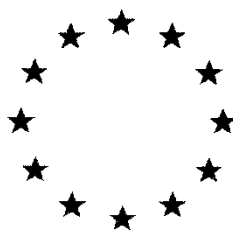


European Commission



**Draft Assessment Report prepared according to the Commission
Regulation (EU) N° 1107/2009**

XDE-729 Methyl (Halauxifen-methyl) Volume 3 – Appendices

**Rapporteur Member State: United Kingdom
Co-Rapporteur Member State: France**

Version History

When	What
2013-12-19	Initial DAR

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

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WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

APPENDIX 1: MATERIAL SAFETY DATA SHEET FOR THE ACTIVE SUBSTANCE.

**Safety Data Sheet**

Dow AgroSciences Limited
Safety Data Sheet according to Reg. (EC) N. 453/2010

Product Name: XDE-729 Methyl Technical Herbicide**Revision Date:** 2012/09/12**Print Date:** 12 Sep 2012

Dow AgroSciences Limited encourages and expects you to read and understand the entire (M)SDS, as there is important information throughout the document. We expect you to follow the precautions identified in this document unless your use conditions would necessitate other appropriate methods or actions.

Section 1. Identification of the substance/preparation and of the company/undertaking**1.1 Product identifiers****Product Name**

XDE-729 Methyl Technical Herbicide

Chemical Name: Methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate**CAS-No.** 943831-98-9**1.2 Relevant identified uses of the substance or mixture and uses advised against****Identified uses**

Plant Protection Product active substance

1.3 Details of the supplier of the safety data sheet**COMPANY IDENTIFICATION**

Dow AgroSciences Limited
A Subsidiary of The Dow Chemical Company
Latchmore Court, Brand Street
SG5 1NH Hitchin
United Kingdom

SDSQuestion@dow.com**1.4 EMERGENCY TELEPHONE NUMBER****24-Hour Emergency Contact:**

0031 115 694 982

Local Emergency Contact:

00 31 115 69 4982

Section 2. Hazards Identification**2.1 Classification of the substance or mixture****Classification - REGULATION (EC) No 1272/2008**

Acute aquatic toxicity	Category 1	H400	Very toxic to aquatic life.
Chronic aquatic toxicity	Category 1	H410	Very toxic to aquatic life with long lasting effects.

Classification according to EU Directives 67/548/EEC or 1999/45/EC

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Product Name: XDE-729 Methyl Technical Herbicide **Revision Date:** 2012/08/12

N R50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

2.2 Label elements**Labelling - REGULATION (EC) No 1272/2008****Hazard pictograms****Hazard statements:****H410** Very toxic to aquatic life with long lasting effects.**Precautionary Statements:****P273** Avoid release to the environment.**P501** Dispose of contents/container in accordance with applicable regulations.**EUH401** To avoid risks to human health and the environment, comply with the instructions for use.**2.3 Other Hazards**

No information available.

Section 3. Composition/information on ingredients**3.1 Substance**

This product is a substance.

CAS-No. / EC-No. / REACH No. Index	Amount	Component	Classification: REGULATION (EC) No 1272/2008
CAS-No. 943831-98-9 EC-No. Not available	— 95.9 %	Methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate	Aquatic Acute, 1, H400 Aquatic Chronic, 1, H410

CAS-No. / EC-No. / Index	Amount	Component	Classification: 67/548/EEC
CAS-No. 943831-98-9 EC-No. Not available	95.9 %	Methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate	N: R50/53

For the full text of the H-Statements mentioned in this Section, see Section 16.
See Section 16 for full text of R-phrases.

Product Name: XDE-729 Methyl Technical Herbicide

Revision Date: 2012/08/12

Section 4. First-aid measures

4.1 Description of first aid measures

General advice: If potential for exposure exists refer to Section 8 for specific personal protective equipment.

Inhalation: No emergency medical treatment necessary.

Skin Contact: Take off contaminated clothing. Rinse skin immediately with plenty of water for 15-20 minutes. Call a poison control center or doctor for treatment advice.

Eye Contact: Hold eyes open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eyes. Call a poison control center or doctor for treatment advice.

Ingestion: No emergency medical treatment necessary.

4.2 Most important symptoms and effects, both acute and delayed

Aside from the information found under Description of first aid measures (above) and Indication of immediate medical attention and special treatment needed (below), no additional symptoms and effects are anticipated.

4.3 Indication of immediate medical attention and special treatment needed

No specific antidote. Treatment of exposure should be directed at the control of symptoms and the clinical condition of the patient. Have the Safety Data Sheet, and if available, the product container or label with you when calling a poison control center or doctor, or going for treatment.

Section 5. Fire Fighting Measures

5.1 Extinguishing Media

Water. Dry chemical fire extinguishers. Carbon dioxide fire extinguishers.

5.2 Special hazards arising from the substance or mixture

Hazardous Combustion Products: During a fire, smoke may contain the original material in addition to combustion products of varying composition which may be toxic and/or irritating. Combustion products may include and are not limited to: Nitrogen oxides. Hydrogen cyanide. Hydrogen chloride. Carbon monoxide. Carbon dioxide.

Unusual Fire and Explosion Hazards: Do not permit dust to accumulate. When suspended in air dust can pose an explosion hazard. Minimize ignition sources. If dust layers are exposed to elevated temperatures, spontaneous combustion may occur.

5.3 Advice for firefighters

Fire Fighting Procedures: Keep people away. Isolate fire and deny unnecessary entry. Soak thoroughly with water to cool and prevent re-ignition. Cool surroundings with water to localize fire zone. Hand held dry chemical or carbon dioxide extinguishers may be used for small fires. Dust explosion hazard may result from forceful application of fire extinguishing agents. Contain fire water run-off if possible. Fire water run-off, if not contained, may cause environmental damage. Review the "Accidental Release Measures" and the "Ecological Information" sections of this (M)SDS.

Special Protective Equipment for Firefighters: Wear positive-pressure self-contained breathing apparatus (SCBA) and protective fire fighting clothing (includes fire fighting helmet, coat, trousers, boots, and gloves). If protective equipment is not available or not used, fight fire from a protected location or safe distance.

Section 6. Accidental Release Measures

6.1 Personal precautions, protective equipment and emergency procedures: Spilled material may cause a slipping hazard. Use appropriate safety equipment. For additional information, refer to Section 8, Exposure Controls and Personal Protection.

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6.2 Environmental precautions: Prevent from entering into soil, ditches, sewers, waterways and/or groundwater. See Section 12, Ecological Information. Spills or discharge to natural waterways is likely to kill aquatic organisms.

6.3 Methods and materials for containment and cleaning up: Contain spilled material if possible. Small spills: Sweep up. Collect in suitable and properly labeled containers. Large spills: Contact Dow AgroSciences for clean-up assistance. See Section 13, Disposal Considerations, for additional information.

Section 7. Handling and Storage

7.1 Precautions for safe handling

Handling

General Handling: Keep out of reach of children. Keep away from heat, sparks and flame. Do not swallow. Avoid contact with eyes, skin, and clothing. Avoid breathing dust or mist. Wash thoroughly after handling. Use with adequate ventilation. Good housekeeping and controlling of dusts are necessary for safe handling of product. See Section 8, EXPOSURE CONTROLS AND PERSONAL PROTECTION.

7.2 Conditions for safe storage, including any incompatibilities

Storage

Store in a dry place. Store in original container. Do not store near food, foodstuffs, drugs or potable water supplies.

7.3 Specific end uses

For use as active substance in a plant protection product.

Section 8. Exposure Controls / Personal Protection

8.1 Control parameters

Exposure Limits

RECOMMENDATIONS IN THIS SECTION ARE FOR MANUFACTURING, COMMERCIAL BLENDING AND PACKAGING WORKERS. APPLICATORS AND HANDLERS SHOULD SEE THE PRODUCT LABEL FOR PROPER PERSONAL PROTECTIVE EQUIPMENT AND CLOTHING. None established

8.2 Exposure controls

Personal Protection

Eye/Face Protection: Use safety glasses (with side shields). Safety glasses (with side shields) should be consistent with EN 188 or equivalent.

Skin Protection: Wear clean, body-covering clothing.

Hand protection: Use gloves chemically resistant to this material when prolonged or frequently repeated contact could occur. Use chemical resistant gloves classified under Standard EN374: Protective gloves against chemicals and micro-organisms. Examples of preferred glove barrier materials include: Polyvinyl chloride ("PVC" or "vinyl"). Neoprene. Nitrile/butadiene rubber ("nitrile" or "NBR"). When prolonged or frequently repeated contact may occur, a glove is recommended to prevent contact with the solid material. NOTICE: The selection of a specific glove for a particular application and duration of use in a workplace should also take into account all relevant workplace factors such as, but not limited to: Other chemicals which may be handled, physical requirements (cut/puncture protection, dexterity, thermal protection), potential body reactions to glove materials, as well as the instructions/specifications provided by the glove supplier.

Respiratory Protection: Under intended handling conditions, no respiratory protection should be needed.

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Ingestion: Use good personal hygiene. Do not consume or store food in the work area. Wash hands before smoking or eating.

Engineering Controls

Ventilation: Use local exhaust ventilation, or other engineering controls to maintain airborne levels below exposure limit requirements or guidelines. If there are no applicable exposure limit requirements or guidelines, general ventilation should be sufficient for most operations.

Section 9. Physical and Chemical Properties**9.1 Information on basic physical and chemical properties****Appearance**

Physical State	Powder
Color	White
Odor	Mild
Odor Threshold	No test data available
pH	6.24 (@ 1 %) <i>pH Electrode</i>
Melting Point	145.5 °C <i>Differential Scanning Calorimetry (DSC)</i>
Freezing Point	Not applicable
Boiling Point (760 mmHg)	Not applicable.
Flash Point - Closed Cup	Not applicable
Evaporation Rate (Butyl Acetate = 1)	Not applicable
Flammability (solid, gas)	No
Flammable Limits In Air	Lower: Not applicable Upper: Not applicable
Vapor Pressure	Not volatile
Vapor Density (air = 1)	Not applicable
Specific Gravity (H₂O = 1)	1.5057 20 °C/4 °C
Solubility in water (by weight)	1.83 mg/l @ 20 °C <i>Column Elution</i> , 20°C, Unbuffered
Partition coefficient, n-octanol/water (log Pow)	3.78
Autoignition Temperature	Not applicable
Decomposition Temperature	221.08 °C
Kinematic Viscosity	Not applicable
Explosive properties	No
Oxidizing properties	No

9.2 Other information

Bulk Density	0.17 g/ml @ 25.2 °C
Henry's Law Constant (H)	1.22E-06 Pa·m ³ /mole.

Section 10. Stability and Reactivity**10.1 Reactivity**

No dangerous reaction known under conditions of normal use.

10.2 Chemical stability

Thermally stable at typical use temperatures.

10.3 Possibility of hazardous reactions

Polymerization will not occur.

10.4 Conditions to Avoid: Exposure to elevated temperatures can cause product to decompose.**10.5 Incompatible Materials:** None known.**10.6 Hazardous decomposition products**

Product Name: XDE-729 Methyl Technical Herbicide**Revision Date:** 2012/08/12

Decomposition products depend upon temperature, air supply and the presence of other materials.

Section 11. Toxicological Information**11.1 Information on toxicological effects****Acute Toxicity****Ingestion**

Very low toxicity if swallowed. Harmful effects not anticipated from swallowing small amounts.

LD50, rat, female > 5,000 mg/kg

Aspiration hazard

Based on physical properties, not likely to be an aspiration hazard.

Dermal

Prolonged skin contact is unlikely to result in absorption of harmful amounts.

LD50, rat, male and female > 5,000 mg/kg

Inhalation

No adverse effects are anticipated from inhalation. For respiratory irritation and narcotic effects: No relevant data found.

The LC50 has not been determined.

Eye damage/eye irritation

Essentially nonirritating to eyes.

Skin corrosion/irritation

Brief contact is essentially nonirritating to skin. Prolonged contact may cause skin irritation with local redness.

Sensitization**Skin**

Did not demonstrate the potential for contact allergy in mice.

Respiratory

No relevant data found.

Repeated Dose Toxicity

In animals, effects have been reported on the following organs: Kidney. Liver. Thyroid.

Chronic Toxicity and Carcinogenicity

For similar active ingredient(s). XDE-729. Did not cause cancer in laboratory animals.

Developmental Toxicity

Has been toxic to the fetus in laboratory animals at doses toxic to the mother. Did not cause birth defects in laboratory animals.

Reproductive Toxicity

For similar active ingredient(s). XDE-729. In animal studies, did not interfere with reproduction.

Genetic Toxicology

In vitro genetic toxicity studies were negative.

Section 12. Ecological Information**12.1 Toxicity**

Material is very toxic to aquatic organisms (LC50/EC50/IC50 below 1 mg/L in the most sensitive species). Material is practically non-toxic to birds on an acute basis (LD50 > 2000 mg/kg). Material is practically non-toxic to birds on a dietary basis (LC50 > 5000 ppm).

