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GUIDELINE DEVELOPED WITHIN THE STANDING COMMITTEE ON PLANT HEALTH WITH REGARD TO THE APPLICABILITY OF GOOD LABORATORY PRACTICE TO DATA REQUIREMENTS ACCORDING TO ANNEXES II, PART A, AND III, PART A, OF COUNCIL DIRECTIVE 91/414/EEC

INTRODUCTION

1. If GLP is mentioned in the first column all tests and analyses have to be performed in accordance with the principles laid down in Council Directive 87/18/EEC. This implies also where relevant the requirements defined in the OECD GLP Consensus Documents "THE APPLICATION OF THE GLP PRINCIPLES TO SHORT-TERM STUDIES", ENVIRONMENT MONOGRAPH NO. 73, 1993, and "THE APPLICATION OF THE PRINCIPLES OF GOOD LABORATORY PRACTICE TO FIELD STUDIES".
2. Where in the first column GLP* is mentioned the derogations of paragraph 2.2 of the introduction to Annex II and of paragraph 2.4 of Annex III of Council Directive 91/414/EEC, amended by Commission Directive 93/71/EEC and Commission Directive 95/35/EEC, apply.
3. For section 6 of Annex III (Efficacy) the provisions of points 2.2 and 2.3 of the introduction to Annex III of Council Directive 91/414/EEC, as amended by Commission Directive 93/71/EEC apply.

Generally the provisions of GLP have to be applied only where experimental data are generated.

This document gives guidance to the Member States in their requirements to applicants performing studies required under Council Directive 91/414/EEC.

ANNEX II

	1.1	Applicant (name, address, etc.)
	1.2	Manufacturer (name, address, including location of plant)
	1.3	Common name proposed or ISO-accepted, and synonyms
	1.4	Chemical name (IUPAC and CA nomenclature)
	1.5	Manufacturer's development code number(s)
	1.6	CAS, EEC and CIPAC numbers (if available)
	1.7	Molecular and structural formula, molecular mass
	1.8	Method of manufacture (synthesis pathway) of the active substance
	1.9	Specification of purity of the active substance in g/kg
	1.10	Identity of isomers, impurities and additives (e.g. stabilizers), together with the structural formula and the content expressed as g/kg
GLP	1.11	Analytical profile of batches
	2.1	Melting point and boiling point
GLP	2.1.1	Melting point
GLP	2.1.2	Boiling point
GLP	2.1.3	The temperature of decomposition or sublimation
GLP	2.2	Relative density
	2.3	Vapour pressure (in Pa), volatility (e.g. Henry's law constant)
GLP	2.3.1	Vapour pressure
GLP	2.3.2	Volatility
	2.4	Appearance (physical state, colour and odour; if known)
	2.4.1	Colour and physical state
	2.4.2	Odour
	2.5	Spectra (UV/VIS, IR, NMR, MS), molecular extinction at relevant wavelengths
GLP	2.5.1	Spectra of active substance
GLP	2.5.2	Spectra of impurities
GLP	2.6	Solubility in water including effect of pH (4 to 10) on solubility
	2.7	Solubility in organic solvents
GLP	2.8	Partition coefficient n-octanol/water including effect of pH (4 to 10)
	2.9	Stability in water, hydrolysis rate, photochemical degradation, quantum yield and identity of breakdown product(s), dissociation constant including effect of pH (4 to 9)
GLP	2.9.1	Hydrolysis rate
GLP	2.9.2	Direct phototransformation
GLP	2.9.3	Quantum yield of direct photodegradation in water
GLP	2.9.4	Dissociation constant(s) (pKa values)
GLP	2.10	Stability in, air, photochemical degradation, identity of breakdown product(s)
	2.11	Flammability including auto-flammability

GLP	2.11.1 Flammability
GLP	2.11.2 Auto-flammability
GLP	2.12 Flash point
GLP	2.13 Explosive properties
GLP	2.14 Surface tension
GLP	2.15 Oxidizing properties
	3.1 Function, e.g. fungicide, herbicide, insecticide, repellant, growth regulator
	3.2 Effects on harmful organisms, e.g. contact poison, inhalation poison, stomach poison, fungitoxic or fungistatic, etc., systemic or not in plants
	3.3 Field of use envisaged, e.g. field, protected crops, storage of plant products, home gardening
	3.4 Harmful organisms controlled and crops or products protected or treated
	3.5 Mode of action
	3.6 Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies
	3.7 Recommended methods and precautions concerning handling, storage, transport or fire
	3.8 Procedures for destruction or decontamination
	3.8.1 Controlled incineration
GLP	3.8.2 Others
	3.9 Emergency measures in case of an accident
	4.1 Analytical methods for the determination of pure active substance and, where appropriate, for relevant breakdown products, isomers and impurities of the active substance and additives (e.g. stabilizers) in the active substance as manufactured
	4.2 Analytical methods including recovery rates and the limits of determination for the determination of residues
	4.2.1 Residues in plants, plant products, foodstuffs, feedingstuffs
	4.2.2 Residues in soil
	4.2.3 Residues in water (including drinking water)
	4.2.4 Residues in air
	4.2.5 Residues in body fluids and tissues of animal and human

