations:
the pest is a problem in areas where there is shortage of moisture and infestation to varying degrees occurs every year in such environments.
Extrapolation:
pests: none
crops: barley and wheat

Pre-verification Protocol 4: Cotton aphids on cotton

Date: August 27, 2011

Trial stage – Pre-verification

Test organism(s): Cotton aphid (*Aphis gossypii*)

Test crop(s): cotton

Experimental unit

Gross: 6.3m x 10m
Inter row spacing: 0.9m
Inter plot spacing : 2m
Net: 5 internal rows = 45m^2

Design

RCBD, 4 replicates
Included treatments: test product, reference product and untreated control

Specific requirements/doses

claimed dose (N), N-0.25N, and N+0.25N

Application timing

crop: 30 days after emergence
pest:30% infested plants

Efficacy assessment(s):

Type:

- number of aphids on 20 randomly chosen plants on a 0-5 scale (0- none, 1- 1-10 aphids, 2- 11-30 aphids, 3- 31-100 aphids, 4- 101-250 aphids, 5- >251 aphids)
- yield; lint weight from 5 internal rows

Time:

- 1 day before for pre-application assessment,
- 2, 5, 7, & 10 days after application for post assessment

Phytotoxicity assessment(s):

- Scoring for leaf scorch on a 0-3 scale (0-no, 1-light, 2-medium, 3-heavy)

Symptom(s) description

- presence of adults and nymphs
- honey dew and leaf curling

Recommendations

- untreated control can be covered by polyethylene sheet during spraying to protect against drift from adjacent treatments

Extrapolation

- crop:none
- pest:none

Pre-verification Protocol 5: Bollworms on cotton

Bollworms on cotton

Trial Stage- Pre-verfifcation
Date: August 27, 2011

Test organism(s): Cotton bollworm (*Helicoverpa armigera*)

Test crop(s): Cotton

Experimental unit/ plot size:
Gross: 6.3 x 10m;
Net: 5 internal rows
Inter row spacing: 0.9m
Inter plot spacing: 2m

Design: RCBD, 4 replicates
Included treatments: Standard (reference product) and untreated control

Specific requirements/ Doses:
Three rates of the test insecticide, Claimed dose (N), N-0.25N and N+0.25N

Application timing:
Crop: starting at initial square stage of crop
Pest: 20 eggs per 20 plants for ovicidal products

5 first to third instar larvae (L1-L3) per 30 plants for larvicidal products

Efficacy assessment(s):
Type:
counting the number of eggs and larvae on 10 randomly chosen plants/plot;
percentage of damaged squares and bolls on 10 randomly chosen plants;
yield; lint weight from 5 internal rows;

Time of assessment for each application:
1 day before for pre-application assessment (for each application);
2, 5, 7, & 10 days after application for post assessment (for each application)

Phytotoxicity assessment(s)
- Score for leaf scorch on a 0-3 scale (0-no, 1-light, 2-medium, 3-heavy)

Symptom(s) description
- premature opening of square
- boreholes on bolls
- presence of frass
- sheeding of bolls and squares (scars on stems; branches)
- presence of eggs and larvae

Recommendations
- untreated control can be covered by polyethylene sheet during spraying to protect against drift from adjacent treatments
- excluded untreated control may also be considered to prevent interference by migration

Extrapolation
- pests:none
- crops:none

Pre-verification Protocol 6: Stalk borer on maize

Stalk borer on maize
Date: 24 August 11
Test Stage: Pre-verification
Test organism (s): Maize stem borer, *Busseola fusca* (Fuller)
Test Crop: Maize (*Zea mays*)

Experimental unit:

Gross: 4m x 4.5m.
Net: 4m x 3m
Inter row spacing: 0.75m
Inter plot spacing: 2m

Experimental design
RCBD replicated four times
Included standard (Lambda cyhalothrin) and untreated checks
Specific treatments
Three rates of the test pesticide (manufacturer's rate (MR), one lower rate (0.75MR), and one higher rate (1.25MR)

Application timing:
Crop: two weeks after crop emergence
Pest: 10% incidence based on visible symptoms on the leaves (all plants considered)
Efficacy assessment
Type: Incidence of stalk borer infestation from central four rows (number of infested plants out of total from the central four rows.
Leaf feeding score on a scale of 1-5 (1- No infestation, 2- light infestation, 3-Moderate infestation, 4-Heavy infestation and 5- Very heavy infestation).
Larvae and pupae from five randomly selected plants from border rows.
Number of holes from the five randomly selected plants from border rows.
At harvest, number of plants with stalk borer damaged cobs and yield from central four rows

Time: at pre spray, a week and two weeks after treatment applications

Phytotoxicity assessment:
Score for leaf scorch on a scale of one to 4 (1=no symptom of leaf scorch, 2= light scorch, 3 = medium and 4 = heavy)

Symptoms
Leaf damage due to larval feeding, stem tunneling, bored stem, larvae and pupae in the stalk,

Recommendations:
For a good level of infestation the trial can be conducted in offseason using irrigation

Extrapolation:
Pests: none
Crops: sorghum

Pre-verification Protocol 7: Weevil in maize storage

Weevil in maize storage

Date : January 27, 2011

Test stage: pre-verification

Test organism(s): maize weevil (*Sitophyllus zeamays*)

Test crop(s): maize (grains)

Experimental unit
jars, beakers, bags of 1 L, containing 250 g grains (dust application)

porous sacks of 100 kg grains (fumigation)

Design
CRD, 4 replications
included standard pesticide and untreated control

Specific requirements
three rates of the test pesticide, producers recommended dose (R), R-0.25R and R+0.25R,

Application timing
Crop: harvested grain/seeds
Pest: according to product claim

Efficacy assessment(s)
type:percentage of pest mortality
percentage of damaged grains out of 100

time:depending on product characteristics
at least one assessment after the claimed residual activity

Phytotoxicity assessment(s)
Not applicable
Symptom(s) description
bored seeds
seed malformation

Recommendations
Infest the grains with 20 individuals (1:1 sex ratio) for dust application
Infest the sacks with 100 individuals (1:1 sex ratio) for fumigation

- at least one third of the containers should be left for air circulation
- applications in airtight polyethylene sheets, at room temperature
- fumigations should be performed by well-trained employees
- sampling should be done from different layers and positions
- safety period should be followed critically
- effectiveness calculation according to Abbott formula if mortality is observed in the untreated control

Extrapolations
pests: none
crops: none

Pre-verification Protocol 8: Red scale on citrus

Red scale on citrus

Date: 24 August 11

Testing stage: Pre-verification

Test organism (s): Red scale, *Aonidiella aurantii* (Maskell)

Test Crop: Orange (Citrus spp.)

Experimental unit
Gross: 5m x 15m (3 trees)
Net 5m x 10m (2 trees). Two trees per treatment per replication. One tree will be planted between each treatment to avoid insecticide drift.
Inter row spacing: 5m
Inter plot spacing: 5m
Experimental design
RCBD in four replicates
Included standard insecticide (methidathion) and untreated check.
Specific treatments
Three rates of the test pesticide (manufacturer's rate (MR), one lower rate (0.75MR), and one higher rate (1.25MR)
Application timing
Crop: established tree/orchard
Pest: Leaf infestation - 20% incidence or trees with red scale out of 30 randomly sampled
Fruit infestation - 10% of fruits infested out of 50 sampled; frequency of application depends on the product claims

Efficacy assessment
- Count the number of live and dead scales from forty randomly picked leaves from a height of about two meters (Ten leaves per quadrant from four quadrants). Assessment be made a day before each treatment application
- Score for severity per tree from two trees(0- no infestation symptom, 1- light infestation, 3 – heavy and 4- very heavy infestation)

Phytotoxicity assessment
Score for leaf scorch on a scale of 1-4 (1- no infestation, 2- light infestation, 3- medium infestation and - heavy infestation)

Symptoms
Leaf with red scale, leaf and twigs drying and dying, fruit infested with red scales, reduced fruit size etc

Recommendations
Efficacy of insecticide evaluations on red scale need to be conducted during red scales peak breeding period of September/October and March/April.

Extrapolation
Pests: other armoured scales
Crops: Other citrus species such as Mandarin and lime

Pre-verification Protocol 9: Apple aphids on apple

Woolly Apple aphid on Apple
Date: 24 August 11
Test stage: Pre-verification
Test organism (s): Woolly Apple Aphid, *Eriosoma lanigerum* (Hausmann)
Test Crop: Apple (*Dovyalis* spp.)
Experimental unit

Gross: 27 m^2
Net: 18 m^2 (Two trees per treatment per replication. One tree will be planted between each treatment to avoid insecticide drift).
Inter row spacing: 3m
Inter plot spacing: 6m (One tree between treatment trees)

Experimental design
RCBD in four replicates.
Included standard reference pesticide and untreated check
Specific treatments
Three rates of the test pesticide (manufacturer's rate (MR), one lower rate (0.75MR), and one higher rate (1.25MR)

Application timing
Crop: Established tree/orchard
First application when WAA is detected and continue application according to the products claim

Efficacy assessment
- Number of WAA colonies from the two lower tier branches per tree out of the two trees prior to treatment application
- Number WAA infested shoots out of five per tree.
- Number of WWA colonies per shoot from three randomly selected shoots
- Scoring for black sooty mold (SM) from 0 (no sooty mold to 3 (heavy sooty mold)
--Number of fruit infested with WAA out of 20 randomly sampled

Phytotoxicity assessment
Score for leaf scorch on a scale of 1 to 4 (1-no symptom, 2-light, 3- medium and 4- heavy scorch)
Symptoms
Aerial infestation in groves and cervices at branching stems and leaf bases, infestation at root stem crowns of trees/seedlings
Recommendations
Conduct efficacy assessment only when there are aerial infestations in groves and cervices at branching stems and in leaf bases (NB. If infestation occurs at the root-stem crowns of trees/seedlings then screening of insecticides is not advisable rather the whole orchard showing this symptom be cleared as such rootstock is susceptible to the WAA).

Extrapolation
Pests: other Apple infesting aphids
Crops: none

Pre-verification Protocol 10: Pea aphids on Lentil

Pea aphid on Lentil
Testing stage-Pre-verification
Test organism(s): Pea aphid (*Acyrthosiphon pisum*)
Test crop(s): lentil (*Lens culinaris*)

Experimental unit
Gross:3 x 4 m, in row crops use border rows
Net:2 x 2 m center rows for row crops
1 x 1 m quadrate for broadcast crops

Inter plot spacing: 2 m

Design
RCBD, 4 replicates
Included standard pesticide (Premicarb) and untreated checks

Specific treatments
Three rates of the pesticide, claimed dose (N), 0.75N, 1.25N

Application timing

Crop: starting from seedling stage

Pest: 10 aphids per plant

Efficacy assessment(s)

Type:

- number of aphids per plant (destructive method) on 10 plants outside of net plot,
- Damage score (leaf clorosis and scratch pattern) on the leaves using 0-5 scale (0- free, 1- <10%, 2- 11-25%, 3- 26-50%, 4- 51-75%, 5- >75%)
- Grains and biomass yield harvested
- Any effects on non- target organisms and/or beneficial organisms should also be recorded

Time:

2 days after spraying, on a weekly base after that

Phytotoxicity assessment(s)
Score for leaf scorch on a scale of 1-4 (0-no symptom, 1-light, 2-medium, 3-heavy

Symptom(s) description
Aphid infestation, plant wilting

Recommendations
Aphid infestation is more severe in dry spells
Use susceptible cultivar grown in the area where the trial is conducted.