Fish Acute & Prolonged ToxicityLC50, rainbow trout (*Oncorhynchus mykiss*), static test, 96 h: 2.01 mg/lLC50, *Pimephales promelas* (fathead minnow), 96 h: > 3.22 mg/l**Aquatic Invertebrate Acute Toxicity**EC50, *Daphnia magna* (Water flea), static test, 48 h, immobilization: 2.12 mg/l**Aquatic Plant Toxicity**The EC50 value is above the water solubility. ErC50, *Pseudokirchneriella subcapitata* (green algae),

96 h: > 3.0 mg/l

ErC50, Other, Growth rate inhibition, 14 d: 0.000393 mg/l

Product Name: XDE-729 Methyl Technical Herbicide**Revision Date:** 2012/08/12**Toxicity to Micro-organisms**

EC50; activated sludge, 1 d: > 981 mg/l

Fish Chronic Toxicity Value (ChV)

Pimephales promelas (fathead minnow), flow-through test, Other, NOEC: 0.259 mg/l

Aquatic Invertebrates Chronic Toxicity Value

Daphnia magna (Water flea), semi-static test, 21 d, number of offspring, NOEC: 0.484 mg/l

Toxicity to Above Ground Organisms

dietary LC50, Colinus virginianus (Bobwhite quail): > 5,620 ppm

dietary LC50, Anas platyrhynchos (Mallard duck): > 5,620 ppm

oral LD50, Colinus virginianus (Bobwhite quail): > 2250 mg/kg bodyweight.

contact LD50, Apis mellifera (bees): > 98.1 ug/bee

oral LD50, Apis mellifera (bees): > 108 ug/bee

Toxicity to Soil Dwelling Organisms

LC50, Eisenia fetida (earthworms), 14 d: > 1,000 mg/kg

12.2 Persistence and Degradability

For similar active ingredient(s). XDE-729. Material is expected to biodegrade only very slowly (in the environment). Fails to pass OECD/EEC tests for ready biodegradability.

OECD Biodegradation Tests: For similar active ingredient(s). XDE-729.

Biodegradation	Exposure Time	Method	10 Day Window
7.7 %	28 d	OECD 310/ISO 14593	Not applicable

12.3 Bioaccumulative potential

Bioaccumulation: Bioconcentration potential is moderate (BCF between 100 and 3000 or Log Pow between 3 and 5).

Partition coefficient, n-octanol/water (log Pow): 3.78

Bioconcentration Factor (BCF): 233; Lepomis macrochirus (Bluegill sunfish)

12.4 Mobility in soil

Mobility in soil: Expected to be relatively immobile in soil ($K_{oc} > 5000$).

Partition coefficient, soil organic carbon/water (K_{oc}): 5,684
Henry's Law Constant (H): 1.22E-06 Pa·m³/mole.

12.5 Results of PBT and vPvB assessment

This substance has not been assessed for persistence, bioaccumulation and toxicity (PBT).

12.6 Other adverse effects

No relevant data found.

Section 13. Disposal Considerations**13.1 Waste treatment methods**

If wastes and/or containers cannot be disposed of according to the product label directions, disposal of this material must be in accordance with your local or area regulatory authorities. This information presented below only applies to the material as supplied. The identification based on characteristic(s) or listing may not apply if the material has been used or otherwise contaminated. It is the responsibility of the waste generator to determine the toxicity and physical properties of the material generated to determine the proper waste identification and disposal methods in compliance with applicable regulations. If the material as supplied becomes a waste, follow all applicable regional, national and local laws.

Product Name: XDE-729 Methyl Technical Herbicide

Revision Date: 2012/08/12

Section 14. Transport Information**ROAD & RAIL****Proper Shipping Name:** ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.**Technical Name:** Substituted aryl pyridine carboxylate ester**Hazard Class:** 9 **ID Number:** UN3077 **Packing Group:** PG III**Classification:** M7**Hazard identification No:** 90**Environmental Hazard:** Yes**OCEAN****Proper Shipping Name:** ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.**Technical Name:** Substituted aryl pyridine carboxylate ester**Hazard Class:** 9 **ID Number:** UN3077 **Packing Group:** PG III**EMS Number:** F-A,S-F**Marine pollutant:** Yes**AIR****Proper Shipping Name:** ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.**Technical Name:** Substituted aryl pyridine carboxylate ester**Hazard Class:** 9 **ID Number:** UN3077 **Packing Group:** PG III**Cargo Packing Instruction:** 956**Passenger Packing Instruction:** 956**Environmental Hazard:** Yes**INLAND WATERWAYS****Proper Shipping Name:** ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.**Technical Name:** Substituted aryl pyridine carboxylate ester**Hazard Class:** 9 **ID Number:** UN3077 **Packing Group:** PG III**Classification:** M7**Hazard identification No:** 90**Environmental Hazard:** Yes**Section 15. Regulatory Information****15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture****European Inventory of Existing Commercial Chemical Substances (EINECS)**

The components of this product are on the EINECS inventory or are exempt from inventory requirements.

15.2 Chemical Safety Assessment

A Chemical Safety Assessment is not required for this substance.

Section 16. Other Information**Hazard statement in the composition section**

H400

Very toxic to aquatic life.

H410

Very toxic to aquatic life with long lasting effects.

Risk phrases in the Composition section

Product Name: XDE-729 Methyl Technical Herbicide**Revision Date:** 2012/08/12

R50/53

Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Revision

Identification Number: 1042032 / 3027 / Issue Date 2012/09/12 / Version: 1.0

Most recent revision(s) are noted by the bold, double bars in left-hand margin throughout this document.

Dow AgroSciences Limited urges each customer or recipient of this (M)SDS to study it carefully and consult appropriate expertise, as necessary or appropriate, to become aware of and understand the data contained in this (M)SDS and any hazards associated with the product. The information herein is provided in good faith and believed to be accurate as of the effective date shown above. However, no warranty, express or implied, is given. Regulatory requirements are subject to change and may differ between various locations. It is the buyer's/user's responsibility to ensure that his activities comply with all federal, state, provincial or local laws. The information presented here pertains only to the product as shipped. Since conditions for use of the product are not under the control of the manufacturer, it is the buyer's/user's duty to determine the conditions necessary for the safe use of this product. Due to the proliferation of sources for information such as manufacturer-specific (M)SDSs, we are not and cannot be responsible for (M)SDSs obtained from any source other than ourselves. If you have obtained an (M)SDS from another source or if you are not sure that the (M)SDS you have is current, please contact us for the most current version.

APPENDIX 2 PROPOSED LABEL FOR REPRESENTATIVE FORMULATION GF-2573

GF-2573 herbicide

A post-emergence herbicide
for use on all varieties of winter cereals (soft wheat, durum wheat, spelt, barley, rye, triticale)
and spring cereals (soft wheat, durum wheat, barley and rye)
for the control of a wide range of broad leaved weeds.

An EC (Emulsifiable Concentrate) containing 7.5 g ae/L of XDE-729 methyl
and 7.5 g/L of cloquintocet-mexyl (safener).

Read all “safety precautions” and “directions for use” before use.

SAFETY PRECAUTIONS

(To be filled in)

WARNING: This document forms part of an EC evaluation data package and should not be relied upon for registration. Registration must not be granted on the basis of this document.

DIRECTIONS FOR USE

CROPS

GF-2573 is a selective post-emergence herbicide for use on all varieties of winter cereals (soft wheat, durum wheat, spelt, barley, rye and triticale) and all varieties of spring cereals (soft wheat, durum wheat, barley and rye).

GF-2573 can be used in malting barley.

Do not use GF-2573 to winter and spring oats.

Do not treat crops under stress. Stress can be caused by many factors including frost, drought, water logging, trace element deficiency, disease and pest attack etc... GF-2573 can sometimes induce slight and transient (2-3 weeks) crop yellowing. This has no impact at all to the yield.

Do not apply to crops undersown with any legume crop (clover etc...). But crops undersown with grass may be sprayed.

TARGET WEEDS

GF-2573 has a foliar activity against a wide range of annual broad leaved weeds, including *Galium aparine*, *Papaver Rhoeas*, *Chenopodium album*, *Lamium purpureum*, *Lamium amplexicaule*, *Fumaria officinalis*, *Geranium spp.*, *Galeopsis tetrahit*, *Consolida orientalis*.....

For best results apply GF-2573 to young weeds which will respond quicker when treated at early stages. Vigorous crop competition enhances control of the difficult to control weeds.

RATES OF USE

GF-2573 can be used at a maximum rate of 1 L/ha when autumn applied and at a maximum rate of 0.8 L/ha when spring applied.

SOIL

GF-2573 can be used to any soil type.

TIMING

The earliest application timing is BBCH 10 (first leaf through coleoptile) for winter cereals and BBCH 13 (three leaves unfolded) for spring cereals.

The latest application timing is BBCH 45 (flag leaf sheath swollen) for all cereal types.

It is possible to apply GF-2573 both in autumn and spring to any winter cereal during the same growing season.

The ideal timing for application is when the weeds are small and actively growing. However, some highly susceptible species can be controlled at advanced growth stages for rescue treatments (Eg. *Galium aparine* and *Lamium purpureum*).

WEATHER CONDITIONS

GF-2573 can be used in cold or warm (from 2 to 25 °C), humid or dry conditions.

RAINFASTNESS

GF-2573 is rainfast one hour after application.

NEIGHBORING CROPS

GF-2573 is of low volatility and is therefore not subject to vapor drift.

Do not spray in windy weather and avoid spray drift onto non-target crops. Spray drift can be injurious to various susceptible crops so that a 5 m buffer zone must be respected when spraying close to vines, orchards, sunflower, legumes, vegetable crops, ornamentals, tobacco, flax, sugar beet, potatoes etc.....

However, under normal conditions, GF-2573 can be sprayed at 1 m from cereals, corn, grasses and oil seed rape.

SPRAY TANK PREPARATION

GF-2573 can be used with any sprayer type. It can be added to the top of the tank or through induction bowls. Add the appropriate amount of GF-2573 to clean water in a half-filled sprayer tank, mix thoroughly and add the remainder of the water. The spray mix must be agitated continuously during mixing and until application is complete.

VOLUME

Using standard nozzles the recommended spray volume is 100 to 400 liters of water per hectare. The lowest water volume should only be used in very open crops on small weeds. On later applications where the crop is dense, the spray volume should be increased to 200-400 liters water per hectare. The minimum recommended pressure is 2 to 3 bars.

EFFICACY

When post-emergence applied, GF-2573 controls various broad leaved weeds which are already emerged. The efficacy is not influenced by the soil type. When sprayed at young stages, the following species can be ranked as follows:

	GF-2573 at 1 L/ha Autumn uses	GF-2573 at 0.8 L/ha Spring uses
Highly susceptible species: efficacy from 95 to 100 %	<i>Centaurea cyanus</i> <i>Fumaria officinalis</i> <i>Geranium dissectum</i> <i>Geranium pusillum</i> <i>Lamium amplexicaule</i> <i>Lamium purpureum</i> <i>Papaver Rhoeas</i>	<i>Consolida orientalis</i> <i>Chenopodium album</i> <i>Galium aparine</i> <i>Geranium dissectum</i> <i>Geranium pusillum</i> <i>Lamium amplexicaule</i> <i>Lamium purpureum</i> <i>Papaver Rhoeas</i> (North EU)
Susceptible species: efficacy from 85 to 94.9 %	<i>Galium aparine</i> <i>Stellaria media</i> <i>Veronica hederaefolia</i> <i>Veronica persica</i>	<i>Fumaria officinalis</i> <i>Papaver Rhoeas</i> (South EU)
Moderately susceptible species: efficacy from 70 to 84.9 %		<i>Galeopsis tetrahit</i> <i>Polygonum convolvulus</i> <i>Stellaria media</i>

AUTUMN APPLICATIONS TO WINTER CEREALS

GF-2573 can be used from crop emergence (BBCH 10 – first leaf through coleoptile) to the beginning of the winter.

GF-2573 is a post-emergence herbicide with a limited pre-emergence control of the weeds. Best results will be achieved when most of the weeds are already emerged. The control of the susceptible weeds is almost not weather dependent (air temperature, soil humidity). GF-2573 can provide a season long control if there are no new emergences in spring.

Weeds controlled with GF-2573 at 0.6 L/ha	Additional weeds controlled with GF-2573 at 0.8 L/ha	Additional weeds controlled with GF-2573 at 1 L/ha
<i>Fumaria officinalis</i>	<i>Galium aparine</i>	<i>Centaurea cyanus</i>
<i>Geranium dissectum</i>		<i>Papaver Rhoeas</i>
<i>Geranium pusillum</i>		<i>Stellaria media</i>
<i>Lamium amplexicaule</i>		<i>Veronica hederaefolia</i>
<i>Lamium purpureum</i>		<i>Veronica persica</i>

SPRING APPLICATIONS TO WINTER CEREALS

GF-2573 can be used from the winter period to the BBCH 45 (flag leaf sheath swollen) growth stage.

As GF-2573 is a mainly post-emergence herbicide, best results will be achieved when most of the weeds are already emerged. It is advised to apply GF-2573 to young weeds which will respond quicker. The control of the susceptible weeds is almost not weather dependent (air temperature, soil and air humidity...).