GLP	5.1 Studies on absorption, distribution, excretion and metabolism in mammals
	5.2 Acute toxicity
GLP	5.2.1 Oral
GLP	5.2.2 Percutaneous
GLP	5.2.3 Inhalation
GLP	5.2.4 Skin irritation
GLP	5.2.5 Eye irritation
GLP	5.2.6 Skin sensitization
	5.3 Short-term toxicity
GLP	5.3.1 Oral 28-day study
GLP	5.3.2 Oral 90-day study
GLP	5.3.3 Other routes

	5.4 Genotoxicity testing
GLP	5.4.1 In vitro studies
GLP	5.4.2 In vivo studies
GLP	5.4.3 In vivo studies in germ cells
GLP	5.5 Long term toxicity and carcinogenicity
	5.6 Reproductive toxicity
GLP	5.6.1 Multi-generation studies
GLP	5.6.2 Developmental toxicity studies
GLP	5.7 Delayed neurotoxicity studies
	5.8 Other toxicological studies
GLP	5.8.1 Toxicity studies of metabolites as referred to in the introduction point
GLP	5.8.2 Supplementary studies on the active substance
	5.9 Medical data
	5.9.1 Medical surveillance on manufacturing plant personnel
	5.9.2 Direct observation, e.g. clinical cases and poisoning incidents
	5.9.3 Observations on exposure of the general population and epidemiological studies if appropriate
	5.9.4 Diagnosis of poisoning (determination of active substance, metabolites), specific signs of poisoning, clinical tests
	5.9.5 Proposed treatment: first aid measures, antidotes, medical treatment
	5.9.6 Expected effects of poisoning
	5.10 Summary of mammalian toxicity and conclusion (including no observed adverse effect level (NOAEL), acceptable daily intake (ADI), acceptable operator exposure level (AOEL)) and maximum admissible concentration in water. Overall evaluation with regard to all toxicological data, and other information concerning the active substance

GLP	6.1 Metabolism, distribution and expression of residue in plants
GLP	6.2 Metabolism, distribution and expression of residue in livestock
GLP*	6.3 Residue trials
GLP	6.4 Livestock feeding studies
	6.5 Effects of industrial processing and/or household preparations
GLP	6.5.1 Effects on the nature of the residue
GLP	6.5.2 Effects on the residue levels
GLP*	6.6 Residues in succeeding crops
	6.7 Proposed maximum residue levels (MRLs) and justification of the acceptability of these residues.
	6.8 Proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses.
	6.9 Estimation of the potential and actual exposure through diet and other means
	6.10 Summary and evaluation of residue behaviour

	7.1 Fate and behaviour in the environment

	7.1.1 Route and rate of degradation
	7.1.1.1 Route of Degradation
GLP	7.1.1.1.1 Aerobic degradation
GLP	7.1.1.1.2 Supplementary studies
	7.1.1.2 Rate of degradation
GLP	7.1.1.2.1 Laboratory studies.
GLP	7.1.1.2.2 Field studies
GLP	7.1.2 Adsorption and desorption
	7.1.3 Mobility in the soil
GLP	7.1.3.1 Column leaching studies
GLP	7.1.3.2 Aged residue column leaching
GLP	7.1.3.3 Lysimeter Studies or Field leaching studies
	7.2 Fate and behaviour in water and air
	7.2.1 Route and rate of degradation in aquatic systems (as far as not covered by point 2.9)
GLP	7.2.1.1 Hydrolytic degradation
GLP	7.2.1.2 Photochemical degradation
	7.2.1.3 Biological degradation
GLP	7.2.1.3.1 Ready biodegradability
GLP	7.2.1.3.2 Water/sediment study
GLP	7.2.1.4 Degradation in the saturated zone
GLP	7.2.2 Rate and route of degradation in air (as far as not covered by point 2.10)
	7.3 Definition of the residue
	7.4 Monitoring data