Extrapolation possibilities
Pests:black bean aphid (*Aphis fabae*)
Crops:other Legumes

Pre-verification Protocol 11: Thrips on onion

Thrips on onion

Date: 28 august 2011

Test organism(s): Onion thrips (*Thrips tabaci*)

Test crop(s): Onion

Experimental unit

Gross:3.6 x 3 m; 6 ridges

Net:The central four ridges

Inter row (ridge) spacing: 0.6m

Inter plot spacing: 2m

- Interplot spacing at least 2 m

Design

RCBD, 4 replicates

Included: Standard insecticide (Profenofos) and untreated checks

Specific treatments

Three rates of the test insecticide, Claimed dose (N), 0..75N, 1.25N

Application timing

Crop: After field transplanting

Pest: 10 thrips per plant

Efficacy assessment(s)

Type

The number of thrips per plant (destructive method) on 10 randomly selected plants from 2nd and 5th ridges ;

Damage score (sucking spots, scratch pattern) on the leaves using 0-5 scale (0- free, 1- <10%, 2- 11-25%, 3- 26-50%, 4- 51-75%, 5- >75%);

Total and marketable bulb yield; weight of harvested bulbs on the 3nd and 4th ridges

Average bulb weight from 10 randomly selected bulbs;

Any effects on non- target organisms and/or beneficial organisms should also be recorded

Time

Prior to treatment application and one and two weeks after treatment application

Phytotoxicity assessment(s)

Score for leaf scorch on a 1-4 scale (1- no symptom, 2-light, 3-medium and 4-heavy scorch)

Symptoms

Leaf wilting and drying, premature drying , silvery appearance of foliage with black excrement of the pest, undersized bulb, etc

Recommendations

Thrips infestation is severe in onion produced using irrigation in the dryer months

Extrapolation

Pests:Other T*hrips* spp.

Crops:shallot and garlic (*Allium* pp.)

Pre-verification Protocol 12: Broadloaf weeds in cereals

Pesticide testing against broadleaf weeds in cereals

Date
January 27, 2011

Testing stage
Pre- verification

Test organism(s)
Broad leaf weeds

Test crop(s)
teff

Experimental unit
gross:3 x 4 m
net:2 x 3 m

interplot spacing at least 2 m

Designs
RCBD, 4 replicates
Included untreated control

Specific treatments
Claimed dose (N), 0.5N and 2N
Include hand weeded untreated control, standard check

Application timing
Based on crop or weed growth stage according to claimed use

Efficacy assessment(s)
Type:visual estimation of percentage weeds control
Counting number of weed plants per species
Yield; weight of grains harvested

Time:every week, starting from application

Phytotoxicity assessment(s)
On a 0-4 scale (no, few, slight, moderate, severe, and very severe)

Symptom(s) description
-described and recorded, if possible symptoms should be photographed

Extrapolations
Pests: none
Crops:effectiveness data (not phytotoxicity) on the susceptible weed species to wheat and barley

Pre-verification Protocol 13: Weeds in perennial tree crops

Weeds in perennial tree crops

Date
January 27, 2011

Stage of testing
Pre-Verification

Test organism(s)
Weeds-Bermuda grass (*Cynodon dactylon*), coach grass *(Digitaria abyssinica*)*, etc.*

Test crop(s)
Perennial tree crops –coffee (coffee arabica), Orange (citrus sinensis), mango (mangifera indica),apple-(malus domestica)

Experimental unit
Gross: 11 x 11m, for fruit tree crops planted in rows
3x3 m quadrate for coffee planted in rows
Net: 2x2 for coffee planted in rows
10 x 10m quadrate for other fruit tree crops planted in rows
Inter-plot spacing as per crop type
All row planted

Design
Single evaluation plot on 5 locations
Including untreated plots

Specific treatments
The effective dose of the test product (N), 0.75N, N and 1.25N
Include hand weeded and untreated control

Application timing
Based on crop or weed growth stage according to claimed use (preferably at young and fast growing stage.

Efficacy assessment(s)
Type: visual assessment of discoloration and gradual death of the claimed weeds.
- For short term efficacy 2-4 weeks after spray
- For medium term efficacy 4-6 weeks after spray
- For long term efficacy 6-8 weeks after spray

Time: every two weeks, starting from application date.

Phytotoxicity assessment(s)
Describe phytotoxicity (symptoms; turbidity, nutrient content, physiological changes, etc. and severity; low, moderate, severe, etc.)

Symptom(s) description
Leaf burn, wilting, leaf discoloration

Recommendations

- do not start treatments when rain is forecasted within 6 hour
- Temperature should be 25 C or above for effective killing.
- use knapsack or motorized sprayer for application.
- working direction shall follow wind direction.
- The claimed product shall be environmentally friendly.
- Finally control result must show at least 85% kill of the claimed weed.

Extrapolation

Pest: grass family weeds species

Crop: effectiveness data can be extrapolated to all perennial tree crops

Pre-verification Protocol 14: Late blight in potato

Late blight in potato
Date: August 25, 2011
Testing stage: Pre-verification
Test organism(s): Late blight (*Phytophthora infestans*)
Test crop(s): Potato (*Solanum tuberosum*)
Experimental unit
Gross: 3m x 3m
Net: 1.5m x 3m (two central rows)
Inter-row spacing is 0.75m; inter-plot spacing is at least 1.5m
Design: RCBD, 4 replications
Include untreated control
Test it at hot-spot site (one location)
Specific treatments
Claimed dose (N), 0.5N and 1.5N
Application time
Crop: at the onset of the disease,
Disease: Never later than 40% foliar damage
Efficacy assessment(s)
Type: blight severity (percentage foliar coverage), infected tubers at harvest, unmarketable tubers, tuber yield per plot
Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description
Very young lesions appear as irregular shaped, small lesions with or without a small surrounding area of collapsed but still green tissue. Lesions later turn brown. Old lesions are larger and are usually not delimited by the veins. These lesions are typically surrounded by a zone of collapsed tissue that is not yet necrotic. If there are many lesions on a single leaflet, the entire leaf can turn chlorotic. Sporulation may be evident on collapsed tissue and on the outermost portions of the necrotic areas of a lesion if it has been in a saturated atmosphere (100% RH) for more than 7 or 8 h.
Recommendations
Late blight infection is more severe in rainy, cool and foggy weather
Extrapolation
Pathogens: none
Crops: Tomato

Pre-verification Protocol 15: Rusts in wheat

Rusts in wheat
Date: August 28, 2011
Testing stage: Pre-verification
Test organism(s): yellow (*Puccinia striiformis*), stem rust (*Puccinia graminis*), leaf rust (*Puccinia recondita*)
Test crop(s): Wheat (*Triticum* spp.)
Experimental unit
Gross: 2.4m x 3.0m
Net: 2.0m x 2.5m (four central rows)
Inter row spacing: 0.2m;
Inter plot spacing: at least 1.5 meters
Design: RCBD, 4 replications
Include untreated control
Specific treatments
Claimed dose (N), 0.5N and 1.5N
Application time
Disease: When the disease starts, never later than 30% foliar damage
Efficacy assessment(s)
Type: pustule density; percentage foliar coverage; 1000-seed weight; biomass, seed yield per plot
Crop stage: flag leaf separately recorded
Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description
Yellow speckles, rust pustules, shriveling of seeds
Recommendations
Yellow (*Puccinia striiformis*) in the highlands
Leaf rust (*Puccinia recondita*) in intermediate altitudes
Stem rust (*Puccinia graminis*) in lower altitudes
Extrapolation
Pathogens: *none*
Crops: effectiveness data to barley and triticale

Pre-verification Protocol 16: Botrytis in rose

Botrytis in rose
Date: August 29, 2011
Testing stage: Pre-verification
Test organism(s): Grey mold (*Botrytis cinerea*)
Test crop(s): Rose (*Rosa* spp.)
Experimental unit
Gross: 3m x 5m
Net: 3m x 5m
Design: RCBD, 4 replications
Include untreated control
Test it at hot-spot site (one location)
Specific treatments
Claimed dose (N), 0.5N and 1.5N
Application time
Crop: at the onset of the disease,
Efficacy assessment(s)
Type: disease severity (percentage foliar coverage), percent infected flowers, percent unmarketable flowers
Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description
Very young lesions appear as circular small lesion on any part of the plant. These spots later form conspicuous circular concentric lesions, which turn grey later. Canker often develops on the stem. Black spots usually occur on petals that reduce the quality of rose flower. Cut flowers with a single spot are often rejected and unacceptable.
Recommendations
Grey mold infection is more severe in rainy, cool and foggy weather
Extrapolation
Pathogens: none
Crops: none

Pre-verification Protocol 17: Powdery mildew in rose

Powdery mildew in rose
Date: August 29, 2011
Testing stage: Pre-verification
Test organism(s): Powdery mildew (*Sphaerotheca pannosa* var. *rosae*)
Test crop(s): Rose (*Rosa* spp.)
Experimental unit
Gross: 3m x 5m
Net: 3m x 5m
Design: RCBD, 4 replications
Include untreated control
Test it at hot-spot site (one location)
Specific treatments
Claimed dose (N), 0.5N and 1.5N
Application time
Crop: at the onset of the disease,
Efficacy assessment(s)
Type: disease severity (percentage foliar coverage), percent infected flowers, percent unmarketable flowers
Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description
Symptoms on leaves begin as small, round, spots, that widen and coalesce, showing white mycelial and conidial growth on leaf surface. The disease causes slight twisting of the foliage sometimes. The leaves and stems, and sometimes the flowers, become distorted, growth is diminished, and chlorosis, yellowing and necrosis of leaves occurs. The white cover of the plant reduce the quality of cut flowers, thus often rejected and unacceptable.
Recommendations
Powdery mildew infection is more severe in dry day and cool night period
Extrapolation
Pathogens: none
Crops: ornamentals

Pre-verification Protocol 18: Powdery mildew in mango

Date

September, 2011

Pre-verification

Test organism

Powdery mildew (*Oidium mangiferae* Berthet)

Test crop

Mango (*Magnifera indica* L.)

Experimental unit

Mango trees

Net; Single tree/plot

Gross; three trees

Inter-plot spacing- At least 7-10 meters

Design

RCBD, single tree plots replicated three times for each treatment

Specific treatments

Three rates of the test fungicide

Manufacturers 'rate (N), (N) , 0.5N and 1.5N

Include standard check (previously recommended pesticide) and untreated control

Application timing

Susceptibility of mango trees to powdery mildew usually starts during flowering stage where elongation of inflorescences are still protected by bracts and extends to Pea-sized fruit where fruits reach approx. 8 mm diameter in size. However, the full-bloom stage is the most susceptible to infection. Hence, the first spray application for mango powdery mildew should start no later than at 50% of full flowering, and spraying should continue after flowering and after fruit set.

Crop: Before flowering, after flowering and after fruit set

Three locations for one season or in one location for two seasons in case three locations or hot spots cannot be found.

Efficacy assessment (s)

Type:

Disease severity; recorded on the four marked panicles in each four directions (E,W,N,S) of each mango tree using 0-5 grade (0 = No disease; 1 = 1-20; 2 = 21-40; 3 = 41-60; 4 = 61-80; and 5 = 81-100% panicles covered by powdery mildew.

The percent of leaves and panicles should arrive at from the evaluation of 100 leaves and panicles from each treatment and cultivar replicated 3 times.

Yield; Number of fruit counted from each tree within each plot. Total number of fruit counted from each treatment and cultivars replicated 3 times and converted in a hectare basis.

Phytotoxicity assessments

On a 0-3 score scale (0 = no; 1-few; 2 = moderate; and 3 = severe)

Symptoms description

1. Chlorosis/necrosis of foliage,
2. Damage and deformation of blossoms
3. Fruitlets and fruit, including color of fruit

Recommendation

- Mango Powdery mildew causes the most serious losses when flowering and growth flushes occur during dry, cool conditions
  The product should normally be applied at the dosage specified for the intended use. Subsequently, in testing fungicides for the control of mango powdery mildew trees should be sprayed till run-off with approximately 20 l of spray solution per tree by using a knapsack/motorized sprayer. However, determining spray volumes through calibration in the field is highly recommended.