Applications from BBCH 13 to BBCH 32 (cereal growth stages):

Weeds controlled with GF-2573 at 0.4 L/ha	Additional weeds controlled with GF-2573 at 0.6 L/ha	Additional weeds controlled with GF-2573 at 0.8L/ha
<i>Geranium pusillum</i>	<i>Chenopodium album</i>	<i>Galeopsis tetrahit</i>
<i>Geranium dissectum</i>	<i>Consolida orientalis</i>	<i>Papaver Rhoeas</i>
<i>Lamium amplexicaule</i>	<i>Fumaria officinalis</i>	<i>Silybum marianum</i>
<i>Lamium purpureum</i>	<i>Galium aparine</i>	

Applications from BBCH 33 to BBCH 45 (rescue treatments):

Weeds controlled with GF-2573 at 0.8L/ha
<i>Galium aparine</i>

SPRING APPLICATIONS TO SPRING CEREALS

GF-2573 can be used from BBCH 13 to BBCH 45 growth stage.

Applications from BBCH 13 to BBCH 32 (cereal growth stages):

Weeds controlled with GF-2573 at 0.4 L/ha	Additional weeds controlled with GF-2573 at 0.6 L/ha	Additional weeds controlled with GF-2573 at 0.8L/ha
<i>Fumaria officinalis</i>	<i>Chenopodium album</i>	<i>Polygonum convolvulus</i>
<i>Galeopsis tetrahit</i>	<i>Galium aparine</i>	<i>Stellaria media</i>
<i>Lamium purpureum</i>		

Applications from BBCH 33 to BBCH 45 (rescue treatments):

Weeds controlled with GF-2573 at 0.8L/ha
<i>Galium aparine</i>

CROP FAILURE

In the event of a crop failure after a crop has been treated with GF-2573, consider all herbicides used on the treated field before deciding the new crop to sow.

Spring barley, spring wheat, spring oil seed rape, ryegrass and corn can be safely sown (with or without ploughing) at least one month after a GF-2573 application.

Sunflower and field beans can be safely sown (with or without ploughing) at least two months after a GF-2573 application.

SUCCEEDING CROPS (normal rotations)

After an autumn application of GF-2573 at 1 L/ha there is no restriction for sowing any succeeding crop sown after the cereal harvest.

After a spring application of GF-2573 at 0.8 L/ha all tested crop (wheat, barley, oat, rye-grass, oil seed rape, transplanted cabbage and tomato, sunflower, potato, onion, leek, flax, carrot, field beans, alfalfa, chicory Witloof, sugar beet, cultivated poppy, fodder pea) can be sown after the cereal harvest and any soil cultivation practice.

Clover and double crop soybean can be sown just after cereal harvest (in summer or autumn) only after ploughing.

MODE OF ACTION and RESISTANCE MANAGEMENT

XDE-729 methyl is the active substance included in GF-2573. XDE-729 methyl belongs to the synthetic auxin herbicide family (Group "O" according to HRAC classification). There is no resistance or cross-resistance issue to XDE-729 methyl of any tested biotype of the susceptible weeds species (*Papaver Rhoeas*, *Stellaria media*, *Galium aparine*...). GF-2573 can be used for controlling all biotypes including those which are resistant to other modes of actions (Eg. *Papaver Rhoeas*, *Stellaria media* etc...).

As the risk of resistance development to GF-2573 is unlikely, as GF-2573 is a post emergence herbicide with a limited pre-emergence control, it is possible to use GF-2573 twice per season in winter cereals: once in Autumn (Eg. for *Papaver Rhoeas* control) and once in Spring (Eg. for Spring emergences of *Galium aparine*).

TANK WASHING

GF-2573 is active to a range of broad-leaved crop species. To avoid subsequent injury to crops other than cereals (wheat, durum wheat, spelt, barley, rye, triticale), all spraying equipment must be thoroughly cleaned both inside and out.

Carefully rinse the GF-2573 bottle after use and pour the rinsing water into the spray tank.

Wash equipment (sprayer, boom, nozzles) thoroughly with water immediately after use.

Rinse the inside of the spray tank with water and pump through spray pipes and nozzles to remove any contamination.

Re-fill spray tank with a minimum of 20% of the total spray tank volume and re-circulate water for approximately 10 minutes. It is advised to use a cleaner such All Clear Extra at 0.5 % v/v or a solution of bleach containing a minimum of 5% hypochlorite. Safely dispose of spray rinse water.

Ensure the empty bottle cannot be re-used and dispose it according to the local law.

SPECIFIC RECOMMANDATIONS

Add any National legal text (local language labels).

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

APPENDIX 3: EFFICACY ASSESSMENT

1.1. Introduction

XDE-729 methyl is a new active substance belonging to a new family of 6-arylpicolinate herbicides. XDE-729 methyl is a member of the pyridine-carboxylic family of herbicidal auxins (HRAC Group O).

XDE-729 methyl is intended for the control of a range of broad-leaved weed species post-emergence at a maximum dose of 7.5 g a.s/ha. It is proposed for use in winter and spring cereals, from early autumn through late spring. It provides a phenotypic response similar to the natural auxins and synthetic auxin herbicides.

The applicant presented a brief summary of studies conducted to date for the XDE-729 methyl active substance approval and this is largely replicated in this section.

(Reference: (Paterson, E; Larelle, D; June 2012)

Additional detailed Zonal Biology Assessments Dossiers will be subsequently submitted in Northern, Central and Southern Zones for product authorizations, in compliance with Annex IIIA data requirements of Regulation (EC) 1107/2009 and to satisfy Member State authorities.

1.2. Preliminary studies/Glasshouse studies

In this chapter, the applicant provided summaries of greenhouse results achieved with technical XDE-729 methyl, dissolved and formulated in an acetone based system in most of the studies.

1.2.1 Herbicidal activity

The herbicidal activity of XDE-729 methyl was summarized in the following reference report, which presents results of an extensive greenhouse study set up to evaluate the XDE-729 efficacy to a range of cereal broad leaved weeds, as well as selectivity to various cereal types (wheat, barley).

Reference report: Satchivi, N., Schmitzer, P. Efficacy and selectivity of XDE-729 applied to cereal crops. Do AgroSciences, unpublished report no. DAI 0978, 12 August 2010. Ref. Bio-1

The main conclusions of this study report were as follows:

1.2.1.1 Effects of XDE-729 methyl to target weeds

XDE-729 methyl was mixed with Crop Oil Concentrate (Agri-Dex adjuvant) to serve as an adjuvant to optimize the herbicidal performance. Weeds were treated when they reached the 2-4 leaf growth stage. In the glasshouse, both the acid and methyl ester of XDE-729 methyl provided control of *Cirsium arvense*, *Galium aparine*, *Lamium purpureum*, *Papaver rhoeas* and *Stellaria media* at rates between 6 and 35 g a.e (acid equivalent)/ha.

XDE-729 methyl demonstrated greater efficacy on several weed species compared to XDE-729 acid. The efficacy of several XDE-729 esters was evaluated on key weed species. Visual observations of the herbicidal activity of esters of XDE-729 on the foliage of broadleaf weeds showed various levels of herbicidal activity depending on both the weed species and the ester tested.

- *Galium aparine*, *Lamium purpureum* and *Papaver rhoeas* were the most susceptible to esters of XDE-729.
- The methyl ester was the only ester that provided control of *Cirsium arvense*, *Kochia scoparia* and *Polygonum convolvulus* at a rate below 35 g a.e/ha in the greenhouse studies.

None of the esters tested provided an acceptable control of *Veronica persica*, *Viola tricolor* or *Matricaria chamomilla* at rates below 35 g a.e/ha.

1.2.1.2 Effects of XDE-729 methyl to target crops

The cereal target crops are wheat (soft and durum), barley, rye, triticale and spelt.

XDE-729 methyl was tested on spring barley (*Hordeum vulgare*) and spring wheat (*Triticum aestivum*). Application rates were 70, 35, 17.5, 8.75 and 4.375 g a.e/ha. Various esters and salts were tested along with the XDE-729 acid form.

Cereal plants were treated when they reached the 2-4 leaf growth stage and plant injury was visually assessed 20-22 days later. Significant and unacceptable head (ear) deformation was caused by XDE-729 methyl, even at low rates. Although the methyl ester form of XDE-729 was visually more injurious to cereal crops than the acid, the difference between both forms of XDE-729 was not statistically significant.

The selectivity of ester and salt forms of XDE-729 showed that the esters were relatively less phytotoxic than the salts. Indeed, the average GR10 (rate providing 10% injury) of the esters varied between 20 and 175 g a.e/ha for both *Triticum aestivum* and *Hordeum vulgare* while the GR10 values of the salts ranged between 15 and 105 g a.e/ha. That difference in selectivity was one of the reasons why the methyl ester form of XDE-729 was selected for development. However, it was identified that the use of a safener was required.

1.2.1.3 Effects of XDE-729 to target crops, when mixed with a safener

The effect of safeners on XDE-729 methyl treated plants is included in the following report:

Reference report: Satchivi, N., Toft, A., Bangel, B. Safener effects on the phytotoxicity of XDE-729 to Wheat and Barley. Dow AgroSciences, unpublished report no. DAI 0979, 12 August 2010. Ref. Bio-2

Greenhouse experiments were conducted to:

- (1) Evaluate the effectiveness of the herbicide safener cloquintocet-mexyl against the phytotoxic effects of XDE-729 methyl applied to cereal crops,

- (2) Compare the ability of forms of cloquintocet, including acid, dimethylamine, triisopropylamine and triethanolamine salts, to protect wheat and barley,
- (3) Evaluate the effects of various herbicide safeners on the phytotoxicity of XDE-729 methyl when applied in mixture to cereal crops.

XDE-729 was applied as ester or salt. These studies are supportive of the following conclusions:

- Cloquintocet-mexyl applied at 1:1 herbicide-to-safener ratio provided complete protection of spring, winter and durum wheat as well as spring and winter barley against the phytotoxicity of XDE-729 (methyl ester, TEA salt, K salt, etc ..) applied at a rate between 35 and 140 g a.e/ha. When XDE-729 was mixed with cloquintocet-mexyl, no seed head deformation was observed at maturity.
- Various forms of cloquintocet such as acid, DMA, TEA and TIPA were also able to provide commercial level safening of XDE-729 methyl ester when applied in mixture.
- Mefenpyr-diethyl and fenchlorazole-ethyl, both safeners used in wheat and barley, could also be used to safen the effects of XDE-729 on wheat and barley. However, these appeared less effective than cloquintocet.
- With the exception of fluxofenim, seed-treatment safeners did not provide enough safening against XDE-729. Dichloroacetamide safeners such as AD-67, benoxacor, dichlormid, dicyclonon and furilazole provided significant safening of wheat and barley against the phytotoxicity of XDE-729 TEA salt when applied in mixture at 1:1 herbicide to safener ratio. However, these safeners were not as effective as cloquintocet.
- The safening effects of cloquintocet-mexyl did not affect the ability of XDE-729 to control weeds.

Field trials set up in the European Union in 2008-2010 to wheat, durum wheat, spelt, barley, rye and triticale have demonstrated that cloquintocet-mexyl is an effective safener when used at a 1:1 herbicide-to-safener ratio. This means a rate of cloquintocet-mexyl of 7.5 g ai/ha for a rate of XDE-729 methyl of 7.5 g a.e/ha. The cloquintocet-mexyl safener does not prevent crop symptoms in oats, at the currently developed rates of XDE-729 methyl.

All laboratory and field studies which were completed have shown that XDE-729 methyl does not present any unacceptable effects on grain quantity and quality (1000 grain weight, protein content etc....). The preliminary processing studies specify that XDE-729 methyl is safe in both bread making and malting / brewery studies.

1.2.2 Fungicidal activity

A study was designed to assess the antifungal activity of XDE-729 (=X11393729, acid form) and XDE-729 methyl (=X11393728) and to determine any potential adverse effects

on non-target fungi. Inhibition of fungal growth and disease control were measured under standard fungicide screening conditions.

Reference report: Davis, G.E. Assessment of antifungal potential of X11393729 and X11393728. Dow AgroSciences, unpublished report # DAI 1102, 11 May 2012. Ref. Bio-3

The anti-fungal activity of XDE-729 and XDE-729 methyl ester was evaluated:

- *in vitro* at 5 ppm on the following fungal species:
 - o *Pyricularia oryzae* (PYRIOR, rice blast)
 - o *Septoria tritici* (SEPTTR, wheat leaf spot)
 - o *Ustilago maydis* (USTIMA, maize blister smut)
- *in planta (in Vivo)* at 200 ppm as a 1 day protectant application to the following species:
 - o *Colletotrichum lagenarium* (COLLLA, anthracnose) on *Cucumis sativus* (CUMSA, cucumber)
 - o *Erysiphe cichoraceum* (ERYSCI, powdery mildew) on *Cucumis sativus* (CUMSA, cucumber)
 - o *Leptosphaeria nodorum* (LEPTNO, glume blotch) on *Triticum aestivum* (TRZAW, wheat)
 - o *Phytophthora infestans* (PHYTIN, late blight) on *Lycopersicon esculentum* (LYPES, tomato)
 - o *Puccinia recondita* (PUCCRT, brown rust) on *Triticum aestivum* (TRZAW, wheat)
 - o *Pyricularia oryzae* (PYRIOR, rice blast) on *Oryza sativa* (ORYSJ, rice)

XDE-729 and XDE-729 methyl did not demonstrate significant *in vitro* growth inhibition (10-30%) when applied to any of the fungi tested. In addition, no disease control was observed for *in planta* tests where host plant selectivity allowed evaluations. In spring 2010, additional field trials were set up in Europe to winter wheat in order to evaluate the fungicidal effect of XDE-729 methyl to diseases such as *Septoria tritici* (SEPTTR) and *Puccinia striiformis* (PUCCST) in field conditions. It was concluded that XDE-729 methyl (applied at 6 and 12 g a.e/ha as formulated product) did not have any fungicidal activity in such conditions.