	8.1 Effects on birds
GLP	8.1.1 Acute oral toxicity
GLP	8.1.2 Short-term dietary toxicity
GLP	8.1.3 Subchronic toxicity and reproduction
	8.2 Effects on aquatic organisms
GLP	8.2.1 Acute toxicity to fish
	8.2.2 Chronic toxicity to fish
GLP	8.2.2.1 Chronic toxicity test on juvenile fish
GLP	8.2.2.2 Fish early life stage toxicity test
GLP	8.2.2.3 Fish life cycle test
GLP	8.2.3 Bioconcentration in fish
GLP	8.2.4 Acute toxicity to aquatic invertebrates
GLP	8.2.5 Chronic toxicity to aquatic invertebrates
GLP	8.2.6 Effects on algal growth
GLP	8.2.7 Effects on sediment dwelling organisms
GLP	8.2.8 Aquatic plants
	8.3 Effects on arthropods
	8.3.1 Bees
GLP*	8.3.1.1 Acute toxicity
GLP*	8.3.1.2 Bee brood feeding test
GLP*	8.3.2 Other arthropods
	8.4 Effects on earthworms
GLP	8.4.1 Acute toxicity
GLP	8.4.2 Sublethal Effects
GLP	8.5 Effects on soil non-target micro organisms
	8.6 Effects on other non-target organisms (flora and fauna) believed to be at risk
GLP	8.7 Effects on biological methods for sewage treatment

	9 Summary and conclusions of points 7 and 8
	10 Proposals for labelling

ANNEX III

	1.1 Applicant (name and address, etc.)
	1.2 Manufacturer of the preparation and the active substance(s) (names and addresses, etc. including location of plants)
	1.3 Trade name or proposed trade name, and manufacturer's development code number of the preparation if appropriate
	1.4 Detailed quantitative and qualitative information on the composition of the preparation (active substance(s), and formulants).
	1.5 Physical state and nature of the preparation (emulsifiable concentrate, wettable powder, solution etc)
	1.6 Function (herbicide, insecticide, etc.)
	2.1 Appearance (colour and odour)
	2.2 Explosivity and oxidizing properties
	2.2.1 Explosive properties of preparations
GLP	2.2.2 Oxidizing properties of preparations
GLP	
	2.3 Flash point and other indications of flammability or
GLP	spontaneous ignition
	2.4 Acidity / alkalinity and if necessary pH value
	2.4.1 Acidity or alkalinity and the pH value
GLP	2.4.2 pH of a 1% aqueous dilution, emulsion or dispersion
GLP	of the preparation
	2.5 Viscosity and surface tension
	2.5.1 Kinematic viscosity of ULV prepararions
GLP	2.5.2 Viscosity for non newtonian liquids
GLP	2.5.3 Surface tension for liquid preparations
GLP	
	2.6 Relative density and bulk density
	2.6.1 Relative density of liquid preparations
GLP	2.6.2 Bulk (tap) density of preparations which are powders or granules
	2.7 Storage stability - stability and shelf-life: Effects of light, temperature and humidity on technical characteristics of the plant protection product
	2.7.1 Stability of the preparation after storage
GLP	**(GLP for chemical stability only if on the basis of theoretical considerations hazardous compounds may be formed during storage)**
	2.7.2 Additionally in the case of liquid preparations, the effect of low temperatures on stability
	2.7.3 The shelf life of the preparation at ambient temperature
	2.8.1 Wettability
	2.8.2 Persistent foaming
	2.8.3 Suspensibility and suspension stability
	2.8.4 Dilution stability
	2.8.5 Dry sieve test and wet sieve test
	2.8.6 Particle size distribution (dustable and wettable powders, granules), content of dust/fines (granules), attrition and friability (granules)
GLP	2.8.6.1 Particle size distribution
GLP	2.8.6.2 Dust content
	2.8.6.3 Friability and attrition

	2.8.7 Emulsifiability, Re-emulsifiability, emulsion stability 2.8.7.1 Emulsifiability, emulsion stability and re-emulsifiability 2.8.7.2 Stability of dilute emulsions and of preparations which are emulsions 2.8.8 Flowability, pourability (rinsability) and dustability 2.8.8.1 Flowability of granular preparations 2.8.8.2 Pourability (including rinsed residue) 2.8.8.3 Dustability of dustable powders 2.9 Physical and chemical compatibility with other products including plant protection products with which its use is to be authorized 2.9.1 Physical compatibility of tank mixes 2.9.2 Chemical compatibility of tank mixes 2.10 Adherence and distribution to seeds 2.11 Summary and evaluation of data presented under points 2.1 to 2.10 --- 3.1 Field of use 3.2 Effects on harmful organisms 3.3 Details of intended use 3.4 Application rate 3.5 Concentration of active substance in material used (e.g. in the diluted spray, baits or treated seed) 3.6 Method of application 3.7 Number and timing of applications and duration of protection 3.8 Necessary waiting periods or other precautions to avoid phytotoxic effects on succeeding crops 3.9 Proposed instructions for use --- 4.1 Packaging (type, materials, size etc.), compatibility of the preparation with proposed packaging materials. 4.1.1 Packaging 4.1.2 The suitability of the packaging, including closures 4.1.3 The resistance of the packaging material to its contents
GLP	4.2 Procedures for cleaning application equipment 4.3 Re-entry periods, necessary waiting periods or other precautions to protect man, livestock and the environment 4.3.1 Where relevant pre-harvest intervals, re-entry periods or withholding periods 4.3.2 Information on any specific agricul-tural, plant health or environmental conditions under which the prepara-tion may or may not be used must be provided. 4.4 Recommended methods and precautions concerning: handling, storage, transport or fire 4.5 Emergency measures in the case of an accident 4.6 Procedures for destruction or decontamination of the plant protection product and its packaging 4.6.1 Possibility of neutralization 4.6.2 Controlled incineration 4.6.3 Others --- 5.1Analytical methods for the determination of pure active substances in the plant protection product and, where appropriate, for relevant breakdown products, isomers and impurities of the active substance and