Extrapolation

No extrapolations for other diseases and crops

Pre-verification Protocol 19: Coffee berry disease in coffee

Date

September, 2011

Pre-verification

Test organism

Coffee berry disease *(CBD) (Colletotrichum kahawae)*

Test crop

Coffee (*Coffea arabica)*

Experimental unit

Coffee trees

Net; 6 trees/plot

Gross; 24 coffee trees

Inter-plot spacing- at least 5 meters

Design

RCBD, 4 replications

Specific treatments

Three rates of the test fungicide

Manufacturers 'rate (N), (N), 0.5N and 1.5N

Included standard check (previously recommended pesticide) and untreated control

Application timing

In Ethiopia, spraying against CBD starts six weeks after main flowering, which usually occurs in March but depends on the pattern of rainfall, and with a four weeks interval.Crop: 6 weeks after flowering Four replications in three locations for one season or in one location for two seasons in case three locations or hot spots cannot be found.

Efficacy assessment (s)

Type:

Berry count; counting the number of infected and healthy berries on three sample branches (each from top, middle and bottom canopy layers at different directions) on each of the six trees. Seven weeks after the first spray at three weeks interval

Visual assessment; of disease severity at peak CBD infection level, usually in mid-August.

Yield; Ripe cherry fresh weight in gram per tree-at final harvest

Phytotoxicity assessments

On a 0-3 scale (0=no, 1=few, 2=moderate, 3=severe)

Symptoms description

4. Premature Leaf fall
5. Premature berry drop
6. Leaf scorch
7. Crinkled leaf
8. Chlorotic types on leaves
9. Necrotic types on leaves

Recommendation

- CBD reaches its peak time in mid-August

In areas of the country where shortage of water does not occur the high volume, 750-1000 ml/ tree, using knapsack sprayer can be used, depending on the size of coffee trees. Low volume application, 200-250 ml/tree, using motorized knapsack sprayer is found useful when spraying tall coffee trees and has an advantage in removing much of the human involvement. Besides, the vertical throw of the droplets is high and thus spray solutions can reach the top of the tree thereby serving the intended purpose.

Extrapolation

No extrapolations for other diseases and crops

Pre-verification Protocol 20: Seed borne diseases in wheat

Seed borne diseases in wheat
Date: August 20, 2011
Testing stage: Pre-verification
Test organism(s): Seedborne diseases (e.g. *Fusarium* spp., *Helminthosporium* spp., etc)
Test crop(s): Wheat (*Triticum* spp.) and other cereals
Experimental unit
Gross: 1.2m x 3.0m
Net: 0.8m x 2.5m (four central rows)
Inter-row spacing: 0.2m
Inter-plot spacing: at least 1m
Design: RCBD, 4 replications
Include untreated control, healthy seed control
Specific treatments
Claimed dose (N), 0.5N and 1.5N
Application time
Crop: seed treatment
Efficacy assessment(s)
Type: seedling infection test in the laboratory (4 replications and 100 seeds in 1 replication), seedling diseases in the field (2.4m x 3.0m plot size)
Time: assessed at seedling, at dough, ripping stage
Crop: emergence percentage, crop stand in percent, seed yield, seed health testing
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe) in two different tests (in germination test in the lab and at seedling stage in the field)
Symptom(s) description
Germination percentage, seedling infection, emergence, scab on the head during ripping, shriveling of seeds, seed infection test after harvest, seed yield
Recommendations
Primary seed infection and contamination determine disease development in the field. Hence, the experiment should include isolation of the pathogens, contamination of the seed to be used for efficacy test, then testing in the lab and ultimately in the field
Extrapolation
Pathogens: Seedborne fungi (*Fusarium* spp., *Helminthosporium* spp., etc)
Crops: barley, triticale

Verification Protocol 1: Red tefworm on tef

Date: 29 August 2011
Testing stage: Verification
Test organism: Red tefworm, *Mentaxya ignicollis* (Walker)
Test crop: Tef
Experimental units:

Gross: 10 m x 10 m, superimposed in tef fields
Net: 1 m x 1 m quadrates
Inter row spacing; Not applicable (broadcast)
Inter plot spacing: 3m (tef covered)

Design:

Single plot with 5 over-site replications
Included standard insecticide in use in the area and an untreated control

Specific treatments:

Insecticide proven effective at the pre-verification stage, to be applied at the effective rate identified

Application time:

Crop: any stage
Pest: a larva per 0.25 m^2 quadrate

Efficacy assessments:

Type: larvae per 1 m^2 quadrate on five randomly taken quadrates per plot
damaged and undamaged panicles per 0.25 m^2 quadrate on five randomly taken quadrates per plot
grain yield per 1 m^2 quadrate on five randomly taken quadrates per plot

Time: pre spray count of larvae to be recorded at dusk
post spray count to be recorded at dusk on the following day
panicle damage to be recorded at pre spray, 7 and 14 days latter

Phytotoxicity assessments:

Scoring for scorch on a scale of 0-4, where 0=no, 1= top leaves 2=entire panicle, 3=top leaves and entire panicle, 4=entire plant scorched

Symptom(s) description:

Chewed leaf edges and panicles lacking growing seed

Recommendations:

The pest is a problem in deeply cracking heavy black clay soils and infestation to varying degrees occurs every year in limited yet major tef growing areas in the country that include Becho Plane and Bechena areas

Extrapolation:

Pests: none

Props: none

Verification Protocol 2: Shootflies on tef

Shootflies on tef
Date: 29 August 2011
Trial stage: verification
Test organism: shootflies (*Atherigonia hyalinipennis* Em and *Delia aramburgi* (Seguy)
Test crop: Tef
Experimental units:

Gross: 10 x 10 m
Net: 1m x 1m quadrates
Inter row spacing: Not applicable (Broadcast)
Inter plot spacing: 1.5m

Design:

Single plot with 3 over site replications
Included standard insecticide in use in the area and an untreated control

Specific treatments:

insecticide proven effective in the pre-verification trial, to be applied at the effective rate identified,

Application timing:

Crop: any stage
Pest: 10% seedling damage per 0.25 m^2 quadrate or 2% damaged panicles per 1 m^2 quadrate

Efficacy assessments
type: damaged and undamaged seedlings per 0.25 m^2 quadrate per plot and in ten randomly taken quadrates
damaged and undamaged panicles per 1 m^2 quadrate in ten randomly taken quadrates per plot
grain yield per 1 m^2 quadrate on five randomly taken quadrates per plot
time:
if damage starts at seedling stage:
pre spray count of damaged and undamaged seedlings
post spray count of damaged and undamaged seedlings after 1 week and carrying out second spray, if required
post spray count of damaged and undamaged seedlings after 1 and 2 weeks from the 2^{nd} spray
if damage starts on panicles:
pre spray count of damaged and undamaged panicles
post spray count of damaged and undamaged panicles after 1 week and carrying out second spray, if required
post spray count of damaged and undamaged panicles after 1 and 2 weeks from the 2^{nd} spray

Phytotoxicity assessments:

scoring for leaf scorch on a scale of 0-4, where 0=no, 1= top leaves 2=entire panicle, 3=top leaves and entire panicle, 4=entire plant scorched

Symptom(s) description:

dead seedlings, which can be clearly seen by the number of seedlings turned yellow and are stacked to the soil.
damaged panicles, which can be confirmed by trying to pull panicles of tef plants contained in the sample quadrates. When the damage is severe, shootfly damaged tef panicles die and turn white and remain in an upright position. Such panicles when threshed by hand are often found being without seeds or may contain prematurely aborted seeds.

Recommendations:

the pest is a major problem in areas where there is shortage of moisture and infestation to varying degrees occurs every year and in other places in seasons of rainfall shortage as well as in times of terminal drought.

Extrapolation:

pests: none

crops: barley and wheat

Verification Protocol 3: Tef Epilachna on tef

Tef Epilachna on tef
Date: 29 August 2011
Testing stage: Verification
Test organism: Tef epilachna, *Epilachna simillis*
Test crop: Tef
Experimental units:

Gross: 10 x 10 m, in a place hotspot to the beetle
Net: 1 x 1 m quadrates
Inter row spacing: Not applicable (broadcast)
Inter plot spacing: 1.5m

Design:

Single plot with 3 over site replications
Included standard insecticide in use in the area and an untreated control

Specific treatments:

insecticide proven effective in the pre-verification trial, to be applied at the effective rate identified

Application timing:

5 larvae and/or adults per 1 m^2 quadrate

Efficacy assessments

type: larvae and adults per 1 m^2 quadrate on five randomly taken quadrates per plot;
skeletonized leaves per plant on fifteen randomly selected plants per plot;
damaged and undamaged plants per 1 m^2 quadrate on five randomly taken quadrates per plot;
grain yield per 1 m^2 quadrate on five randomly taken quadrates per plot

time: pre spray count of larvae and adults;
post spray count of larvae and adults after 24 hours;
at pre spray, 7 and 14 days latter count of number of skeletonized leaves per plant;
damaged and undamaged plants at pre spray, 7 and 14 days latter

Phytotoxicity assessments:

scoring for leaf scorch on a scale of 0-4, where 0=no, 1= top leaves 2=entire panicle, 3=top leaves and entire panicle, 4=entire plant scorched

Symptom(s) description:

skeletonized leaves

Recommendations:

the pest is a problem in areas where there is shortage of moisture and infestation to varying degrees occurs every year in such environments.

Extrapolation:

pests: none
crops: barley and wheat

Verification Protocol 4: Cotton aphids on cotton

Aphids in cotton

Date: August, 27, 2011

Test organism(s): cotton aphid (*Aphis gossypii*)

Test crop(s): cotton

Experimental unit/ plot size:
Gross:10.8m x 10m;
Net:10 internal rows
Inter row spacing: 0.9m
Inter plot spacing: 2m

Design
single plot over 3 sites
Included untreated control and another standard control plot (commonly used by farmers and if possible with the same mode of action as the test product)

Specific treatments:
the effective dose of the test product at pre-verification stage

Application timing
- crop: 30 days after emergence
- pest:30% infested plants

Efficacy assessment(s)
Type:
- number of aphids on 20 randomly chosen plants on a 0-5 scale (0- none, 1- 1-10 aphids, 2- 11-30 aphids, 3- 31-100 aphids, 4- 101-250 aphids, 5- >251 aphids)
- yield; lint weight from 10 internal rows

Time:
- 1 day before for pre-application assessment (For each application)
- 2, 5, 7, and 10 days after application for post application assessment (For each application)

Phytotoxicity assessment(s)
- Score for leaf scorch a scale of on a 0-3 scale (0-no, 1-few, 2-moderate, 3-severe)

Symptom(s) description
- presence of adults and nymphs
- honey dew and leaf curling

Recommendations
- untreated control can be covered by polyethylene sheet during spraying to protect against drift from adjacent treatments

Extrapolation
- crop:none
- pest:none

Verification Protocol 5: Bollworms on cotton

Bollworm in cotton

Date: August 27, 2011

Test organism(s): Cotton bollworm (*Helicoverpa armigera*)

Test crop(s): Cotton

Experimental unit/ plot size:
Gross:10.8m x 10m
Net:10 internal rows
Inter row spacing: 0.9m
Inter plot spacing: 2m

Design
single plot over 3 sites
Included reference product and untreated control

Specific treatments:
the effective dose of the test product at pre-verification stage

Application timing:
Crop: starting at initial square stage of crop
Pest: 10 eggs per 20 plants for ovicidal products

5 first to third instar larvae (L1-L3) per 20 plants for larvicidal products

Efficacy assessment(s):

Type:
counting the number of eggs and larvae on 10 randomly chosen plants/plot;
percentage of damaged squares and bolls on 20 randomly chosen plants;
yield; lint weight from 10 internal rows