1.2.3 Insecticidal activity

A study was designed to assess the insecticidal activity of XDE-729 (=X11393729, acid form), XDE-729 methyl ester (=X11393728) and the major XDE-729 metabolite determined in soils and tolerant plant species (=X11449757) to evaluate any potential significant insecticidal effects on key insect pest species.

Reference report: Wessels, F., Schmitzer, P. Insecticidal Assessment of X11393729, X11393728 and X11449757. Dow AgroSciences, unpublished report # DAI 1101, 22 February 2012. Ref. Bio-4

The insecticidal activity was evaluated to:

- *Spodoptera exigua* (LAPHEG, beet armyworm)
- *Aedes aegypti* (AEDSAE, yellow fever mosquito)
- *Drosophila melanogaster* (DROSME, common fruit fly)

These tests are designed to give the compounds the best chance of inducing insect mortality, either by contact or by ingestion. The high concentration of compound combined with prolonged insect exposure and the possibility of ingestion increase the likelihood of finding a positive result. The lack of insecticidal activity associated with XDE-729 methyl ester, XDE-729 and its major metabolite X11449757 in these assays strongly suggests that these compounds are not acutely toxic to the species tested.

In spring 2010, additional field trials were set up in Greece to cotton crops in order to evaluate the insecticidal effect of XDE-729 methyl to insects such as *Aphis gossypii* (APHIGO, cotton aphid), *Helicoverpa armigera* (HELIAR, cotton bollworm) and *Frankliniella occidentalis* (FRANOC, alfalfa thrips) in field conditions. It is concluded that XDE-729 methyl (applied at 7.5 ga.e/ha as formulated product) did not have any insecticidal activity in such conditions.

1.2.1. Field of Use

XDE-729 methyl containing products are proposed for use in agriculture as post-emergent foliar sprays to winter and spring cereal crops.

1.3.1 Treated crops

Field trials set up from 2008 to 2011 in the European Union (Northern, Central and Southern zones) have demonstrated that XDE-729 methyl containing products, which also include the safener cloquintocet-mexyl (applied at the currently developed autumn and spring rates), are safe to winter and spring cereals (except winter and spring oats) without any varietal restriction.

The crop list includes:

- Winter cereals: soft wheat, durum wheat, barley, rye, spelt, triticale.
- Spring cereals: soft wheat, durum wheat, barley, rye.

Proposed application timings where crop safety has been observed were at growth stages from BBCH 10 (emergence: coleoptile penetrates soil surface =cracking stage) to BBCH 45 (late boot stage: flag leaf sheath swollen), even under dry or humid conditions, cold or warm conditions.

1.3.2 Method of application

XDE-729 methyl containing products can be applied through all conventional sprayers including tractor mounted or self propelled hydraulic sprayers. Supported spray volumes are from 100 to 400 L/ha.

An adjuvant may be recommended for use with XDE-729 methyl to optimize effectiveness.

Reference report: Satchivi, N., Bangel, B. Effects of adjuvants on the efficacy and selectivity of XDE-729 applied to cereal crops. Dow AgroSciences, unpublished report # DAI 0981. 10 August 2010. Ref. Bio-5

Evaluations were conducted in a greenhouse to determine the effects of various adjuvants on the efficacy of the foliar applied herbicide XDE-729 methyl ester.

XDE-729 methyl ester applied at 5 g a.e/ha alone or in combination with various adjuvant types was investigated on several key broad leaved weed species; *Lamium purpureum*, *Matricaria chamomilla*, *Papaver rhoeas*, *Sinapis arvensis*, *Stellaria media* and *Viola tricolor*.

Data presented in this report indicate that any nonionic surfactant, crop oil concentrate adjuvant, methylated seed oil adjuvant, organosilicone surfactant, petroleum hydrocarbons based surfactant, blend or nonionic fluorinated surfactant, can be used with XDE-729 methyl ester to provide maximum herbicidal activity. When applied with an adjuvant at a rate between 0.125 and 1% v/v, the activity of XDE-729 methyl ester on these weeds was significantly enhanced.

As a consequence, several XDE-729 methyl containing products developed in Europe will include adjuvants (methylated seed oil or non ionic surfactant). Alternatively, when such an adjuvant cannot be incorporated into the formulation, tank mixing an adjuvant with XDE-729 methyl containing products may be recommended to users.

1.4.1 Supported uses

All formulations which will be developed to cereals in Europe will include XDE-729 as the methyl ester and cloquintocet-mexyl as the safener (always with a 1:1 herbicide-to-safener ratio).

The first representative and lead formulation is GF-2573, containing XDE-729 methyl at 7.5 g a.e/L (maximum rates to be applied: 1 L/ha in autumn and 0.8 L/ha in spring). This EC formulation contains also 7.5 g ai/L of cloquintocet-mexyl and 750 g/L of methylated seed oil (see sections 6.2.1 & 6.3.2).

Two co-formulations are also in development;

- GF-2644: XDE-729 + florasulam (6+5 g a.e/L) with a maximum rate of 1 L/ha in spring. Interest is a very broad spectrum product, with florasulam adding the important Compositae and Cruciferae species to the XDE-729 profile. This OD formulation contains also 6 g ai/L of cloquintocet-mexyl and 727 g/L of methylated seed oil.
- GF-2819: XDE-729 + fluroxypyr (12 + 280 g a.e/L) with a maximum rate of 0.5 L/ha in spring. Interest is for development of a non-ALS mixture with a great flexibility of use to control *Galium aparine* (the broad leaved weed number one in North and West Europe), and adding species such as POLCO, POLAV, volunteer SOLTU. This EC formulation contains also 12 g ai/L of cloquintocet-mexyl and the co-formulants which play the role of adjuvant.

Dow AgroSciences will intend to develop various formulations (mixtures) which can be used either in autumn, or in spring or both in autumn and spring.

Table 1: intended uses of XDE-729 methyl in the **Northern Zone**

Crops	Application		Max rate per application	Remarks
	Growth stage	Number per season	g a.e./ha	
Winter cereals - wheat - barley - rye - triticale	Autumn (Sept 1 st – Dec 31 st) BBCH 09-29 and Spring (March 1 st – June 20 th) BBCH 13-45	1 - 2	7.5* followed by 6.0*	The applications are made: - in autumn only - or in spring only - or in both autumn and spring.
Spring cereals - wheat - barley	Spring (March 1 st – June 20 th) BBCH 13-45	1	6.0*	The application is made in spring only

* 7.5 g a.e./ha equals 7.82 g/ha of XDE-729 methyl ester

* 6.0 g a.e./ha equals 6.25 g/ha of XDE-729 methyl ester

Table 2: intended uses of XDE-729 methyl in the **Central Zone**

Crops	Application		Max rate per application	Remarks
	Growth stage	Number per season	g a.e./ha	
Winter cereals - wheat (soft) - wheat (durum) - barley - spelt - rye - triticale	Autumn (Sept 1 st – Dec 31 st) BBCH 09-29 and Spring (March 1 st – June 30 th) BBCH 13-45	1 - 2	7.5* followed by 6.0*	The applications are made: - in autumn only - or in spring only - or in both autumn and spring.
Spring cereals - wheat (soft) - wheat (durum) - barley - rye	Spring (Jan 1 st – June 30 th) BBCH 13-45	1	6.0*	The application is made in spring only

* 7.5 g a.e./ha equals 7.82 g/ha of XDE-729 methyl ester

* 6.0 g a.e./ha equals 6.25 g/ha of XDE-729 methyl ester

Table 3: intended uses of XDE-729 methyl in the **Southern Zone**

Crops	Application		Max rate per application	Remarks
	Growth stage	Number per season	g a.e./ha	
Winter cereals - wheat (soft) - wheat (durum) - barley - spelt - rye - triticale	Autumn (Sept 1 st – Dec 31 st) BBCH 09-29 and Spring (March 1 st – May 31 st) BBCH 13-45	1 - 2	7.5* followed by 6.0*	The applications are made: - in autumn only - or in spring only - or in both autumn and spring.
Spring cereals - wheat (soft) - wheat (durum) - barley - rye	Spring (Feb 1 st – May 31 st) BBCH 13-45	1	6.0*	The application is made in spring only

* 7.5 g a.e/ha equals 7.82 g/ha of XDE-729 methyl ester

* 6.0 g a.e/ha equals 6.25 g/ha of XDE-729 methyl ester

1.4.1 **Effectiveness including dose justification**

Reference report : Satchivi, N., Schmitzer, P. Efficacy and selectivity of XDE-729 applied to cereal crops. Dow AgroSciences, unpublished report no. DAI 0978, 12 August 2010. Ref. Bio-1

Data from this preliminary screen demonstrate that *Galium aparine*, *Lamium purpureum*, *Papaver rhoeas* and *Stellaria media* are susceptible to post-emergence applications of XDE-729 methyl. Of these species *G. aparine* and *L. purpureum* are the most sensitive to XDE-729 methyl, with *Matricaria chamomilla*, *Veronica persica* and *Viola tricolor* being the most tolerant to post emergence applications of XDE-729 methyl.

Table 4: GR 90 values and relative susceptibility to XDE-729 methyl (applied rates from 4.375 to 70 g a.e./ha) of various European broad leaf weed species

Target weed	GR 90 (g a.e./ha)
<i>Galium aparine</i>	6
<i>Lamium purpureum</i>	7
<i>Papaver rhoeas</i>	8
<i>Stellaria media</i>	26
<i>Matricaria chamomilla</i>	118
<i>Veronica persica</i>	129
<i>Viola Tricolor</i>	140

1.4.1.1 Autumn uses

Zonal Biology Assessment Dossiers will be submitted to support the authorization of XDE-729-methyl in each of the three European zones. In the autumn, the applicant considers that a key target is *Stellaria media* (increasing ALS resistance in Denmark, UK etc...) requiring the highest proposed maximum dose (7.5 g a.e./ha) of active substance.

The field trials data supporting effectiveness against this target comprised 14 trials conducted over 2 years. The trials were undertaken by Officially Recognised Organisations, all of which follow EPPO guidelines. Trials were conducted in the following Member States: Denmark, France, Germany and the UK. These are representative of the following EPPO zones according to EPPO Standard PP1/241 (1); Maritime and Mediterranean and the Northern, Central and Southern EC regulation 1107/2009 work sharing zones.

XDE-729 methyl, as GF-2573, was tested at a range of doses from 3 to 9 g a.e./ha in order to determine the most appropriate dose for the control of *S. media* in the autumn. Data presented below in table 5 demonstrate an improvement in the efficacy of XDE-729 methyl when applied at the proposed field rate of 7.5 g a.e./ha (1N) compared to the 0.6 N and 0.8 N rates. This improved efficacy was also associated with a reduced variation in the level of control observed at each rate with a Standard Deviation of 12.6 at the 1 N rate compared to a Standard Deviation of 21 at the 0.6 N rate. Additional data and a detailed summary on dose rate justification will be presented in the zonal BADs.

Table 5 : Dose response of XDE-729 methyl applied (as GF-2573) to winter cereals in Autumn to several key broad leaf weeds (EU field results, across zones)

Target weed	Number of trials	Summary of control (%) achieved with XDE-729 methyl at		
		4.5 g a.e/ha (0.6 N)	6 g a.e/ha (0.8 N)	7.5 g a.e/ha (1 N)
<i>Stellaria media</i>	All zones: 14 trials	84 %	89 %	93 %
<i>Veronica hederifolia</i>	All zones: 19 trials	83 %	88 %	91 %
	Southern zone: 6 trials	92 %	94 %	98 %

1.4.1.2 Spring uses

Zonal Biology Assessment Dossiers will be submitted to support the authorization of XDE-729-methyl in each of the three European zones. In the spring, one of the most challenging susceptible targets is considered by the applicant to be *Papaver rhoeas* (increasing ALS resistance in Spain, Italy, France, UK, Belgium...) requiring the highest proposed maximum dose (6 g a.e/ha) of active substance.

The field trials data supporting effectiveness against this target comprised 7 trials conducted over 2 years. The trials were undertaken by Officially Recognized Organizations, all of which follow EPPO guidelines. Trials were conducted in the following Member States: France, Italy, Spain, Poland and UK. These are representative of the following EPPO zones according to EPPO Standard PP1/241 (1); Maritime, North East and Mediterranean and the Central and Southern EC regulation 1107/2009 zones.

XDE-729 methyl was tested at a range of doses from 3 to 6 g a.e./ha in order to determine the most appropriate dose for the control of *P. rhoeas* in the spring. Data presented below in Table 6 demonstrate an improvement in the efficacy of XDE-729 methyl when applied at the proposed field rate of 6 g a.e/ha (1N) compared to the 0.75 N and 0.5 N rates. Additional data and a detail summary on dose rate justification will be presented in the zonal BADs.