		additives (e.g. stabilizers) and formulants
	5.2	Analytical methods for the determination of residues

		6Efficacy data (see introduction point 3)

		7.1Acute toxicity
	7.1.1	Oral
	7.1.2	Percutaneous
GLP	7.1.3	Inhalation
GLP	7.1.4	Skin irritation
GLP	7.1.5	Eye irritation
GLP	7.1.6	Skin sensitization
GLP	7.1.7	Supplementary studies for combinations of plant
GLP		protection products
GLP		
	7.2	Data on exposure
	7.2.1	Operator exposure
	7.2.1.1	Estimation of operator exposure
	7.2.1.2	Measurement of operator exposure
	7.2.2	Bystander exposure
GLP	7.2.3	Worker Exposure
GLP	7.2.3.1	Estimation of worker exposure
	7.2.3.2	Measurement of worker exposure
GLP	7.3	Dermal absorption
GLP	7.4	Available toxicological data relating to non-active substances

GLP*	8.1	Residue trials
GLP	8.2	Livestock feeding studies
GLP*	8.3	Residues in succeeding crops
	8.4	Proposed maximum residue levels (MRLs) and justification of the acceptability of these residues.
	8.5	Proposed pre-harvest intervals for envisaged uses, or withholding periods or storage periods, in the case of post-harvest uses.
	8.6	Estimation of the potential and actual exposure through diet and other means
	8.7	Summary and evaluation of residue behaviour

	9.1	Fate and behaviour in the environment
	9.1.1	Rate of Degradation in Soil
GLP	9.1.1.1	Laboratory studies
GLP	9.1.1.2	Field studies
	9.1.2	Mobility in the Soil
GLP	9.1.2.1	Laboratory studies
GLP	9.1.2.2	Lysimeter Studies or Field leaching studies
	9.1.3	Estimation of expected concentrations in soil
	9.2	Fate and behaviour in water
	9.2.1	Estimation of concentrations in Groundwater
	9.2.2	Impact on water treatment procedures
GLP	9.2.3	Estimation of concentrations in Surface Water
	9.3	Fate and behaviour in air
GLP		---
	10.1	Effects on birds
	10.1.1	Acute oral toxicity
GLP	10.1.2	Supervised cage or field trials
GLP	10.1.3	Acceptance of bait, granules, or treated seeds by

GLP		birds
	10.1.4	Effects of secondary poisoning.
GLP		
	10.2	Effects on aquatic organisms
	10.2.1	Acute toxicity to fish,aquatic invertebrates or
GLP		effects on algal growth.
	10.2.2	Microcosm or Mesocom study
GLP	10.2.3	Residue data in fish
GLP	10.2.4	Additional studies
GLP		
	10.3	Effects on terrestrial vertebrates other than birds
GLP		
	10.4	Effects on bees
	10.4.1	Acute oral and contact toxicity
GLP*	10.4.2	Residue test
GLP*	10.4.3	Cage Tests
GLP*	10.4.4	Field tests
GLP*	10.4.5	Tunnel tests
GLP*		
	10.5	Effects on arthropods other than bees
	10.5.1	Laboratory, extended laboratory and semi-field tests
GLP*	10.5.2	Field tests
GLP*		
	10.6	Effects on earthworms and other soil non-target macro-organisms, believed to be at risk.
	10.6.1	Effects on earthworms
GLP	10.6.1.1	Acute toxicity tests
GLP	10.6.1.2	Tests for sublethal effects
GLP	10.6.1.3	Field studies
GLP	10.6.2	Effects on other soil non-target macro-organisms
	10.7	Effects on soil non-target micro-organisms
GLP	10.7.1	Laboratory Testing
GLP	10.7.2	Additional Testing
	10.8	Available data from biological primary screening in summary form
	11.	SUMMARY AND EVALUATION OF SECTIONS 9 AND 10
	12.	Further Information