Time:
1 day before for pre-application assessment (for each application);
2, 5, 7, & 10 days after application for post assessment (for each application);

Phytotoxicity assessment(s)
Score for leaf scorch on a 0-3 scale (0-no, 1-light, 2-medium, 3-heavy);

Symptom(s) description
- premature opening of square
- boreholes on bolls
- presence of frass
- sheeding of bolls and squares (scars on stems; branches)
- presence of eggs and larvae

Recommendations
- untreated control can be covered by polyethylene sheet during spraying to protect against drift from adjacent treatments
- excluded untreated control may also be considered to prevent interference by migration

Extrapolation
- pests:none
- crops:none

Verification Protocol 6: Stalk borer on maize

Stalk borer on maize
Date: 24 August 11
Test Stage: Verification
Test organism (s): Maize stem borer, *Busseola fusca* (Fuller)
Test Crop: Maize (*Zea ma*
Experimental unit
Mmaize plot of 10 m x 10 m

Experimental design
Single plot in three sites
Included standard insecticide (Lambda cyhalothrin) and untreated check
Specific treatments
Recommended rate of the test insecticide l
Application timing:
Crop: two weeks after crop emergence
Pest: 10% incidence based on visible symptoms on the leaves (all plants considered)
Efficacy assessment
Type: Incidence of stalk borer infestation from central four rows (number of infested plants out of total from the central four rows.
Leaf feeding score on a scale of 1-5 (1- No infestation, 2- light infestation, 3-Moderate infestation, 4-Heavy infestation and 5- Very heavy infestation).
Larvae and pupae from five randomly selected plants from border rows.
Number of holes from the five randomly selected plants from border rows.
At harvest, number of plants with stalk borer damaged cobs and yield from central four rows

Time: at pre spray, a week and two weeks after treatment applications

Phytotoxicity assessment:
Score for leaf scorch on a scale of one to 4 (1=no symptom of leaf scorch, 2= light scorch, 3 = medium and 4 = heavy)

Symptoms
Leaf damage due to larval feeding, stem tunneling, bored stem, larvae and pupae in the stalk,

Recommendations:
For a good level of infestation the trial can be conducted in offseason using irrigation

Extrapolation:
Pests: none
Crops: sorghum

Verification Protocol 7: Weevil in maize storage

Weevil in maize storage

Date : January 27, 2011

Test stage: Verification

Test organism(s): maize weevil (*Sitophyllus zeamays*)

Test crop(s): maize (grains)

Experimental unit

jars, beakers, bags of 1 L, containing 250 g grains (dust application)

porous sacks of 100 k

Design

- CRD, 4 replication per concentrations
- Untreated control included

Specific requirements

Recommended rate will be compared with the standard insecticide and untreated check

Application timing

- According to product claim

Type:

- Percentage of pest mortality
- Percentage of damaged grains

Time:

- Depending on product characteristics
- At least one assessment after the claimed residual activity

Phytotoxicity assessment(s)

---none----

Symptom(s) description

- bored seeds
- Seed malformation

Recommendations

- At least one third of the containers should be left for air circulation
- Applications in air tight polyethylene sheets, at room temperature
- Fumigations should be performed by well-trained employees and air tight plastic sheets
- Sampling should be done from different layers and positions of stack
- Safety period should be followed critically
- Effectiveness calculation according to Abbott's formula (1925) if mortality is observed in the untreated control

Extrapolation

- Pests: none
- Crops: none

Verification Protocol 8: Red scale on citrus

Red scale on citrus
Date: 24 August 11
Testing stage: Verification
Test organism (s): Red scale, *Aonidiella aurantii* (Maskell)
Test Crop: Orange (Citrus spp.)
Experimental unit
Gross: 25m x 25m (16 trees)
Net 10m x 10m (4 trees). four trees per treatment per replication.
Inter row spacing: 5m
Inter plot spacing: 5m
Experimental design
Single plot replicated over four orchards
Included standard insecticide (methidathion) and untreated check.
Specific treatments
Recommended rate of the test insecticide
Application timing
Crop: established tree/orchard
Pest: Leaf infestation - 20% incidence or trees with red scale out of 30 randomly sampled
Fruit infestation - 10% of fruits infested out of 50 sampled; frequency of application depends on the product claims

Efficacy assessment
- Count the number of live and dead scales from forty randomly picked leaves from a height of about two meters (Ten leaves per quadrant from four quadrants). Assessment be made a day before each treatment application
- Score for severity per tree from two trees(0- no infestation symptom, 1- light infestation, 3 – heavy and 4- very heavy infestation)

Phytotoxicity assessment
Score for leaf scorch on a scale of 1-4 (1- no infestation, 2- light infestation, 3- medium infestation and - heavy infestation)

Symptoms
Leaf with red scale, leaf and twigs drying and dying, fruit infested with red scales, reduced fruit size etc

Recommendations
Efficacy of insecticide evaluations on red scale need to be conducted during red scales peak breeding period of September/October and March/April.

Extrapolation
Pests: other armoured scales
Crops: Other citrus species such as Mandarin and lime

Verification Protocol 9: Apple aphids on apple

Woolly Apple aphid on Apple
Date: 24 August 11
Test stage: Verification
Test organism (s): Woolly Apple Aphid, *Eriosoma lanigerum* (Hausmann)
Test Crop: Apple (*Dovyalis* spp.)

Experimental unit
Gross : 9m x 15 m (15 trees)
Net : 3mx 9m (9trees).

Experimental design
Single plot replicated over four orchards
Included standard pesticide and untreated checks
Specific treatments
Recommended rate of the test insecticide
Application timing
Crop: Established tree/orchard
First application when WAA is detected and continue application according to the products claim

Efficacy assessment
- Number of WAA colonies from the two lower tier branches per tree out of the two trees prior to treatment application
- Number WAA infested shoots out of five per tree.
- Number of WWA colonies per shoot from three randomly selected shoots
- Scoring for black sooty mold (SM) from 0 (no sooty mold to 3 (heavy sooty mold)
--Number of fruit infested with WAA out of 20 randomly sampled

Phytotoxicity assessment
Score for leaf scorch on a scale of 1 to 4 (1-no symptom, 2-light, 3- medium and 4- heavy scorch)
Symptoms
Aerial infestation in groves and cervices at branching stems and leaf bases, infestation at root stem crowns of trees/seedlings
Recommendations
Conduct efficacy assessment only when there are aerial infestations in groves and cervices at branching stems and in leaf bases (NB. If infestation occurs at the root-stem crowns of trees/seedlings then screening of insecticides is not advisable rather the whole orchard showing this symptom be cleared as such rootstock is susceptible to the WAA).

Extrapolation
Pests: other Apple infesting aphids
Crops: none

Verification Protocol 10: Pea aphids on Lentil

Pea aphid on Lentil
Date: August 28, 2011
Testing stage: Verification
Test organism(s): Pea aphid (*Acyrthosiphon pisum*)
Test crop(s): lentil (*Lens culinaris*)

Experimental unit

Gross:10 x 10 m
Net:5 x 5 m or using quadrat for broadcast crops
Inter plot spacing: 2 m

Design
Single plot replicated over thre sites
Included standard pesticide (Premicarb) and untreated checks

Specific treatments
The effective dose of the test product from pre verification trial, with known reference product as standard check and untreated check

Application timing

Crop: starting from seedling stage
Pest: 10 aphids per plant

Efficacy assessment(s)
Type:

- number of aphids per plant (destructive method) on 10 plants outside of net plot,
- Damage score (leaf clorosis and scratch pattern) on the leaves using 0-5 scale (0- free, 1- <10%, 2- 11-25%, 3- 26-50%, 4- 51-75%, 5- >75%)
- Grains and biomass yield harvested
- Any effects on non- target organisms and/or beneficial organisms should also be recorded

Time:

2 days after spraying, on a weekly base after that

Phytotoxicity assessment(s)
Score for leaf scorch on a scale of 1-4 (0-no symptom, 1-light, 2-medium, 3-heavy
Symptom(s) description
Aphid infestation, plant wilting

Recommendations
Aphid infestation is more severe in dry spells
Use susceptible cultivar grown in the area where the trial is conducted.

Extrapolation possibilities
Pests:black bean aphid (*Aphis fabae*)
Crops:other Legumes

Verification Protocol 11: Thrips on onion

Thrips on onion
Date: 28 august 2011
Test stage: Verification
Test organism(s): Onion thrips (*Thrips tabaci*)
Test crop(s): Onion
Experimental unit
Gross:10m x 10m
Net:5m x 5m
Inter row (ridge) spacing: 0.6m
Inter plot spacing: 2m
- Interplot spacing at least 2 m

Design
Single evaluation plot over 3 sites
Included: Standard insecticide (Profenofos) and untreated checks
Specific treatments
The recommended rate of the taste pesticide
Application timing
Crop: After field transplanting
Pest: 10 thrips per plant
Efficacy assessment(s)
Type
The number of thrips per plant (destructive method) on 10 randomly selected plants from 2nd and 5th ridges ;
Damage score (sucking spots, scratch pattern) on the leaves using 0-5 scale (0- free, 1- <10%, 2- 11-25%, 3- 26-50%, 4- 51-75%, 5- >75%);
Total and marketable bulb yield; weight of harvested bulbs on the 3nd and 4th ridges
Average bulb weight from 10 randomly selected bulbs;
Any effects on non- target organisms and/or beneficial organisms should also be recorded

Time
Prior to treatment application and one and two weeks after treatment application

Phytotoxicity assessment(s)
Score for leaf scorch on a 1-4 scale (1- no symptom, 2-light, 3-medium and 4-heavy scorch)

Symptoms
Leaf wilting and drying, premature drying , silvery appearance of foliage with black excrement of the pest, undersized bulb, etc

Recommendations
Thrips infestation is severe in onion produced using irrigation in the dryer months

Extrapolation
Pests:Other T*hrips* spp.
Crops:shallot and garlic (*Allium* pp.)

Verification Protocol 12: Broadloaf weeds in cereals

Date
January 27, 2011

(Pre-) verification
Verification

Test organism(s)
Broadleaf weeds

Test crop(s)
Teff

Experimental unit
Gross:10m x 10 m
Net:9m x 9 m
interplot spacing at least 2 m

Design
Single evaluation plot on 3 locations

Specific treatments
The effective dose of the test product (N) and 2N
Include hand weeded untreated control, standard check

Application timing
Based on crop or weed growth stage according to claimed use

Efficacy assessment(s)
Type:visual estimation of percentage weeds control
Counting number of weed plants per species
Yield; weight of grains harvested
Time:every week, starting from application

Phytotoxicity assessment(s)
On a 0-4 scale (no, few, slight, moderate, severe, very severe)

Symptom(s) description
- described and recorded, if possible symptoms should be photographed

Extrapolations
Pests: none
Crops: effectiveness data (not phytotoxicity) on the susceptible weed species to wheat and barley

Verification Protocol 13: Weeds in perennial tree crops

Date
January 27, 2011

Stage of test
Verification

Test organism(s)
Weeds-Bermuda grass *cynodon dactylon*-(Star grass), *Digitaria abyssinica*-(coach grass)

Test crop(s)
Perennial tree crops –coffee (coffee arabica), Orange (*Citrus sinensis*), mango (mangifera indica),apple-(malus domestica)

Experimental unit
Gross: 11 x 11m, for fruit tree crops planted in rows
3 x 3 m quadrate for coffee planted in rows
Net: 2x2 for coffee planted in rows
10 x 10m quadrate for other fruit tree crops planted in rows
Inter-plot spacing as per crop type
All row planted

Design
Single evaluation plot on 5 locations
Including untreated plots

Specific treatments
The effective dose of the test product (N), 0.75N, N and 1.25N
Include hand weeded and untreated control

Application timing
Based on crop or weed growth stage according to claimed use (preferably at young and fast growing stage.