Table 6.: Dose response of XDE-729 methyl applied (as GF-2573) to winter cereals in Spring to *Papaver rhoeas* (EU field results, across zones)

Target weed	Number of trials	Summary of control (%) achieved with XDE-729 methyl at		
		3 g a.e/ha (0.5 N)	4.5 g a.e/ha (0.75 N)	6 g a.e/ha (1 N)
<i>Papaver rhoeas</i>	All zones : 14 trials	77 %	81 %	87 %

1.5 Mode of Action –Effects on harmful organisms

Reference report: Walsh, T.A., et al. Mutations in an auxin receptor homolog AFB5 and in SGT1b confer resistance to picolinate auxins but not to 2,4-D or IAA in Arabidopsis. Dow AgroSciences, unpublished report # DAI 0656. 14 Sept 2005. Ref Bio 26

A wide range of chemistries have been shown to exert auxinic effects, which include structurally distinct classes such as: the aryloxypropionates, picolinates, benzoates and the quinoline carboxylates. These herbicidal auxins exhibit a broad range of efficacy and selectivity profiles in important European cereal and grassland markets

XDE-729 methyl will be the first member of a new structural class of chemistry, known as the arylpicolinates, to be developed for the European cereal market. Although XDE-729 methyl is a member of the pyridine carboxylic (picolinate) family of herbicidal auxins (group O) it differs from aminopyralid, picloram and clopyralid in the presences of a 6-phenyl substitution on the pyridine ring. The binding site of the picolinate auxins also differs from the oxy-acetates (for example 2,4-D, fluroxypyr and triclopyr).

XDE-729 methyl is a product, that when applied to sensitive species, will present auxin-like properties. Natural auxins are used by the plant to regulate minute amount of hormones which bind to specific receptor proteins turning on and off vital plant processes. XDE-729 methyl moves systemically throughout the target weed binding to receptor sites normally used by these plant hormones. This causes a disruption of normal plant growth processes via the binding of XDE-729 to the receptors. This binding results in the deregulation of plant growth metabolic pathways and thus causes uneven cell division and growth, culminating in plant death.

Symptoms of XDE-729 methyl herbicide damage to sensitive species normally occur within a couple of hours. Symptoms of herbicide damage include: cessation of growth, epinasty, leaf cupping, chlorosis, swelling/thickening of stems, callus tissue and distortion of the meristems and eventually plant death.

Numerous field trials were set up from 2008 to 2011 in the European Union (Northern, Central and Southern zones) to determine the efficacy profile of XDE-729 methyl in both winter and spring cereals. Detailed summaries of these trials will be presented and discussed in the zonal Biology Assessment Dossiers.

XDE-729 methyl has a wide spectrum of activity on broadleaf weeds species, with some activity on certain perennial weed species. Control can be influenced by weed size with smaller stages more easily controlled. However, the activity of XDE-729 methyl on target weeds is not significantly influenced by environmental conditions and is active under cold (inactive periods of growth) and warm conditions with active growth. Hence it can be used in both the autumn and spring with late spring applications (up to crop growth stage BBCH 39-45) to control certain species such as *Galium aparine*.

Primary target weeds in Europe are as follows (in alphabetic order)

- **Autumn applications of XDE-729 methyl in winter cereals:**

Highly susceptible species to XDE-729 methyl (95-100%)

- *Centaurea cyanus*(CENCY)
- *Fumaria officinalis* (FUMOF)
- *Geranium dissectum* (GERDI)
- *Geranium pusillum* (GERPU)
- *Lamium amplexicaule* (LAMAM)
- *Lamium purpureum* (LAMPU)
- *Papaver rhoeas* (PAPRH)
- *Stellaria media* (STEME)

Susceptible species to XDE-729 methyl (85-94.9%)

- *Galium aparine* (GALAP)
- *Veronica hederifolia* (VERHE)
- *Veronica persica* (VERPE)

- **Spring applications of XDE-729 methyl to either winter or spring cereals:**

Highly susceptible species to XDE-729 methyl (95-100%)

- *Chenopodium album* (CHEAL)
- *Galium aparine* (GALAP)
- *Geranium dissectum* (GERDI)
- *Geranium pusillum* (GERPU)
- *Lamium amplexicaule* (LAMAM)
- *Lamium purpureum* (LAMPU)
- *Papaver rhoeas* (PAPRH) (northern EU)

Susceptible species to XDE-729 methyl (85-94.9%)

- *Papaver rhoeas* (PAPRH) (southern EU)
- *Fumaria officinalis* (FUMOF)

The above species are susceptible to XDE-729 methyl at dose rates ranging between 4.5 to 7.5 g ae /ha depending on the species and growth stage at application. Performance details will be presented in the zonal Biology Assessments Dossiers, document M3, chapter IIIA.6 (“Efficacy data and information”).

There are also some frequent cereal weeds which are not controlled by XDE-729 methyl:

- *Bassica napus* (volunteer oil seed rape)
- *Capsella bursa-pastoris*(CAPBP)
- *Matricaria inodora* (MATIN)
- *Matricaria chamomilla* (MATCH)
- *Matricaria matricarioides* (MATMT)
- *Sinaps arvensis* (SINAR)
- *Viola arvensis* (VIOAR)

1.5.1 Translocation in plants

Reference Reports:

- DeBoer, G.J, et al. Understanding metabolism, uptake and translocation of XDE-729 and its methyl ester (XDE-729 ME) in wheat, *L. Purpureum* and *V. persica* and the effect of safener on wheat selectivity. Dow AgroSciences, unpublished report number DAI 1026, 24 May 2011. Ref Bio-7
- Brockmann, A, et al. Standardized bioassay for the determination of ED₁₀ (NOEL) and ED₅₀ values for GF-2573 (XDE-729, 7.5 g a.e/L, EC) and selected following crop species. Unpublished report, Agrocheck, Germany study id AC/10/219, DAS study id EA10D2C069, 4 July 2011. Ref. Bio-8
- Davis, J. Determination of the foliar No Observable Effect Level (NOEL) of XDE-729 (GF-2573 7.5 g a.e/L) to a range of crop species. Unpublished report Stockbridge Technology Centre, Yorks, UK. Study id STC/11/E646 DAS study id EA11D2C077, 2 August 2011. Ref. Bio-9

The biological activity of the commercially available synthetic auxins such as fluroxypyr-1-MHE and 2, 4-D is believed to require the free carboxylic acid. These herbicides therefore, need to undergo either de-esterification or β -oxidation, to release the active moiety and are considered to be pro-herbicides. The herbicide XDE-729 methyl would also need to undergo de-esterification in order to release its active acid form and can also be considered to be a pro-herbicide.

Translocation of XDE-729 methyl was studied in the reference report (# DA1 1026. Ref. Bio-7), in which radiolabelled ¹⁴C-XDE-729 methyl was applied as 1- μ L droplets to the adaxial surface of the second fully expanded leaf and harvested at 0, 4, 24 and 48 hours after application. The results have been used to understand translocation of XDE-729 methyl within the plant following foliar applications, in three test species namely; wheat, *Veronica persica* and *Lamium purpureum*.

The study demonstrated that the translocation of radiolabelled C ¹⁴ out of the treated leaf was similar in wheat and *V. persica* at each harvest time, whereas radiolabelled C ¹⁴ translocation increased with time in *L. purpureum*. This difference in translocation was explained by the fact that less free acid (XDE-729) was available for translocation out of the leaf in wheat and *V. persica* than in *L. purpureum*. Phosphor images of the translocation of foliar applied ¹⁴C-XDE-729 methyl showed only classic phloem movement in *L. purpureum* and *V. persica*, with the active moiety being translocated though out the plant.

In the Pestemer study (EA10D2C069. Ref. Bio-8) air dried soil was treated with XDE-729 methyl (GF-2573, 7.5 g a.e/L EC) at rates ranging from 37 to 9000 ml pr/ha and incorporated. Pre-germinated monocotyledon and dicotyledon seedlings of the following crop species; wheat (*Triticum aestivum*), pea (*Pisum sativum*), oil seed rape (*Brassica napus*), sugar beet (*Beta vulgaris*), sunflower (*Helianthus annuus*), maize (*Zea mays*), oat (*Avena sativa*) and white mustard (*Sinapis alba*) were transplanted into the treated soil and allowed grow.

All plants were assessed for visual injury; whilst survival and shoot fresh weight was measured at the end of the study. Field pea was the most sensitive species with significant levels of visual injury and shoot fresh weight reduction reported. This study provides evidence that XDE-729 methyl can also be taken up by the roots and redistributed through the plant. No additional data has been provided to support this proposed method of redistribution, within the plant. Data from this Pestemer study are consistent with results of a foliar XDE-729 methyl NOEL study in which peas were identified as a highly susceptible species to XDE-729 methyl (data not presented. Ref. Bio-9).

1.5.2 **Description of biochemical and biological mode of action**

Reference report: Walsh, T.A., et al. Mutations in an auxin receptor homolog AFB5 and in SGT1b confer resistance to picolinate auxins but not to 2,4-D or IAA in *Arabidopsis*. Dow AgroSciences, unpublished report # DAI 0656. 14 Sept 2005. Ref. Bio-6

In 2006, Walsh et al isolated two lines of *Arabidopsis* with reduced sensitivity to the experimental 6-arypicolinate herbicide DAS534, which through screening were used to identify *Arabidopsis* with the AFB5 and SGT1b genes. These artificial mutations were used to determine the binding sites in sensitive plants.

A major component of the herbicidal activity of XDE-729 methyl is mediated via interactions with a SCF^{AFB5} ubiquitin ligase which is involved with auxin signaling and other pathways. This molecular target for XDE-729 AFB5 was found to be in the same family of genes as transport inhibitor response 1 (TIR1), the molecular target for indole acetic acid (IAA) and the herbicide 2,4-D (Dharmasiri et al., 2005; Kepinski et al., 2005). Research with TIR1 indicates that natural auxins as well as 2,4-D allow TIR1 to bind the transcription repressor Aux/IAA. This binding allows the F-box protein to ubiquitinate the Aux/IAA. The ubiquitinated Aux/IAA is then degraded by the proteasome. Degradation of the Aux/IAA repressor allows for unregulated transcription of the genes that would usually be repressed by Aux/IAA (Badescu et al., 2006).

The homolog of AFB5 to TIR1 suggests that XDE-729 methyl allows for Aux/IAA to bind to AFB5 much like 2,4-D allows Aux/IAA to bind to TIR1, allowing for the unregulated transcriptions of genes which would normally be suppressed by Aux IAA. A line of *Arabidopsis* was mutagenized to be resistant to XDE-729 (afb5). The lack of resistance of afb5 *Arabidopsis* to 2,4-D indicates that the molecular recognition site of the oxyacetate auxin herbicide 2,4-D is different from that of the picolinate auxin herbicides (XDE-729).

1.5.3 **Metabolism in plants (weeds and crops)**

Reference report : DeBoer, G.J, et al. Understanding metabolism, uptake and translocation of XDE-729 and its methyl ester (XDE-729 ME) in wheat, *L. Purpureum* and *V. persica* and the effect of safener on wheat selectivity. Dow AgroSciences, unpublished report number DAI 1026, 24 May 2011. Ref Bio-7

A series of metabolism, uptake and translocation studies were conducted to understand the mechanism(s) of selectivity in spring wheat and two broadleaf weed species namely;

Lamium purpureum and *Veronica persica* (reference report # DAI 1026). Studies were also performed to elucidate the mechanism(s) of the improved selectivity of XDE-729 methyl to spring wheat.

XDE-729 methyl was metabolized in all three test species by the conversion of the acid (active form) which was subsequently O-demethylated and conjugated with glucose and malonate.

In wheat this process was slow and selectivity of wheat to XDE-729 methyl is most likely due to slow de-esterification coupled with O-demethylation and conjugation of the acid and the ester. When XDE-729 methyl was applied to wheat with the safener a number of processes occurred; first there was a slight reduction in uptake, secondly there was a significant reduction in translocated radioactive material and thirdly there was an increased rate of the O-demethylation and subsequent conjugation of the ester without increasing the de-esterification. This third effect would have significantly reduced the amount of active moiety available for translocation and thus improving selectivity in wheat.

Of the two weed species tested *V. persica* was the least sensitive to applications of XDE-729 methyl. In this species ring hydroxylation was a major pathway for metabolism unlike wheat where it was only a minor pathway. It was concluded that the higher tolerance of *V. persica* to XDE-729 methyl was due to its ability to offset the fast conversion of the acid in the plant by rapid O-demethylation of the acid and ring hydroxylation of the ester.

In contrast XDE-729 methyl was rapidly converted to acid and not metabolized further in the highly sensitive species *L. purpureum*. The addition of the safener had no effect on the XDE-729 methyl uptake, translocation and metabolism in *L. purpureum*.

1.5.4 Herbicidal activity of the main metabolites

Reference reports:

- Davies, J. Determination of the Soil No Observable Effect Level (NOEL), EC₁₀ and EC₅₀ of XDE-729 and its M-757 metabolite to a range of rotational crop species. Stockbridge Technology Centre. Unpublished report # STC/10/E583 (Dow AgroSciences study Id EA10D2C067), 11 February 2011. Ref. Bio-10
- Brougham, K, et al. Determination of the foliar No Observable Effect Level (NOEL) ED 10 and ED 50 values of XDE-729 methyl metabolite M-757 to a range of crop species. Unpublished Dow AgroSciences study id EA11D2C079, 16 May 2012. Ref. Bio-11

Two studies were established to determine the biological activity of the M-757 metabolite to that of XDE-729 methyl, formulated as GF-2573 (XDE-729 methyl at 7.5 g a.e/L, EC).

The first of these studies was designed to evaluate the soil activity of M-757 on key European monocotyledon and dicotyledon rotational crop species. These crop species included; *Allium cepa*, *Brassica napus*, *Glycine max*, *Trifolium alba*, *Beta vulgaris* and *Linum usitatissimum*, representing the following plant families: Brassicaceae, Leguminosae, Liliaceae, Linaceae, Chenopodiaceae and Umbelliferae.

Test soil was treated with either M-757 or XDE-729 methyl at rates ranging from 0.0206 to 15 µg ae/kg of air dried soil. Crop species were then sown into the treated soil and assessed for any phototoxic effects relative to the untreated control.

The second of these studies was designed to evaluate the foliar activity of M-757 on key European monocotyledon and dicotyledon crop species. These crop species included *Lycopersicon esculentum*, *Beta vulgaris*, *Glycine max* and *Lactuca sativa* representing the following plant families: Solanaceae, Chenopodiaceae, Leguminosae and Asteraceae.

M-757 and XDE-729 methyl were applied as foliar sprays at rates ranging from 0.003 to 7.5 g a.e/ha to the test species once they reached the BBCH12-14 growth stage. They were later assessed for any phototoxic effects relative to the untreated control.

- M-757, applied at the highest rates tested in both the soil and foliar NOEL studies (15 µg ae/kg or 7.5 g a.e/ha respectively), did not result in 50 % injury to any of the test species. In comparison injury with the parent XDE-729 methyl applied at an equivalent rate in both studies resulted in more than 50 % injury to all test species.
- ED₅₀ values for visual control and fresh weight reduction could not be calculated for M-757 applied to any of test species in the soil and foliar NOEL studies because of the lack of a 50 % effect. ED₅₀ values for visual injury and foliar fresh weight were therefore, considered to be > 15 µg ae/kg air dried soil or > 7.5 g a.e/ha in the foliar study, the highest rates tested in either study. These ED₅₀ values were significantly more than 3 times that of the parent XDE-729 methyl, for the most sensitive species (*L. esculentum*, *G. Max*, *L. Sativa*, *L. usitatissimum* and *T. alba*). It was not possible to determine the 3X ED₅₀ value for the less sensitive species, because the 3X value exceeded the highest rate tested. However, it must be noted that the M-757 metabolite applied at the highest rate tested resulted in < 10 % visual injury compared to 61 to 100 % injury with parent.

In conclusion, based on guidance given in by the Federal Environment Agency (UBA) in “Assessment of the Relevance of Metabolites in Groundwater in Context of National Approval Procedures of Plant Protection Products” and “Groundwater metabolites – guidance on efficacy aspects” published by CRD, UK, the M-757 metabolite is not considered to be biologically active.

1.6 Unacceptable effects

1.6.1 Adjacent crops

Risk evaluation due to XDE-729 methyl vapors

The vapour pressure of XDE-729 methyl, when compared to existing herbicides in general and to 2,4-D ethyl hexyl ester (EHE) in particular, is relatively low. Thus, issues associated with non-target volatile movement are anticipated to be very low.

Vapour pressure values at 25°C:

- XDE-729 methyl: 1.5×10^{-8} Pa (1.1 x 10⁻¹⁰ mm Hg)
- 2,4-D ethyl hexyl ester: 48000×10^{-8} Pa (36000 x 10⁻¹⁰ mm Hg)

To confirm this “very low volatility” from a Biology standpoint, the risk to induce injuries by XDE-729 methyl volatility (vapors coming from a treated field) was evaluated in a greenhouse study.

Reference report: Gifford, J., Ouse, D, Bingham-Burr, D. Volatility of XDE-729 methyl (GF-2573, EC, 7.5 g a.e/L) compared to 2,4-D ethyl hexyl ester (GF-1387, EC, 600 g a.e/L). Dow AgroSciences, unpublished Powerpoint document, 1 Sept. 2011. Ref. Bio-14

The volatility of XDE-729 methyl was compared to that of 2,4-D ethyl hexyl ester (EHE). This standard was selected because its potential risks are well known when sprayed close to susceptible crops. Three crop species were selected for this study: European grape (*Vitis vinifera*), lentil (*Lespedeza cuneata*) and tomato (*Lycopersicon esculentum*). These species are susceptible to very low rates of both XDE-729 methyl and 2,4-D EHE when foliar applied. It was checked in separate studies that grapes, lentils and tomatoes are amongst the most susceptible species to XDE-729 methyl.

Method: Wheat plants were sprayed with XDE-729 methyl or 2,4-D EHE at 6 and 1120 g a.e/ha respectively. Then these treated cereal plants were placed in a growth chamber at 30°C together with susceptible broad leaved crops for 24 hours. After exposure of plants to vapors, plants were moved to a 16°C glasshouse for two weeks. Injuries were assessed up to 15-16 days after treatment (DAA). Pictures can be seen in the reference report.

Results: Two weeks after treatments, the visual injury levels were as follows:

Table 7 : Visual injury levels due to XDE-729 methyl or 2,4-D EHE vapors.

	% injury (0-100 scale)		
	Untreated	XDE-729 methyl at 6 g a.e/ha	2,4-D EHE at 1120 g a.e/ha
Grapes	0	0	83
Lentils	0	3	72
Tomatoes	0	0	70

Conclusion: The data presented in this table confirm that 2,4-D EHE is highly injurious to some susceptible crop species (grapes, lentils, tomatoes). Plants exhibit obvious auxin symptoms including epinasty, thickened and brittle stems, stunting and death. Under the same conditions, these susceptible plants exhibit very little or no symptoms when exposed to XDE-729 methyl vapors, demonstrating it is unlikely that XDE-729 methyl induces injuries to adjacent crops due to volatility.

Spray drift

Various post-emergence field replicated trials were set up in France, Germany and the UK in 2010 and 2011 (French CEB method n° 212) to evaluate the safe distance (buffer zone) to be advised on labels to avoid damaging adjacent susceptible crops. XDE-729 methyl was used as GF-2573 (7.5 g a.e/L).

Autumn 2010 trials were set up to evaluate the risks to neighboring autumn sown crops.

- Tested crops were oil seed rape, field beans and winter fodder peas.
- XDE-729 methyl was applied at 2 to 6 leaf stage of the crops.
- XDE-729 methyl was applied at the following rates (calculated in consideration to a maximum rate of 7.5 g a.e/ha, according to the supported GAP):
 - 0.0150 g a.e/ha (corresponding to a 15 m buffer zone)
 - 0.0225 g a.e/ha (corresponding to a 10 m buffer zone)
 - 0.045 g a.e/ha (corresponding to a 5 m buffer zone)
 - 0.075 g a.e/ha (corresponding to a 3 m buffer zone)
 - 0.3 g a.e/ha (corresponding to a 1 m buffer zone)
 - 0.6 g a.e/ha

The visual injury results which were assessed allowed drawing the following conclusions:

- A 1 m safe distance is required when spraying XDE-729 methyl to winter cereals close to:
 - oilseed rape, winter fodder peas.
- A 3 m safe distance is required when spraying XDE-729 methyl to winter cereals close to:
 - field beans.

Spring 2010 and 2011 trials were set up to evaluate the risks to neighboring spring sown crops.

- Tested crops were fodder peas, soybean, sunflower, sugar beets, spring oil seed rape, transplanted vines, onions, flax, lentils and corn.
- XDE-729 methyl was applied at 2 to 4 leaf stage of the crops.
- XDE-729 methyl was applied at the following rates (calculated in consideration to a maximum rate of 6 g a.e/ha, according to the supported GAP):
 - 0.012 g a.e/ha (corresponding to a 15 m buffer zone)
 - 0.018 g a.e/ha (corresponding to a 10 m buffer zone)
 - 0.036 g a.e/ha (corresponding to a 5 m buffer zone)
 - 0.06 g a.e/ha (corresponding to a 3 m buffer zone)
 - 0.24 g a.e/ha (corresponding to a 1 m buffer zone)
 - 0.48 g a.e/ha

The visual injury results which were assessed allowed drawing the following conclusions:

- A 1 m safe distance is required when spraying XDE-729 methyl to winter cereals close to:
 - spring oil seed rape, onion, flax, corn, sunflower, sugar beets.
- A 3 m safe distance is required when spraying XDE-729 methyl to winter cereals close to:
 - spring fodder peas, soybean, lentils.
- A 5 m safe distance is required when spraying XDE-729 methyl to winter cereals close to:
 - vineyards.

Conclusion: These field results show that safe distances from 1 to 5 m (depending on crops) will be recommended to avoid spray drift damages to adjacent susceptible crops. These 1 to 5 m buffer zone values are very similar to those of most of the herbicides which are currently sold as broad leaved weed killers in cereals. Thus when respecting these recommendations, it is unlikely that XDE-729 methyl will cause any unexpected and unacceptable injuries to adjacent crops due to drift.

1.6.2 Succeeding crops

1.6.2.1 Crop failure

It can happen a farmer has to plough a cereal crop which was recently sprayed with an herbicide, because of unexpected damages to the cereal crop due to frost, flood, insects etc. Several field trials have been set up in 2010 and 2011 to evaluate which crops a farmer can sow after a XDE-729 methyl application. These studies were set up across various EU geographies (France, Germany, UK, Hungary and Denmark), mixing soil types and weather conditions.

XDE-729 methyl was tested at 1X and 2X rates (7.5 and 15 g a.e/ha for autumn applications; 6 and 12 g a.e/ha for spring applications).

➤ Autumn applications of XDE-729 methyl :

In most of the cases, XDE-729 methyl was applied in November and succeeding crops were sown in March-April after ploughing (4-5 months after treatment). XDE-729 methyl was safe to all tested crops, whatever the local conditions. Thus, after an autumn application of XDE-729 methyl, all tested crops (spring barley, spring wheat, spring oil seed rape, maize, sunflower, ryegrass, field beans or peas) can be safely sown after ploughing in spring.

➤ Spring applications of XDE-729 methyl :

XDE-729 methyl was applied either in March or in April. Succeeding crops were sown 1 or 2 months later. Two soil cultivation practices were tested: either plough or minimum tillage before sowing the succeeding crops. Results which have been achieved specify that after a spring application of XDE-729 methyl, it is possible to sow :

- 1 month after application (whatever the soil cultivation practice):
 - Spring wheat
 - Spring barley
 - Maize
 - Faba beans
 - Spring oil seed rape
- 2 months after application (whatever the soil cultivation practice) :
 - Sunflower

Conclusion: In case of unexpected crop failure, XDE-729 persistence in soil is short enough to allow farmers sowing a wide range of frequent crops, after either autumn or spring applications, whatever the soil cultivation practices (plough or minimum tillage).

1.6.2.2 Rotational succeeding crops

When applied to soil and plants, XDE-729 methyl is metabolized to XDE-729 (acid form) first and then to M-757. The susceptibility of various crop species to these three compounds has been evaluated in greenhouse conditions. One study has compared the efficacy of XDE-729 acid vs. XDE-729 methyl to a range of crop species.

Reference report: Davies, J. Determination of the Soil No Observable Effect Level (NOEL) of XDE-729 (GF-2573, 7.5 g a.e/L EC) to a range of rotational spring species. Stockbridge Technology Centre. Unpublished report # STC/10/E572, 9 Dec. 2010. Ref. Bio-15

Another study has compared the efficacy of the M-757 metabolite vs XDE-729 methyl to another range of crop species.

Reference report: Davies, J. Determination of the Soil No Observable Effect Level (NOEL), EC₁₀ and EC₅₀ of XDE-729 and its M-757 metabolite to a range of rotational crop species. Stockbridge Technology Centre. Unpublished report # STC/10/E583, 11 Feb. 2011. Ref. Bio-16

In both studies, compounds were mixed to the soil at different concentrations. Then seeds were sown under controlled conditions. Injuries to plants were regularly assessed after crop emergence.

Comparison of XDE-729 (acid) to XDE-729 methyl:

Table 8: XDE-729 methyl and XDE-729 acid rates (µg ae/kg soil) inducing either no injury at all (NOEL) or 10% injury (EC₁₀), based on visual assessments.

Tested crops	XDE-729 methyl		XDE-729 acid	
	EC ₁₀ (µg ae/kg soil)	NOEL (µg ae/kg soil)	EC ₁₀ (µg ae/kg soil)	NOEL (µg ae/kg soil)
Maize	27.70	15	23.51	15
Sorghum	14.49	5	7.46	<5
Lentil	0.108	0.185	0.033	<0.555
Linseed	0.119	0.555	0.0016	<0.555
Oilseed rape	3.07	0.555	1.28	0.555
Potato	2.77	1.666	0.663	<0.555
Soybean	1.27	0.185	0.647	<0.555
Sugar beet	1.15	0.185	0.60	<0.555
Sunflower	2.64	0.0617	2.54	1.666
Tomato	3.65	0.555	2.83	1.666
White clover	0.054	0.0206	0.00002	<0.555

Note: The range of rates tested in these studies did not allow calculating all NOEL values accurately.