Efficacy assessment(s)
Type: visual assessment of discoloration and gradual death of the claimed weeds.
- For short term efficacy 2-4 weeks after spray
- For medium term efficacy 4-6 weeks after spray
- For long term efficacy 6-8 weeks after spray

Time: every two weeks, starting from application date.

Phytotoxicity assessment(s)
Describe phytotoxicity (symptoms; turbidity, nutrient content, physiological changes, etc. and severity; low, moderate, severe, etc.)

Symptom(s) description
Leaf burn, wilting, leaf discoloration

Recommendations

- do not start treatments when rain is forecasted within 6 hour
- Temperature should be 25 C or above for effective killing.
- use knapsack or motorized sprayer for application.
- working direction shall follow wind direction.
- The claimed product shall be environmentally friendly.
- Finally control result must show at least 85% kill of the claimed weed.

Extrapolation

Pest: grass family weeds species

Crop: effectiveness data can be extrapolated to all perennial tree crops

Verification Protocol 14: Late blight in potato

Late blight in potato
Date: August 25, 2011
Testing stage: Verification
Test organism(s): Late blight (*Phytophthora infestans*)
Test crop(s): Potato (*Solanum tuberosum*)
Experimental unit
Gross: 10m x 10m
Net: 9m x 8m (twelve central rows)
Inter-row spacing is 0.75 m; inter-plot spacing at least 1.0 m
Design: Un-replicated single plot

Tested at three hot-spot sites (locations)

Include untreated control, another standard check plot (the best product that farmers use at present having the same mode of action)

Specific treatments
Claimed dose (or the dose recommended by the pre-verification test)
Application time
Crop: when the disease starts,
Disease: Never later than 50% foliar damage
Efficacy assessment(s)

Type: blight severity (percentage foliar coverage), infected tubers, unmarketable tubers, tuber yield per plot

Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description

Very young lesions appear as irregular shaped, small lesions with or without a small surrounding area of collapsed but still green tissue. Lesions later turn brown. Old lesions are larger and are usually not delimited by the veins. These lesions are typically surrounded by a zone of collapsed tissue that is not yet necrotic. If there are many lesions on a single leaflet, the entire leaf can turn chlorotic. Sporulation may be evident on collapsed tissue and on the outermost portions of the necrotic areas of a lesion if it has been in a saturated atmosphere (100% RH) for more than 7 or 8 h.

Recommendations
Late blight infection is more severe in rainy, cool and foggy weather
Extrapolation
Pathogens: *none*
Crops: efficacy data to tomato

Verification Protocol 15: Rusts in wheat

Rusts in wheat
Date: August 28, 2011
Testing stage: Verification
Test organism(s): yellow (*Puccinia striiformis*), stem rust (*Puccinia graminis*), leaf rust (*Puccinia recondita*)
Test crop(s): Wheat (*Triticum* spp.)
Experimental unit
Gross: 10m x 10m
Net: 9m x 9m
Inter row spacing: 0.2m
Inter plot spacing: at least 1m
Design: Un-replicated single plot
Tested at three hot-spot sites (locations)
Include **untreated control** and another **standard control plot** (the best product under use by farmers having the same mode of action)
Specific treatments
The effective dose of the test product
Application time
Crop: record growth stage of the host
Disease: at the onset of rust; never later than 30% foliar damage
Efficacy assessment(s)
Type: pustule density; estimation of disease severity; 1000-seed weight; biomass grain weight per plot
Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description
Yellow speckles, rust pustules, shriveling of seeds
Recommendations
Yellow (*Puccinia striiformis*) in the highlands
Leaf rust (*Puccinia recondita*) in intermediate altitudes
Stem rust (*Puccinia graminis*) in lower altitudes
Extrapolation
Pathogens: *none*
Crops: effectiveness data to barley and triticale rusts

Verification Protocol 16: Botrytis in rose

Botrytis in rose
Date: August 28, 2011
Testing stage: Verification
Test organism(s): Grey mold (*Botrytis cinerea*)
Test crop(s): Rose (*Rosa* spp)
Experimental unit
Gross: 10m x 30m
Net: 10m x 30m
Design: single plot
Include untreated control;
Test it at three hot-spot sites (locations)
Specific treatments
The effective dose of the test product
Application time
Crop: at the onset of the disease
Efficacy assessment(s)
Type: disease severity (percentage foliar coverage), percent infected flowers, percent unmarketable flowers
Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description
Very young lesions appear as circular small lesion on any part of the plant. These spots later form conspicuous circular concentric lesions, which turn grey later. Canker often develops on the stem. Black spots usually occur on petals that reduce the quality of rose flower. Cut flowers with a single spot are often rejected and unacceptable.
Recommendations
Grey mold infection is more severe in rainy, cool and foggy weather
Extrapolation
Pathogens: none
Crops: none

Verification Protocol 17: Powdery mildew in rose

Powdery mildew in rose
Date: August 29, 2011
Testing stage: Verification
Test organism(s): Powdery mildew (*Sphaerotheca pannosa* var. *rosae*)
Test crop(s): Rose (*Rosa* spp.)
Experimental unit
Gross: 10m x 30m
Net: 10m x 30m
Design: un-replicated single plot
Include untreated control; and another standard product as a control
Test it at three hot-spot sites (locations)
Specific treatments
The effective dose of the test product
Application time
Crop: at the onset of the disease,
Efficacy assessment(s)
Type: disease severity (percentage foliar coverage), percent infected flowers, percent unmarketable flowers
Time: every week starting from first treatment application date
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe)
Symptom(s) description
Symptoms on leaves begin as small, round, spots, that widen and coalesce, showing white mycelial and conidial growth on leaf surface. The disease causes slight twisting of the foliage sometimes. The leaves and stems, and sometimes the flowers, become distorted, growth is diminished, and chlorosis, yellowing and necrosis of leaves occurs. The white cover of the plant reduce the quality of cut flowers, thus often rejected and unacceptable.
Recommendations
Powdery mildew infection is more severe in dry day and cool night periods of the year
Extrapolation
Pathogens: none
Crops: ornamentals

Verification Protocol 18: Powdery mildew in mango

Date

September, 2011

Verification

Test organism

Powdery mildew (*Oidium mangiferae* Berthet)

Test crop

Mango (*Magnifera indica* L.)

Experimental unit

Mango trees

5 mango trees/plot

Inter-plot spacing- at least 20 meters

Design

Two non- replicated evaluation plots (treated and untreated)

Specific treatments

Recommended rate and frequency of the test fungicide would be compared with untreated control

Application timing

Crop: Before flowering, after flowering and after fruit set

The experiment will be carried out at least at three sites in one season. In case three locations or hot spots cannot be found, it will be carried out at one site.

Efficacy assessment (s)

Type:

Disease severity; recorded on the four marked panicles in each four directions (E,W,N,S) of each mango tree using 0-5 grade (0 = No disease; 1 = 1-20; 2 = 21-40; 3 = 41-60; 4 = 61-80; and 5 = 81-100% panicles covered by powdery mildew.

The percent of leaves and panicles should arrive at from the evaluation of 100 leaves and panicles from each treatment.

Yield; Number of fruit counted from each tree within each plot. Total number of fruit counted from each treatment and cultivars and converted in a hectare basis. All data should be subjected to analysis of variance and the means compared by Duncan's multiple range test

Phytotoxicity assessments

On a 0-3 score scale (0 = no; 1-few; 2 = moderate; and 3 = severe)

Symptoms description

10. Chlorosis/necrosis of foliage,
11. Damage and deformation of blossoms
12. Fruitlets and fruit, including color of fruit

Recommendation

- Mango Powdery mildew causes the most serious losses when flowering and growth flushes occur during dry, cool conditions

Extrapolation

No extrapolations for other diseases and crops

Verification Protocol 19: Coffee berry disease in coffee

Date

September, 2011

Verification

Test organism

Coffee berry disease (CBD) (Colletotrichum kahawae)

Test crop

Coffee (*Coffea arabica)*

Experimental unit

30-40 Coffee trees, (depending on availability)/Plot

Inter-plot spacing- at least 10 meters

Design

Two non-replicated evaluation plots (treated and untreated)

Specific treatments

Recommended rate and frequency of the test fungicide should be compared with untreated control

Application timing

Crop: 6 weeks after flowering

The experiment should be carried out at least at three sites in one season. In case three locations or hot spots cannot be found the experiment can be carried out at one site.

Efficacy assessment (s)

Type:

Berry count; counting the number of infected and healthy berries on three sample branches (each from top, middle and bottom canopy layers at different directions) on each of the six trees. Seven weeks after the first spray at three weeks interval.

Visual assessment; of disease severity- at peak CBD infection level, usually in mid-August.

Yield; Ripe cherry fresh weight in gram per tree -at final harvest

Phytotoxicity assessments

On a 0-3 scale (0=no, 1=few, 2=moderate, 3=severe)

Symptoms description

13. Premature Leaf fall
14. Premature berry drop
15. Leaf scorch
16. Crinkled leaf
17. Chlorotic types on leaves
18. Necrotic types on leaves