Conclusions:

- In most of the cases, the acid form of XDE-729 was slightly more injurious than the XDE-729 methyl ester. However the herbicidal activities of both compounds are of a similar magnitude.
- The most susceptible species to both XDE-729 methyl and its acid form were linseed and legume crops (lentil, soybean and white clover). Grass crops such as maize and sorghum were tolerant to both XDE-729 methyl and its acid form.

Comparison of M-757 (first XDE-729 metabolite) to XDE-729 methyl:

Table 9: XDE-729 methyl and its M-757 metabolite injury levels, when incorporated at 5 µg ae/kg of soil, based on visual assessments 35 days after crop emergence.

Tested crops	% injury* (35 days after crop emergence)	
	XDE-729 methyl (at 5 µg ae/kg of soil)	M-757 metabolite (at 5 µg ae/kg of soil)
Oilseed rape	14	0
Soybean	69	0
White clover	100	0
Sugar beet	79	0
Onion	82	0
Carrot	100	0
Linseed	100	0

* 0= no injury, 100= plant death

** Note: 5 µg ae/kg of soil corresponds to a field rate of 7.5 g a.e/ha, assuming a soil density of 1.5 and a uniform incorporation of the active substance within the top 10 cm of soil.

Conclusions:

- Data from this study demonstrate that the test species chosen were susceptible to the parent XDE-729 methyl (except oilseed rape). At the 35 day assessment, plants growing in soil treated with 5 µg ae/kg of soil concentration of XDE-729 methyl were exhibiting between 69 and 100% visual injury (except oil seed rape, 14% injury only).
- In comparison the M-757 metabolite at the 5 µg ae/kg of soil concentration did not induce any injury to any crop, clearly demonstrating a lack of herbicidal activity against a range of sensitive test species from M-757.
This demonstrates that M-757, the primary metabolite, would pose a very low probability of causing injury to non-target plants. XDE-729 is not a “pro-herbicide” that degrades to herbicidally active compounds.

The overall conclusion of these two studies is that the potential impact on following crops may come from XDE-729 methyl or from XDE-729 acid, and not from the primary soil metabolite, M-757.

Field results: Risks to succeeding crops, after XDE-729 methyl applications in cereals.

The first carry over trials were set up in Europe in autumn 2008. Since then, many field trials have been set up every autumn and every spring to evaluate the risk of XDE-729 methyl uses across EU countries to key succeeding crops, when applied to cereals.

In all trials, after cereal harvest, the straw was incorporated to soil before sowing the succeeding crops. This precautionary approach was decided from the very first carry over trial set up in 2008, taking into account the unlikely case that there are some remaining herbicidal residues in straw at harvest. In practice, since that date, the applicant stated that this precautionary approach was not necessary as cereal straw at harvest does not contain any herbicidal residue level which can induce any problem to crops sown where this straw is incorporated to soil.

Detailed field results will be presented in the zonal Biology Assessment Dossiers. This document only presents an up to date summary of the potential risks and label restrictions.

- Autumn applications of XDE-729 methyl (7.5 g a.e/ha according to supported GAP)

XDE-729 methyl was applied to winter cereals at tillering stage from October to December.

- Succeeding autumn crops were sown after minimum tillage (most frequent farmer practice) about 7-12 months after application:
 - Grasses: winter wheat, winter barley, rye-grass.
 - Cruciferae: winter oil seed rape, mustard (catch crop).
 - Legumes: field bean, clover, soybean (double crop).
- Succeeding spring crops were sown after plough (most frequent farmer practice) about 15-18 months after application:
 - Grasses: maize, spring barley, spring oat.
 - Cruciferae: spring oil seed rape
 - Compositae: sunflower
 - Solanaceae: potato
 - Chenopodiaceae: sugar beet
 - Alliaceae: onion
 - Papaveraceae: poppy (*Papaver somniferum*)
 - Legumes: field bean, fodder pea, lentil, clover, soybean (double crop).

Conclusion: None of the tested crops were visually injured after an autumn application of XDE-729 methyl at 7.5 g a.e/ha. Thus, after an autumn application of XDE-729 methyl at 7.5 ga.e/ha, all tested succeeding crops can be sown without any restriction.

- Spring applications of XDE-729 methyl (6 g a.e/ha according to supported GAP)

XDE-729 methyl was applied to cereals from tillering to BBCH 45 growth stages, from February to May depending on geographies.

- Succeeding autumn crops were sown either after minimum tillage or after plough, about 3-6 months after application:
 - Grasses: winter wheat, winter barley, rye-grass
 - Cruciferae: winter oil seed rape, mustard (catch crop), transplanted cabbage (broccoli)
 - Compositae: sunflower (double crop)
 - Solanaceae: transplanted tomato, potato (double crop)
 - Alliaceae: onion, leek
 - Linaceae: flax
 - Umbelliferae: carrot
 - Legumes: field bean, alfalfa, lentil, clover, soybean (double crop)

The majority of the above crop species were selected because they were considered as the most susceptible species to XDE-729 methyl in the greenhouse soil NOEL studies.

Conclusion regarding the autumn crops sown after a spring application (this corresponds to the shortest 3-6 month interval tested):

➤ Soil ploughed before sowing:

None of the tested crops were visually injured after a spring application of XDE-729 methyl at 6 g a.e/ha.

Thus, after a spring application of XDE-729 methyl at 6 g a.e/ha, all tested succeeding crops can be sown after ploughing without any restriction.

➤ Minimum tillage before sowing:

- Some visual injuries (growth inhibition) were assessed to the following legume crop species (clover and double crop soybean only). Legumes appear to be the most susceptible botanic family to XDE-729 methyl and these results are consistent with the preliminary greenhouse screening studies.

However, susceptibility variations have to be noted amongst the large family of legume crops, as there was no injury to field beans and alfalfa, which can be sown after harvest in autumn after a spring application of XDE-729 methyl at 6 g a.e/ha.

- There was no visual injury to all other tested species (except for clover and double crop soybean).

Thus, after a spring application of XDE-729 methyl at 6 g a.e/ha, all tested succeeding crops can be sown in summer or autumn after harvest and minimum tillage, except clover and soybean.

- Succeeding spring crops were sown after plough (most frequent farmer practice) about 10-12 months after application:
 - Grasses: maize, spring barley, spring oat
 - Cruciferae: spring oil seed rape
 - Compositae: sunflower, chicory Witloof
 - Solanaceae: potato
 - Chenopodiaceae: sugar beet
 - Alliaceae: onion
 - Papaveraceae: poppy (*Papaver somniferum*)
 - Linaceae: flax
 - Legumes: fodder pea, lentil, clover, soybean

Conclusion regarding the spring crops sown after a spring application (this corresponds to a 10-12 months interval):

- None of the spring crops sown 10-12 months after a XDE-729 methyl spring application at 6 g a.e/ha was visually injured. Thus, after a spring application of XDE-729 methyl at 6 g a.e/ha, all tested succeeding spring crops can be sown 10-12 months after application without any restriction.
- Some of these trials were harvested. There was no yield penalty at all to any tested crop (field bean, sugar beet, potato).

As an overall conclusion, after a spring application of XDE-729 methyl at 6 g a.e/ha, even applied at the latest growth stage (BBCH 45) which is supported in GAP, all tested crop species can be sown after harvest and any soil cultivation practice, either in autumn or in spring. There are two exceptions: Clover and double crop soybean which can be sown just after cereal harvest (in summer or autumn) only after ploughing.

- Autumn followed by Spring applications of XDE-729 methyl (7.5 followed by 6 g a.e/ha)

As the proposed supported GAP includes the possibility to apply XDE-729 methyl both in autumn and spring during the same growing season of winter cereals, studies have been conducted to determine whether the carry over profile of a spring application of XDE-729 methyl at 6 g a.e/ha is modified by a previous autumn application of XDE-729 methyl at 7.5 g a.e/ha.

These trials were carried out in various EU geographies (across the three zones) to the same crops as above.

Conclusion: An autumn application of XDE-729 methyl at 7.5 g a.e/ha does not increase the potential of injury of a spring application of XDE-729 methyl at 6 g a.e/ha to

succeeding crops. The restrictions to succeeding crops are only driven by the spring applications of XDE-729 methyl. Thus the same restrictions to clover and double crop soybean sown after harvest and minimum tillage remain valid (See above paragraph).

This chapter has analyzed the risks to succeeding crops after XDE-729 methyl applications to cereal crops, according to the supported GAP. This analysis clearly demonstrates that XDE-729 methyl applied according to the GAP with the highest potential for succeeding crop injury does not have any unacceptable effects on succeeding crops (normal rotations or crop failures). The anticipated very rare and limited restrictions cannot be considered as “unacceptable effects”.

1.7 Possible occurrence of the development of resistance or cross-resistance

Reference reports:

- Satchivi, N, et al. Response of herbicide resistant corn poppy (*Papaver rhoeas*) to application of XDE-729 methyl ester. Unpublished Dow AgroSciences report number DAI 1072, 1 Nov 2011. Ref. Bio-12
- Riches, C. XDE-729 *Papaver Rhoeas* baseline monitoring –Europe 2010. Dow AgroSciences study Id EA10D2C071. AgHerba Consultants UK, July 2011. Ref. Bio-13

A total of 14 auxinic herbicides are currently registered in the European Union for the control weeds species in a range of crops including cereals and grasslands. Many of these herbicides have been on the market for decades. Despite the length of time these herbicides have been on the EU market, resistance to this class of herbicide is still relatively low. Especially when compared to high risk groups such as the ALS herbicides.

In Europe, two annual broadleaf weed species have developed significant resistance to auxinic herbicides: *Stellaria media* to mecoprop in the UK and *Papaver rhoeas* to 2,4-D (and MCPA) in Spain and Italy.

Considering the length of time these auxinic herbicides have been on the market, their wide geographic spread of use and a relatively low number of confirmed cases of resistance, this chemistry can be considered to be a low risk in terms of resistance developing.

Two glasshouse studies were conducted to provide data on the resistance profile of XDE-729 methyl and to generate baseline data. The test species used in these studies was *Papaver rhoeas* because it is susceptible to XDE-729 methyl and there are many EU biotypes which are resistant to either sulfonylureas, or to 2,4-D or to both sulfonylureas and 2,4-D. A summary of these studies is given below.

A more detailed summary, including data on *Stellaria media* and *Galium aparine*, plus field data will be presented in the zonal biology dossiers, document M3, chapter IIIA.6 (“Efficacy data and information”).

In the first of these studies conducted by Satchivi et al, seven *P rhoeas* biotypes from locations in Northern Spain, with reported poor efficacy to either 2, 4-D or tribenuron-

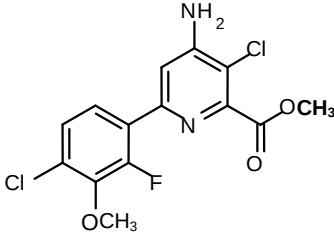
methyl (sulfonylurea, ALS mode of action) were tested with XDE-729 methyl formulated as GF-2353 (XDE-729 methyl, 95.94 g a.e/L SC). Other treatments in this study included 2,4-D amine, mecoprop-P amine, MCPA amine, florasulam, thifensulfuron-methyl and tribenuron-methyl. Data presented in this report demonstrated resistance to 2,4-D applied at 1600 g ae /ha in four Spanish biotypes.

XDE-729 methyl applied at the purposed maximum registered rate of 7.5 g a.e/ha to the same populations achieved between 82 and 90 % control. The absence of cross resistance between 2,4-D and XDE-729 methyl can be explained by the difference of the perception of both types of auxinic herbicides at the molecular level. In the study previously discussed by Walsh et al (description of biochemical and biological mode of action) it was indicated that 2,4-D and the picolinic herbicide DAS534 do not bind to the same receptors. Thus differential binding between XDE-729 methyl and 2,4-D could explain why 2,4-D resistant biotypes of *Papaver rhoeas* were susceptible to applications of XDE-729 methyl.

In the second study conducted by Riches C. of Agherba, twenty one biotypes of *P. rhoeas* collected from sites throughout Europe (Belgium, France, Germany, Greece, Hungary, Italy, Spain and the UK) were used to establish the baseline sensitivity of XDE-729 methyl to *P. rhoeas*. The study also evaluated potential cross resistance between 2,4-D and ALS resistant biotypes.