Recommendation

- CBD reaches its peak time in mid-August

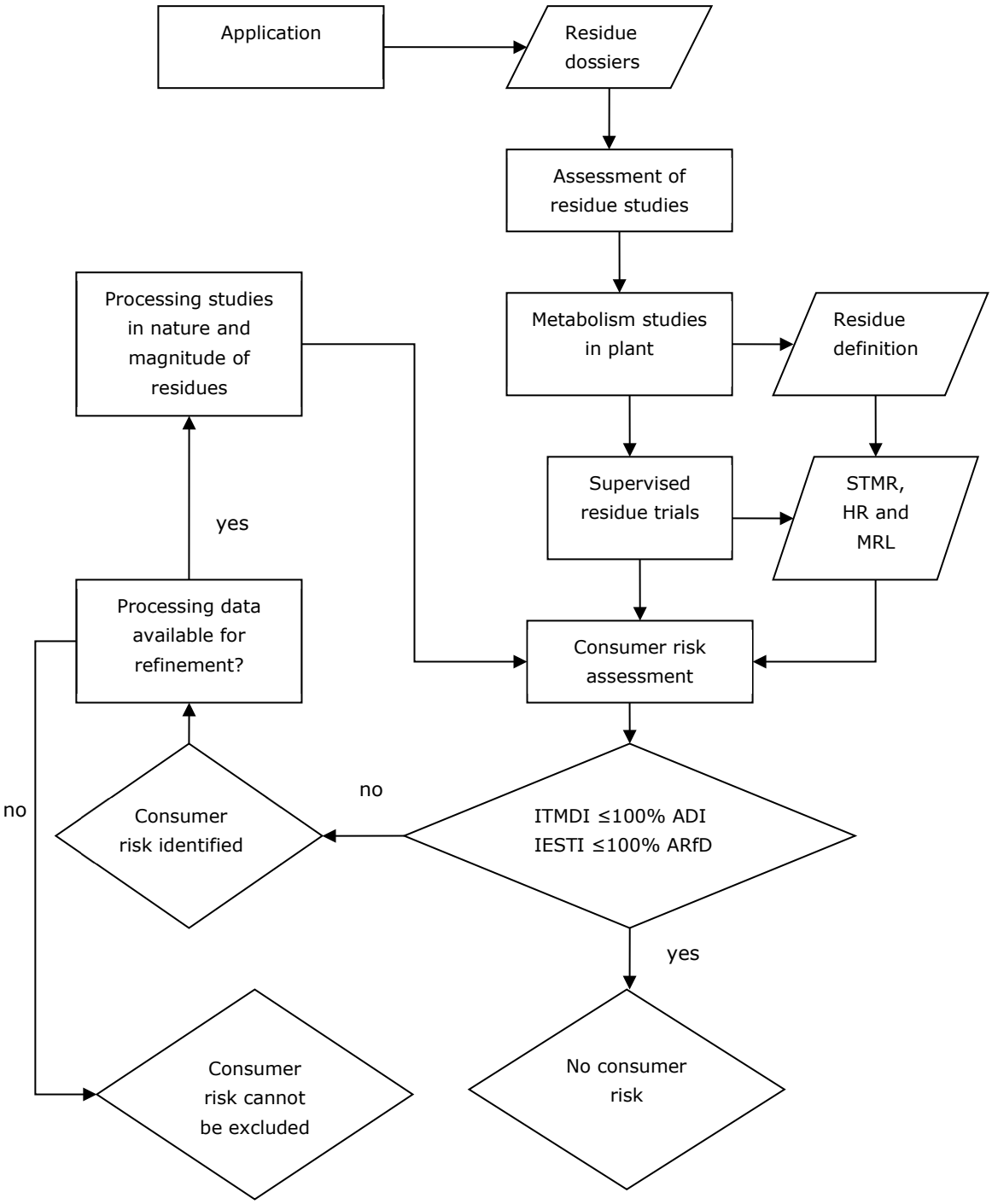
Extrapolation

No extrapolations for other diseases and crops

Verification Protocol 20: Seed borne diseases in wheat

Seed borne diseases in wheat
Date: August 22, 2011
Testing stage: Verification
Test organism(s): Seedborne diseases (e.g. *Fusarium, Helminthosporium* etc)
Test crop(s): Wheat (*Triticum* spp.)
Experimental unit
Gross: 10m x 10m
Net: 8m x 8m
Inter-row spacing: 0.2m
Inter-plot spacing: at least 0.5m
Design: Un-replicated single plot
Include untreated control, healthy seed control, and standard seed treatment product
Test it at three sites
Specific treatments
The effective dose of the product
Application time
Crop: seed treatment,
Efficacy assessment(s)
Type: seedling infection in the laboratory (4 replications and 100 seed per replication), and seedling diseases in the field
Time: at seedling, at dough, ripping stage
Crop: emergence percentage, crop stand in percent, seed yield, seed health
Phytotoxicity assessment(s)
On a 0 – 3 rating scale (0 = no, 1 = few, 2 = moderate, and 3 = severe) in two different tests (in germination test in the lab and at seedling stage in the field)
Symptom(s) description
Germination percentage, seedling infection, emergence, scab on the head during ripping, shriveling of seeds, seed infection test after harvest, seed yield
Recommendations
Primary seed infection and contamination determine disease development in the field. Hence, the experiment should include isolation of the pathogens, contamination of the seed to be used for efficacy test, testing in the lab and ultimately in the field
Extrapolation
Pathogens: Seedborne fungi (*Fusarium* spp., *Helminthosporium* spp., etc)
Crops: barley, triticale

Annex 3 Flowchart for residue assessment



Annex 4 Manuals for the consumer exposure spreadsheets

The very detailed manuals for the WHO Gems models 2006 can be found in the models themselves in the worksheet 'manual' and the 2009 FAO Manual, chapter 7.

Spreadsheet models: http://www.who.int/foodsafety/chem/acute_data/en/index1.html
2009 FAO
Manual: http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/FAO_manual2nded_Oct07.pdf

Please note:

- Enable macros. Without macros the model calculates properly, but an overview table cannot be generated.
- In Office 2007 and up, click the buttons on top of the screen to run the macros, for Office 97, choose 'tools' > macro >> macros
- Check Regional Settings (windows) or Regional and Language Options (Windows XP) or Clock, Language and Region (Windows Vista) for decimal and separator setting (see manuals for 'computer settings'
- For chronic intake:
  - use all the established and calculated MRLs, but only fill in the cells that corresponds with the commodities. When no MRL is present, leave the cell empty.
  - The EDI is the sum of the EDI of all commodities.
- For acute intake:
  - use only the commodities that are being evaluated and not all the established MRLs or already authorized uses in Ethiopia.
  - the HR or STMR can be used, depending on the commodity (raw, processed, bulk etc). See the manual in the spreadsheet for the different cases.
  - Only the highest IESTI value is selected, composed of one commodity. The rationale behind this is that the model considers large portions and that an individual will not eat all the crops in the intended use and its processed products and animal products at the level of the large portion which then also contain residues at the HR.
- Do not select and drag cells or cut and paste cells, otherwise the formulas in the worksheet become corrupt and the calculation does not run properly.

Annex 5 Data requirements for toxicology

Requirement		Remark
a. Reference values	ADI (mg/kg bw/d)	
	ARfD (mg/kg bw)	e.g. Guidance for the setting of an Acute Reference Dose (ARfD) [3]
	AOEL (mg/kg bw/d)	e.g. EU Guidance for the setting and application of Acceptable Operator Exposure Levels (AOELs). AOEL is used in the EU for risk assessments of pesticides [4]
b. Acute oral toxicity (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 401, 423, 425
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LD50 (mg/kg bw)	Rat is the preferred species
c. Acute dermal toxicity (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 402
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LD50 (mg/kg bw)	Rat is the preferred species
d. Acute inhalation toxicity (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 403, 436
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LC50 (mg/kg bw)	As the exposure time in the study is usually 4 or 6h, the LC50 should be expressed as mg/kg bw/4h or mg/kg bw/6h
e. Skin irritation (rabbit)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 404
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Classification skin irritation: yes/no	Indicate the classification of the skin irritation
f. Eye irritation (rabbit)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 405
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Classification eye irritation: yes/no	Indicate the classification of the eye
g. Skin sensitisation (guinea pig)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 406, 429, 442A/B
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Classification skin sensitisation: yes/no	Indicate the classification
h. Reproduction multi-generation study (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 415, 416, 443
	GLP: yes/no[2]	Indicate whether study was performed according

		to GLP.
	NOAELpar (mg/kg bw/d) NOAELdev (mg/kg bw/d) NOAELrepro (mg/kg bw/d)	NOAEL for parents, offspring and reproduction effects should be mentioned
i. Subchronic toxicity 90 day (rat or dog)	According to international guideline: yes/no Indicate guideline[1]	At least one study (in rats) should be provided; preferably 2 studies (in rats and dogs) are submitted. Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 408, 409
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	NOAEL (mg/kg bw/d)	
j. Chronic toxicity (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 452, 453
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	NOAEL (mg/kg/day)	
k. Carcinogenicity (life time) (rat or mouse)	According to international guideline: yes/no Indicate guideline[1]	At least one study (in rats) should be provided; preferably 2 studies (in rats and mice) are submitted. Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 451, 453
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	NOAEL (mg/kg/day) Carcinogenic: yes/no	
l. Neurotoxicity (specify species and duration)	According to international guideline: yes/no Indicate guideline[1]	Acute or short-term neurotoxicity studies may be required if there are indication for neurotoxicity in the other toxicity studies. Delayed neurotoxicity studies are required for insecticides with structures related to those known to cause delayed neurotoxicity, such as organophosphates. Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 418/419 (organophosphates), or 424
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	NOAEL (mg/kg bw/d)	
m. Teratogenicity (rat or rabbit)	According to international guideline: yes/no Indicate guideline[1]	At least one study should be provided; preferably 2 studies (in rats and rabbits) are submitted. Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 414
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	NOAELmat (mg/kg bw/d) NOAELdev (mg/kg bw/d) NOAELterato (mg/kg bw/d)	NOAEL for maternal, offspring and developmental effects should be mentioned
	Teratogenic: yes/no	Indicate classification for teratogenicity
n. Mutagenicity / Genotoxicity	According to international guideline: yes/no Indicate guideline[1]	In vitro for gene mutation and chromosomal damage. If any in-vitro tests indicative positive results, in-vivo genetic toxicity studies should also be carried out. Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 471-488
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Genotoxic: yes/no	Indicate classification for mutagenicity and/or genotoxicity

o. Metabolism (rat)	According to international guideline: yes/no Indicate guideline[1]	Provide the oral absorption value at the relevant dose level, i.e. around the lowest NO(A)EL used for setting of the AOEL Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 417
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Oral absorption (%)	Indicate% oral absorption
p. Other studies		Provide further information relevant to the toxicity profile of the product.

1 The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.

2 Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 6 Data requirements for residues

Requirement		Remark
a. Metabolism	According to international guideline: yes/no Indicate guideline[1] GLP: yes/no[2]	Indicate whether study was performed according to international guidelines and indicate which guideline e.g.: OECD Test No. 501: Metabolism in Crops Lundehn Appendix A (SANCO 7028/VI/95 rev 3) OPPTS Guideline 860.1300 Indicate whether study was performed according to GLP
b. Major metabolites/residue definition		Argumentation for the residue definition for (1) MRL setting and monitoring and (2) risk assessment If (2) is more extended than is (1) give conversion factor
c. Magnitude of residues	According to international guideline: yes/no Indicate guideline[1] GLP: yes/no[2]	Indicate whether study was performed according to international guidelines and indicate which guideline e.g.: OECD Test No. 509: Crop Field Trial Lundehn appendix B (SANCO 7029/VI/95 rev 5) Lundehn appendix D 9SANCO 7525/VI/95 rev 9) OPPTS Guideline 860.1500 Indicate the action and the persistence of the metabolites in the plant The residue level at the proposed critical GAP (dose, number of applications, interval, PHI) should be derived from the residue trials with the crop of interest (or a closely related crop for extrapolation) The objectives of magnitude of residue trials in plants shall be the following: to quantify the highest likely residue levels of all components of the different residue definitions in treated crops, at harvest or outloading from store, in accordance with the proposed GAP and GLP. Applicant to submit relevant JMPR reports for the intended use, in case a CXL was set for the relevant crop/active substance combination. Indicate whether study was performed according to GLP
d. Storage stability	According to international guideline: yes/no Indicate guideline[1] GLP: yes/no[2]	In case samples from studies in plants are not analysed within 30 days after sampling (stored frozen), trials to assess the stability of the active compounds and relevant residues needs to be submitted. To verify the stability of residues in sampled commodities during (frozen) storage. The duration and conditions of the studied storage must correspond with the maximum duration and storage conditions in the supervised residue trials and the metabolism studies. Indicate whether study was performed according to international guidelines and indicate which guideline e.g.: OECD Test No 506: Stability of Pesticide Residues in Stored Commodities Lundehn appendix H (SANCO 7032/VI/95 rev 5.) OPPTS 860.1380 Storage Stability Data Furthermore, indicate the matrix tested. Indicate whether study was performed according to GLP

e. MRL codex and/or other country together with their critical GAPs		Give the MRLs set for the crops of interest together with their respective GAPs. If the uses applied for have been covered by these GAPs these MRLs could be adopted. Codex Pesticides Residues in Food Online Database EU pesticides database USDA MRL database
f. Method of residue analysis	According to international guideline: yes/no Indicate guideline[1] GLP: yes/no[2]	A full description shall be submitted for methods of residues in food and drinking water in accordance with e.g. guidance document SANCO/825/00. or OPPTS Guideline 860.1340 (a)the determination of all components included in the monitoring residue definition in order to enable to determine compliance with established maximum residue levels (MRLs); they shall cover residues in or on food of plant origin; (b)the determination of all components included for monitoring purposes in the residue definitions for water As far as practicable these methods shall employ the simplest approach, involve the minimum cost, and require commonly available equipment. The specificity of the methods shall be determined and reported. It shall enable all components included in the monitoring residue definition to be determined. Validated confirmatory methods shall be submitted if appropriate. The linearity, recovery and precision (repeatability) of methods shall be determined and reported. Data shall be generated at the limit of quantification (LOQ) and either the likely residue levels or ten times the LOQ. The LOQ shall be determined and reported for each component included in the monitoring residue definition. Indicate whether study was performed according to GLP
g. additional information for refinement of intake	According to international guideline: yes/no Indicate guideline[1] GLP: yes/no[2]	Additional information can be provided when the first tier risk assessment results in an exceeded ADI and/or ARfD. (NEDI>100% ADI, IESTI>100%ARfD. For refinement of intake assessment, processing data are generally the most appropriate. Additional information can be provided when the first tier risk assessment results in an exceeded ADI and/or ARfD. For refinement of intake assessment, generally processing data are the most appropriate. e.g. OECD Test No. 507 and No 508 Lundehn Appendix E (7035/VI/95 rev. 5) OPPTS 860.150

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 7 Data requirements for the formulated product

Requirement		Remark
a. Acute oral toxicity (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD 401, 423, 425
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LD50 (mg/kg bw)	Rat is the preferred species
b. Acute dermal toxicity (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD 402
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LD50 (mg/kg bw)	Rat is the preferred species
c. Acute inhalation toxicity (rat)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD 403, 436
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LC50 (mg/kg bw)	As the exposure time in the study is usually 4 or 6h, the LC50 should be expressed as mg/kg bw/4h or mg/kg bw/6h
d. Skin irritation (rabbit)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 404 The skin irritancy of the active substance must be determined except where it is likely, as indicated in the test guideline, that severe skin effects may be produced or that effects can be excluded.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Classification skin irritation[3]:	Indicate the classification
e. Eye irritation (rabbit)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 405 Eye irritation tests must be conducted except where it is likely, as indicated in the test guideline, that severe effects on the eyes may be produced.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Classification eye irritation[3]:	Indicate the classification
f. Skin sensitisation (guinea pig)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 406, 429, 442A/B The test must always be carried out except where the substance is a known sensitizer.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Classification skin sensitisation[3]:	Indicate the classification
g. WHO classification		WHO classification is revised in 2009 (see WHO, 2010)
h. Other toxicological studies		Provide further information relevant to the mammalian toxicity profile of the product.
h1.Dermal absorption study	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline E.g. OECD 427, 428 The test may be performed, or default values to be used. The representative product should be tested.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.

	Value for concentrate Value for spray dilution	Values for dermal absorption for the concentrated product and for the spray dilution should be provided: either by using the default value of 100% or value based on the study data.

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.
3For guidance on classification and labelling for irritation/sensitisation, the GHS rules are used. See below.

Annex 8 Data requirements for the risk assessment of ground and surface water used for drinking water purposes or for the protection of the aquatic ecosystem

Data requirements for the active ingredient with regard to surface water risk assessment, fate in surface water.

Requirement		Remark
Behaviour, ways of degradation, degradation products in water.		
Hydrolytic degradation of the active substance and major metabolites	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 111: Hydrolysis as a Function of pH The hydrolysis rate of purified active substances shall be determined and reported at 20°C or 25°C. Studies on hydrolytic degradation shall also be performed for degradation and reaction products which account at any time for more than 10% of the amount of active substance added in the hydrolysis study, unless sufficient information on their degradation is available from the test performed with the active substance. No additional hydrolysis information on degradates shall be required if they are considered to be stable in water.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Degradation pathways DT50 active substance and major metabolites	Describe the pathways
Photochemical degradation of the active substance and major metabolites	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 316: Phototransformation of Chemicals in Water - Direct Photolysis For compounds with a molar (decadic) absorption coefficient (ε) > 10 L mol^{-1} cm^{-1} at a wavelength (λ) ≥ 295 nm direct phototransformation of purified active substances shall be determined and reported unless the applicant shows that contamination of surface water will not occur. Studies on direct photochemical degradation shall also be performed for metabolites, breakdown and reaction products which account at any time for more than 10% of the amount of active substance added in the photolysis study, unless sufficient information on their degradation is available from the test performed with the active substance. No additional photolysis information on degradates shall be required if they are considered to be stable under photolytic conditions.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Degradation pathways DT50 active substance and major metabolites	Describe the pathways
Water/sediment study	According to international guideline: yes/no	Indicate whether study was performed according to international guidelines and indicate which guideline.

	Indicate guideline[1]	E.g. OECD Test Guideline 308: Aerobic and Anaerobic Transformation in Aquatic Sediment Systems The degradation pathway or pathways shall be reported for two water/sediment systems. The two sediments selected shall differ with respect to organic carbon content and texture, and where relevant, with respect to pH. The duration of the study shall be at least 100 days. It shall be longer where this is necessary to establish the degradation pathway and water/sediment distribution pattern of the active substance and its metabolites, breakdown and reaction products. If more than 90% of the active substance is degraded before the period of 100 days expires, the test duration may be shorter. The degradation pattern of potentially relevant metabolites occurring within the water sediment study shall be established either by extension of the study for the active substance, or by conducting a separate study for potentially relevant metabolites.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Degradation pathways DT50 active substance and major metabolites	Describe the pathways

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Data requirements for the active ingredient with regard to ground water risk assessment, fate in soil

Requirement		Remark
Behaviour, ways of degradation, degradation products in soil		Remark
Aerobic route and route of degradation active substance	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 307: Aerobic and anaerobic transformation in soil. Studies on the degradation pathway or pathways shall be reported for at least one representative soil. Oxygen levels shall be maintained at levels that do not restrict micro-organisms ability to metabolise aerobically. If there is reason to believe that the route of degradation is dependent on one or more properties of the soil, such as pH or clay content, the route of degradation shall be reported for at least one additional soil for which dependent properties are different. The duration of the study shall be at least 120 days, except where after a shorter period the levels of non-extractable residues and CO_2 are such that they can be extrapolated in a reliable way to 100 days. It shall be longer where this is necessary to establish the degradation pathway of the active substance and its metabolites, breakdown or reaction products. Studies on the rate of aerobic degradation of the active substance shall be reported for three representative soils in addition to the one required to investigate the route of degradation. Reliable DegT50 and 90 values shall be available for a minimum of four different representative soils.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Pathways of aerobic degradation DegT50 and DegT90 of the active substance	Describe the pathways
Anaerobic route and rate of degradation active substance	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 307: Aerobic and anaerobic transformation in soil. An anaerobic degradation study shall be submitted unless the applicant shows that exposure of the plant protection products containing the active substance to anaerobic conditions is unlikely to occur for the intended uses.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Pathways of anaerobic degradation DegT50 and DegT90 of the active substance	Describe the pathways
Soil photolysis	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. SETAC 1995 – Procedures for assessing the environmental fate and ecotoxicity of pesticides. A soil photolysis study shall be submitted unless the applicant shows that deposition of the active substance on the soil surface is unlikely to occur or that photolysis is not expected to contribute significantly to the degradation of the active substance in soil for example due to low light absorbance of the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Pathways of degradation by soil photolysis	Describe the pathways
Aerobic degradation rate of major metabolites	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 307: Aerobic and anaerobic transformation in soil. Aerobic degradation, DegT50 and 90 values from a minimum of three different soils shall be provided for

		metabolites, breakdown and reaction products which occur in soil if one of the following conditions is fulfilled: A) they account for more than 10% of the amount of active substance added at any time during the studies; B) they account for more than 5% of the amount of active substance added in at least two sequential measurements; C) the maximum of formation is not reached at the end of the study but accounts for at least 5% of the active substance at the final measurement; Studies shall not be required where three DegT50 and 90 values can be reliably determined from the results of the degradation studies where the active substance is applied as test substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	DegT50 and DegT90 major metabolites	
Adsorption and desorption of the active substance	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 106: Adsorption - Desorption Using a Batch Equilibrium Method OECD Test Guideline 121: Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC) Studies on the active substance shall be reported for at least four representative soils.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Koc or Kom	
Adsorption and desorption of major metabolites	According to international guideline: yes/no Indicate guideline[1]	
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Koc or Kom	

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 9 An overview of the required data on toxicity towards aquatic organisms

Active Ingredient

Requirement		Remark
Acute toxicity to fish (1 species; preferably rainbow trout)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 203: Fish, Acute Toxicity Test
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LC_{50} (mg as/L)	
Chronic toxicity to fish (1 species; preferably rainbow trout)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 210: Fish, Early-Life Stage Toxicity Test A long-term or chronic toxicity study on fish shall be provided for all active substances where exposure of surface water is likely and the substance is deemed to be stable in water, that is to say there is less than 90% loss of the original substance over 24 hours via hydrolysis. A fish early life stage study shall be provided in these circumstances.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	NOEC reproduction (mg as/L)	
Bioconcentration in fish	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 305, Bioconcentration: Flow-through fish test The bioconcentration of the substance, shall be assessed where: the log Pow is greater than 3 or there are other indications of bioconcentration; and the substance is considered stable, that is to say there is less than 90% loss of the original substance over 24 hours via hydrolysis.
	BCF value	Bioconcentration factors shall be expressed as a function of both total wet weight and of the lipid content of the fish.
Acute toxicity to Daphnia	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 202: Daphnia sp. Acute Immobilisation Test A test shall be provided on the 24 and 48-hour acute toxicity of the active substance to *Daphnia magna*, expressed as the median effective concentration (EC_{50}) for immobilisation, and where possible, the highest concentration causing no immobilisation.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	EC50 (mg as/L)	
Acute toxicity to an additional aquatic invertebrate species (e.g. Chironomid larvae or Mysidopsis bahia)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. US EPA OPPTS 850.1035 Mysid Acute Toxicity Test For active substances with an insecticidal mode of action or which show insecticidal activity a second species shall be tested, for example Chironomid larvae or Mysid shrimps (Americamysis bahia).
	GLP: yes/no[2]	Indicate whether study was performed according to GLP

	EC50 (mg/L)	
Chronic toxicity to Daphnia	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 211: Daphnia magna Reproduction Test A long-term or chronic toxicity study on aquatic invertebrates shall be provided for all active substances where exposure of surface water is likely and the substance is deemed to be stable in water, that is to say there is less than 90% loss of the original substance over 24 hours via hydrolysis.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	NOEC (mg as/L)	
Chronic toxicity to an additional aquatic invertebrate species (e.g. Chironomid larvae)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. US EPA OPPTS 850.1350 Mysid Chronic Toxicity Test or OECD Test Guideline 219: Sediment-Water Chironomid Toxicity Using Spiked Water A chronic toxicity study shall be submitted on one aquatic invertebrate species. If acute tests have been conducted on two aquatic invertebrate species the acute endpoints shall be taken into account in order to determine the appropriate species to be tested in the chronic toxicity study. If the active substance is an insect growth regulator, an additional study on chronic toxicity shall be carried out using relevant non-crustacean species such as Chironomus spp.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	NOEC (mg as/L)	
Effects on algae	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 201: Algae growth inhibition test Testing shall be carried out on one green alga (such as Pseudokirchneriella subcapitata, synonym Selenastrum capricornutum). For active substances that exhibit herbicidal activity a test on a second species from a different taxonomic group shall be performed such as a diatom, for example Navicula pelliculosa.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	EC50 (mg as/L) NOEC (mg as/L)	
Effects on aquatic macrophytes	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 221: Lemna sp. Growth Inhibition Test ASTM E1913-04: Standard Guide for Conducting Static, Axenic, 14-Day Phytotoxicity Tests in Test Tubes with the Submersed Aquatic Macrophyte, Myriophyllum sibiricum Komarov Development of a proposed test method for the rooted aquatic macrophyte Myriophyllum sp. In: Maltby L, Arnold D, Arts G, Davies J, Heimbach F, Pickl C, Poulsen V. (2010). Aquatic Macrophyte Risk Assessment for pesticides. SETAC Press & CRC Press, Taylor & -Francis Group, Boca Raton, London, New York., p. 46-56. Davies, et al., 2003. Pest management Science, Vol 59, Issue 2, 231-237. A laboratory test with Lemna species shall be performed for herbicides and plant growth regulators. Additional aquatic macrophyte species tests may be

		undertaken on a dicotyledonous species, such as Myriophyllum spicatum, Myriophyllum aquaticum or a monocotyledonous species, such as aquatic grass Glyceria maxima, as appropriate. The need to perform such studies shall be discussed with the national competent authorities.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	EC50 (mg as/L) NOEC (mg as/L)	