Data from this study demonstrated consistent control of all 21 biotypes by XDE-729 methyl, with a maximum of a 3 X variation for both the ER₅₀ and ER₈₀ values based on percent visual control. The study also demonstrated no cross resistance between XDE-729 methyl and the ALS herbicide tribenuron-methyl and auxinic herbicide 2,4-D, with good control (> 78 %) of all 2,4-D and ALS resistant biotypes by XDE-729 methyl applied at 6 g a.e/ha, 28 days after application

SUMMARY OF EFFECTIVENESS AND CROP SAFETY DATA SUPPORTING EFFICACY

Active substance	XDE-729 methyl
Chemical name (IUPAC)	Methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl) pyridine-2-carboxylate)
Chemical structure	
Chemical family	6-arylpicolinate herbicide
Mode of action	XDE-729 methyl is a member of the pyridine-carboxylic family of herbicidal auxins (group O) and results in typical auxinic symptoms of herbicide damage. As a member of the group O herbicides it has been shown to control ALS (group B) resistant <i>Papaver rhoeas</i> .
Absorption and translocation	Following post-emergence application XDE-729 methyl will undergo de-esterification to release the activity moiety (XDE-729 acid form). The acid can then be translocated throughout the plant via the phloem. Evidence has also been provided to demonstrate that XDE-729 can also be taken into the plant via the root system.
Crop tolerance	Winter and spring cereals (wheat, durum wheat, spelt, barley, rye, triticale – except oats) show excellent tolerance to XDE-729 methyl applied from BBCH 09 to BBCH 45 at projected label rates (7.5 g a.e/ha in autumn, 6 g a.e/ha in spring), when a safener (cloquintocet-mexyl) is used in the formulated product.
Weed control	When autumn applied in winter cereals XDE-729 methyl controls a range of annual broad leaved weed species: - <i>Centaurea cyanus</i> - <i>Galium aparine</i> - <i>Geranium spp</i> - <i>Lamium spp</i> - <i>Papaver Rhoeas</i> - <i>Stellaria media</i> - <i>Veronica spp</i> When spring applied in winter cereals XDE-729 methyl controls a range of annual broad leaved weed species: - <i>Chenopodium album</i> - <i>Fumaria officinalis</i> - <i>Galium aparine</i>

	- <i>Geranium spp</i> - <i>Lamium spp</i> - <i>Papaver Rhoeas</i>
Minimum Effective Dose	Autumn uses: the 7.5 g a.e/ha rate of XDE-729 methyl provides acceptable levels of control of <i>Stellaria media</i> and <i>Veronica spp</i> Spring uses: the 6 g a.e/ha rate of XDE-729 methyl provides acceptable levels of control of <i>Papaver Rhoeas</i>
Neighboring crops	Volatility: XDE-729 methyl does not present a risk to susceptible adjacent crops. Spray drift: depending on crops a safe buffer zone of 1 to 5 m is recommended to avoid injuries to susceptible adjacent crops.
Crop rotation	XDE-729 methyl rapidly degrades and residues in the soil generally do not persist long enough to injure crops the following season. It requires adequate moisture and temperature for breakdown to occur.

RMS assessment

Regulation (EC) No 1107/2009 is divided into Chapter II on the approval of active substances and Chapter III on the authorisation of plant protection products containing approved active substances.

Regulation (EC) No 1107/2009 states in Chapter II, Article 4(3), that ‘a plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use, shall meet the following requirements: a) it shall be sufficiently effective and c) it shall not have any unacceptable effects on plants or plant products. The Regulation also states in article 8 that a summary dossier shall include information with respect to one or more representative uses on a widely grown crop in each zone of at least one plant protection product containing the active substance, demonstrating that the approval criteria provided for in Article 4 are met i.e. Sufficiently effective and with no unacceptable effects on plants or plant products.

XDE-729 methyl is a new active substance belonging to a new family of 6-arylpicolinate herbicides. XDE-729 methyl is a member of the pyridine-carboxylic family of herbicidal auxins (HRAC Group O).

XDE-729 methyl, as GF-2573, is intended for use in winter and spring cereals (wheat, durum wheat, spelt, barley, rye triticale – except oats) for the post-emergence control of a range of broad-leaved weeds. The intended use is post-emergence of the crop from BBCH 10 to BBCH 45. The proposed dose is 7.5 g a.e/ha in autumn and/or 6 g a.e/ha in spring and use is intended in all three EU regulatory zones. This EC formulation contains also 7.5 g ai/L of cloquintocet-mexyl and 750 g/L of methylated seed oil

The applicant provided the results the preliminary testing to demonstrate the absence of insecticidal or fungicidal effects. In addition, the results of preliminary tests were summarised to indicate that XDE-729 methyl requires the use of a safener. Field trials set up in the European Union in 2008-2010 to wheat, durum wheat, spelt, barley, rye and triticale have demonstrated that cloquintocet-mexyl is an effective safener when used at a

1:1 herbicide-to-safener ratio. The cloquintocet-mexyl safener does not prevent crop symptoms in oats, at the currently developed rates of XDE-729 methyl.

The applicant indicated that an adjuvant may be recommended for use with XDE-729 methyl to optimize effectiveness. As a consequence, several XDE-729 methyl containing products developed in Europe will include adjuvants (methylated seed oil or non ionic surfactant). Alternatively, when such an adjuvant cannot be incorporated into the formulation, tank mixing an adjuvant with XDE-729 methyl containing products may be recommended to users. Detailed data are not available to evaluate the claim that effectiveness is increased with the use of an adjuvant and this will need to be considered at the product stage for specific claims.

Data from preliminary screening demonstrated that *Galium aparine*, *Lamium purpureum*, *Papaver rhoeas* and *Stellaria media* are susceptible to post-emergence applications of XDE-729 methyl. Of these species *G. aparine* and *L. purpureum* are the most sensitive to XDE-729 methyl, with *Matricaria chamomilla*, *Veronica persica* and *Viola tricolor* being the most tolerant to post emergence applications of XDE-729 methyl.

The applicant summarised the results of field trials conducted over 2 years in **winter cereals** using an autumn application of GF-2573 applied at 3 to 9 g a.e/ha. The applicant considered the control of *Stellaria media* and *Veronica hederifolia*. Both of these weed species are common targets in cereals in the Northern, Central and Southern EC regulation 1107/2009 work sharing zones.

Results demonstrated an acceptable level of control of both species at the proposed dose of 7.5 a.e/ha. In the control of *Stellaria media* there was some evidence from the 14 trials of a dose response between the proposed dose and lower doses of 4.5 and 6 g a.e/ha. Data were also presented for *Veronica hederifolia* from 19 trials across all zones. GF-2573 at 7.5 g a.e/ha also gave acceptable control of this species although when trials from the Southern zone were considered separately (n=6) there was less evidence of a dose response compared to taking data from across all zones.

The applicant also summarised the results of 7 trials conducted over 2 years in **winter cereals** where GF-2573 was applied in the spring at 3 to 6 g a.e/ha. The applicant considered the effectiveness against *Papaver rhoeas*. This is a major target in the Northern, Central and Southern EC regulation 1107/2009 work sharing zones. Results demonstrated an acceptable level of control of *Papaver rhoeas* at the proposed dose of 6.0 a.e/ha, with some evidence of lower levels of control at 3 and 4.5 g a.e/ha.

Field trials set up in the European Union in 2008-2010 to wheat, durum wheat, spelt, barley, rye and triticale have demonstrated that cloquintocet-mexyl is an effective safener when used at a 1:1 herbicide-to-safener ratio. All laboratory and field studies which were completed have shown that XDE-729 methyl does not present any unacceptable effects on grain quantity and quality (1000 grain weight, protein content etc...). The preliminary processing studies specify that XDE-729 methyl is safe in both bread making and malting / brewery studies.

The applicant also considered other potential unacceptable effects in terms of the risk to adjacent and succeeding crops.

From the information provided by the applicant it appears unlikely that XDE-729 methyl poses a significant risk to adjacent crops due to volatility. In terms of spray drift various post-emergence field replicated trials were set up in France, Germany and the UK in 2010

and 2011 (French CEB method n° 212) to evaluate the safe distance (buffer zone) to be advised on labels to avoid damaging adjacent susceptible crops. XDE-729 methyl was used as GF-2573 (7.5 g a.e/L). These field results show that safe distances from 1 to 5 m (depending on crops) will be recommended to avoid spray drift damages to adjacent susceptible crops.

In terms of the risk of damage to succeeding crops several field trials have been set up in 2010 and 2011 to evaluate which crops a farmer can sow after a XDE-729 methyl application. These studies were set up across various EU geographies (France, Germany, UK, Hungary and Denmark), mixing soil types and weather conditions. XDE-729 methyl was tested at 1X and 2X rates (7.5 and 15 g a.e/ha for autumn applications; 6 and 12 g a.e/ha for spring applications). These trials include a range of crops commonly grown in arable rotations across the EU and indicate that any risks to succeeding crops can be satisfactorily managed using cultivations and appropriate planting intervals.

When applied to soil and plants, XDE-729 methyl is metabolized to XDE-729 (acid form) first and then to M-757. Two studies were established to determine the biological activity of the M-757 metabolite to that of XDE-729 methyl, formulated as GF-2573 (XDE-729 methyl at 7.5 g a.e/L, EC) to consider the biological relevance of M-757. The M-757 metabolite is not considered to be biologically relevant from the results of the preliminary tests submitted.

For approval of an active substance 'a plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use, shall meet the following requirements: a) it shall be sufficiently effective and c) it shall not have any unacceptable effects on plants or plant products'. The applicant has addressed this requirement.

List of reference reports used in the XDE-729 methyl Biology Dossier

Section ¹	Author	Report Date	Title	Source ²	Company Report No.	GLP/GEP Y/N			Owner ³
						N	N	Published Y/N	
								Data Protection Claimed Y/N	
2.A and 6.C Ref. Bio-1	Satchivi, N, Schmitzer, P	12 Aug 2010	Efficacy and selectivity of XDE-729 applied to cereal crops	applicant	DAI 0978	N	N	Y	Applicant
2.A.c Ref. Bio-2	Satchivi, N, et al	12 Aug 2010	Safener effects on the phytotoxicity of XDE-729 to Wheat and Barley	applicant	DAI 0979	N	N	Y	Applicant
2.B Ref. Bio-3	Davis, G E	11 May 2012	Assessment of antifungal potential of X11393729 and X11393728	applicant	DAI 1102	N	N	Y	Applicant
2. C Ref. Bio-4	Wessels, F et al	22 Feb 2012	Insecticidal assessment of X11393729, X11393728 and X11449757	applicant	DAI 1101	N	N	Y	Applicant
3.B Ref. Bio-5	Satchivi, N, et al	10 Aug 2010	Effects of adjuvants on the efficacy and selectivity of XDE-729 applied to cereal crops	applicant	DAI 0981	N	N	Y	Applicant
4 and 4.C Ref. Bio-6	Walsh, T.A, et al	14 Sept 2005	Mutations in an auxin receptor homolog AFB5 and SGT1b confer resistance to picolinate auxins but not 2,4-D or IAA in Arabidopsis	applicant	DAI 0656	N	N	Y	Applicant
4.B and 4.D Ref. Bio-7	DeBoer, G.J, et al	24 May 2011	Understanding metabolism, uptake and translocation of XDE-729 and its methyl ester (XDE-729 ME) in wheat, L purpureum and V. persica and the effect of safener on wheat selectivity.	applicant	DAI 1026	N	N	Y	Applicant
4.B Ref. Bio-8	Brockmann, A, et al	4 July 2011	Standardized bioassay for the determination of ED ₁₀ (NOEL) and ED ₅₀ values for GF-2573 (XDE-729, 7.5 g a.e/L, EC) and selected following crop species.	Agrocheck	EA10D2C069	Y	N	Y	Applicant
4.B Ref. Bio-9	Davis, J	2 Aug 2011	Determination of the foliar No Observable Effect Level (NOEL) of XDE-729 (GF-2573 7.5 g a.e/L EC) to a range of crop species.	STC	EA11D2C077	Y	N	Y	Applicant
4.E Ref. Bio-10	Davis, J	11 Feb 2011	Determination of the soil No Observable Effect Level (NOEL), EC ₁₀ and EC ₅₀ of XDE-729 and its M-757 metabolite to a range of rotational crop species.	STC	EA10D2C067	Y	N	Y	Applicant
4.E Ref. Bio-11	Brougham, K, et al	16 May 2012	Determination of the foliar No Observable Effect Level (NOEL), ED ₁₀ and ED ₅₀ of XDE-729 and its M-757 metabolite to a range of crop species.	applicant	EA11D2C079	Y	N	Y	Applicant
5 Ref. Bio-12	Satchivi, N, et al	1 Nov 2011	Response of herbicide resistant corn poppy (<i>Papaver rhoeas</i>) to application of XDE-729 methyl ester.	applicant	DAI 1072	N	N	Y	Applicant
5 Ref. Bio-13	Riches, J	July 2011	XDE-729 <i>Papaver rhoeas</i> baseline monitoring – Europe 2010	AgHerba consultants	EA10D2C071	Y	N	Y	Applicant
8 Ref. Bio-14	Gifford, J, et al	1 Sept 2011	Volatility of XDE-729 methyl (GF-2573, EC 7.5 g a.e/L) compared to 2,4-D ethyl hexyl ester (GF-1387, EC 600 g a.e/L)	applicant	N/A	N	N	Y	Applicant

¹ Include all relevant Annex points² Where different from applicant³ Applicant company, public etc.

Section ¹	Author	Report Date	Title	Source ²	Company Report No.	GLP/GEP Y/N			
						Published Y/N	Data Protection Claimed Y/N	Owner ³	
8.B.b Ref. Bio-15	Davis , J.	9 Dec 2010	Determination of the soil No Observable Effect Level (NOEL) XDE-729 (GF-2573, 7.5 g a.e/L EC) to a range of rotational spring species	STC	STC/10/E572	Y	N	Y	Applicant
8.B.b Ref. Bio-16	Davis, J.	11 Feb 2011	Determination of the soil No Observable Effect Level (NOEL) EC 10 and EC 50 of XDE-729 and its metabolite to a range of rotational crop species	STC	STC/10/E583	Y	N	Y	Applicant

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