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Formulated product

Requirement		Remark
Effects on aquatic organisms	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding questions for the active substance. Possible effects on aquatic species (fish, aquatic invertebrates, algae and in the case of herbicides and plant growth regulators also aquatic macrophytes) shall be investigated except where the possibility that aquatic species will be exposed can be ruled out. Testing shall be performed where: the acute toxicity of the plant protection product cannot be predicted on the basis of the data for the active substance; or the intended use includes direct application on water; extrapolation on the basis of available data for a similar plant protection product is not possible. However, where the available information permits to conclude that one of these groups is clearly more sensitive, tests on only the relevant group shall be performed. If the plant protection product contains two or more active substances, and the most sensitive taxonomic groups for the individual active substances are not the same, testing on all three/four aquatic groups, that is to say fish, aquatic invertebrates, algae and, where relevant, macrophytes, shall be required. Other remarks: see corresponding questions for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	L(E)C50 (mg/L)	

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 10 Data requirements for birds

Active ingredient

Requirement		Remark
Acute oral toxicity to birds (1 species, preferably Bobwhite quail)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline No 223: Avian acute oral toxicity study or US EPA OPPTS 850.2100: Avian oral toxicity test The highest dose used in tests shall not exceed 2000 mg substance/kg body weight, however, depending on the expected exposure levels in the field following the intended use of the compound, higher doses may be required.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LD50 (mg as/kg bw) NOEL (mg as/kg bw)	
Chronic toxicity to birds (1 species, preferably Bobwhite quail)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 206: Avian Reproduction Test or US EPA OPPTS 850.2300: Avian Reproduction Test The sub-chronic and reproductive toxicity of the active substance to birds shall be investigated, unless the applicant shows that exposure of adults, or exposure of nest sites during the breeding season is unlikely to occur. Such a justification shall be supported by information showing that no exposure or delayed effects will occur during the breeding season.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	NOEL reproduction (mg as/kg bw/d)	

1 The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.

2 Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Formulated product

Requirement		Remark
i. Acute oral toxicity to birds	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding question for the active substance. The acute oral toxicity of the plant protection product shall be investigated if toxicity cannot be predicted on the basis of the data for the active substance, or where results from mammalian testing give evidence of higher toxicity of the plant protection product compared to the active substance, unless the applicant shows that it is not likely that birds are exposed to the plant protection product itself. Other remarks: see corresponding question for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LD50 (mg/kg bw)	

Annex 11 Data requirements for risk assessment to bees

Active ingredient

Requirement		Remark
Acute toxicity to bees (acute oral as well as acute contact toxicity)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. EPPO standard PP 1/170 (4): Side-effects on honeybees OECD Test Guideline 213: Honeybees, Acute Oral Toxicity Test OECD Test Guideline 214: Honeybees, Acute Contact Toxicity Test
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	Oral LD_{50} (ug as/bee) Oral NOEC (ug as/bee) Contact LD_{50} (ug as/bee) Contact NOEC (ug as/bee)	
Bee brood study	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. Aupinel et al (2007): A new larval in vitro rearing method to test effects of pesticides on honey bee brood. *Redia* XC: 87-90 Oomen PA, de Ruijter A and van der Steen J, 1992. Method for honeybee brood feeding tests with insect growth - regulating insecticides. Bulletin OEPP/EPPO Bulletin 22, 613-616. A bee brood study shall be conducted to determine effects on honeybee development and brood activity. The bee brood study shall provide sufficient information to evaluate possible risks from the active substance on honeybee larvae. The test shall be carried out for active substances for which sub-lethal effects on growth or development cannot be excluded, unless the applicant shows that it is not possible that honeybee brood will be exposed to the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	NOEC (mg as/kg food)	

1. The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2. Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Formulated product

Requirement		Remark
k. Effects on bees	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding questions for the active substance. Testing shall be required if: the plant protection product contains more than one active substance; the toxicity of a plant protection product cannot be reliably predicted to be either the same or lower than the active substance. Other remarks: see corresponding questions for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	Oral LD_{50} (ug as/bee) Oral NOEC (ug as/bee) Contact LD_{50} (ug as/bee) Contact NOEC (ug as/bee) NOEC (mg/kg or g as/ha)	Oral and contact LD50 and NOEC values are endpoints from acute oral and contact toxicity studies with bees. NOEC values could be from bee brood test or cage, tunnel and field tests with bees.

1 The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.

2 Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 12 Data requirements for non-target arthropods

Active ingredient

Requirement		Remark
Effects on non-target arthropods other than bees (*Aphidius rhopalosiphi* and *Typhlodromus pyri*)	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. M.P. Candolfi, S. Blümel, R. Forster et al. (2000): Guidelines to evaluate side-effects of plant protection products to non-target arthropods. IOBC, BART and EPPO Joint Initiative. ISBN: 92-9067-129-7. Guidance Document on Regulatory Testing and Risk Assessment Procedures for Plant Protection Products With Non-Target Arthropods: From the Escort 2 Workshop (European Standard Characteristics of Non-Target Arthropod Regulatory Testing) ISBN 1-880611-52-x.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	LR_{50} A. rhopalosiphi (g as/ha) NOER A. rhopalosiphi (g as/ha) LR_{50} T. pyri (g as/ha) NOEC T. pyri (g as/ha)	

1 The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2 Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Formulated product

Requirement		Remark
I. Effects on non-target arthropods other than bees (*Aphidius rhopalosiphi* and *Typhlodromus pyri*)	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding questions for the active substance. Testing shall be required if: the plant protection product contains more than one active substance; the toxicity of a plant protection product cannot be reliably predicted to be either the same or lower than the active substance. Other remarks: see corresponding questions for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LR_{50} A. rhopalosiphi (g as/ha) NOER A. rhopalosiphi (g as/ha) LR_{50} T. pyri (g as/ha) NOEC T. pyri (g as/ha)	LR50 and NOER values for the 2 standard organisms are endpoints from (extended) lab studies. If there is a risk (semi-)field studies may be necessary.

1 *The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.*
2 *Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.*

Annex 13 Data requirements for soil macro-organisms

Active ingredient

Requirement		Remark
Acute toxicity to earthworms	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline207, Earthworm, acute toxicity test
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	NOEC (mg as/kg soil)	
Chronic toxicity to earthworms	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 222: Earthworm Reproduction Test (Eisenia fetida/Eisenia andrei)
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	NOEC (mg as/kg soil)	

1 The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2 Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Formulated product

Requirement		Remark
Acute toxicity to earthworms	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding question for the active substance. Testing shall be required if: the plant protection product contains more than one active substance; the toxicity of a plant protection product cannot be reliably predicted to be either the same or lower than the active substance. Other remarks: see corresponding question for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	LC50 (mg as/kg soil)	
Chronic toxicity to earthworms	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding question for the active substance. Testing shall be required if: the plant protection product contains more than one active substance; the toxicity of a plant protection product cannot be reliably predicted to be either the same or lower than the active substance. Other remarks: see corresponding question for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	NOEC (mg as/kg soil)	

1 The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2 Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 14 Data requirements for soil micro-organisms

Active ingredient

Requirement		Remark
Effects on soil nitrogen transformation	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. OECD Test Guideline 216: Soil Microorganisms: Nitrogen Transformation Test Soils used shall be freshly sampled agricultural soils. The sites from which soil is taken shall not have been treated during the previous two years with any substance that could substantially alter the diversity and levels of microbial populations present, other than in a transitory manner.

Formulated product

Requirement		Remark
Effects on soil nitrogen transformation	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding question for the active substance. The effects of plant protection products on soil microbial function shall be investigated if the toxicity of the plant protection product cannot be predicted on the basis of data for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 15 Data requirements for non-target terrestrial plants

Active ingredient

Requirement		Remark
Effects of terrestrial non-target higher plants	According to international guideline: yes/no Indicate guideline[1]	Indicate whether study was performed according to international guidelines and indicate which guideline. E.g. Seedling emergence and seedling growth: OECD Test Guideline 208: Terrestrial Plant Test: Seedling Emergence and Seedling Growth Test Terrestrial plant vegetative vigour testing: OECD Test Guideline 227: Terrestrial Plant Test: Vegetative Vigour Test For active substances that exhibit herbicidal or plant growth regulator activity, vegetative vigour and seedling emergence concentration/response tests shall be provided for at least 6 species representing families for which herbicidal/plant growth regulatory action has been found. Where, from the mode of action, it can be clearly established that either seedling emergence or vegetative vigour is effected, only the relevant study shall be conducted.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP
	ER50 (g as/ha)	

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Formulated product

Requirement		Remark
Effects of terrestrial non-target higher plants	According to international guideline: yes/no Indicate guideline[1]	Testing Guidelines: see corresponding question for the active substance. Studies of effects on non-target plants shall be required for herbicide and plant growth regulator plant protection products, when the risk cannot be reliably predicted on the basis of the active substance data Other remarks: see corresponding question for the active substance.
	GLP: yes/no[2]	Indicate whether study was performed according to GLP.
	ER50 (g as/ha)	

1The data should be based on internationally recognized testing guidelines and methods, such as those published by OECD or USEPA, among others.
2Data should be generated following the principles of good laboratory practice (GLP), whenever applicable. Experiments performed after 25 July 1993 must have been performed in accordance with GLP.

Annex 16 Example Format for a Table of Intended Uses, OECD GAP Form

SUMMARY OF GOOD AGRICULTURAL PRACTICES FOR PESTICIDE USES
(Application on agricultural and horticultural crops)

Address 1
Address 2
Address 3
Pesticide(s) (common name(s)) :
EEC, CIPAC and CCPR No(s). :
Trade name(s) :
Main uses e.g. insecticide, fungicide :
Applicant :

Date :
Page :
Country :

Use Pattern

1	2	3	4	5	6			7			8	9
Crop and / or situation	F G or I	Pest or group of pests controlled	Formulation Type	Conc. of a.i.	Application method, kind	growth stage	number (range)	Application rate per treatment kg a.i. / hectoliter	water l/ha	kg a.i./ha	PHI (days)	Remarks
(a)	(b)	(c)	(d - f)	(i)	(f - h)	(j)					(k)	(l)

Remarks:(a)In case of group of crops the Codex classification should be used
(b)Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c)e.g. biting and sucking insects, soil born insects, foliar fungi
(d)e.g. wettable powder (WP), emulsifiable concentration (EC), granule (GR)
(e)Use CIPAC/FAO Codes where appropriate
(f)All abbreviations used must be explained
(g)Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h)Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants
(i)g/kg or g/l
(j)Growth stage at last treatment
(k)PHI = Pre-harvest interval
(l)Remarks may include: Extent of use/economic importance/restrictions (e.g. feeding, grazing)/minimal intervals between applications; for seed treatments specify the dose in kg a.i. per kg seed and number of seeds per kg seed

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Alterra Wageningen UR is the research institute for our green living environment. We offer a combination of practical and scientific research in a multitude of disciplines related to the green world around us and the sustainable use of our living environment, such as flora and fauna, soil, water, the environment, geo-information and remote sensing, landscape and spatial planning, man and society.

The mission of Wageningen UR (University & Research centre) is 'To explore the potential of nature to improve the quality of life'. Within Wageningen UR, nine specialised research institutes of the DLO Foundation have joined forces with Wageningen University to help answer the most important questions in the domain of healthy food and living environment. With approximately 30 locations, 6,000 members of staff and 9,000 students, Wageningen UR is one of the leading organisations in its domain worldwide. The integral approach to problems and the cooperation between the various disciplines are at the heart of the unique Wageningen Approach.

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