004076

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MEMORANDUM 04-NOV-1984

SUBJECT: Pydrin® 4 Insecticide ULV Concentrate. EPA File No. 201-URT (201-417) Active Ingredient 47.9%. Accession No. 252652. (Generic name is Fenvalerate).

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

Tox Chem. No. 77A

FROM: Albin B. Kocialski, Ph.D.
Section Head, Section VII
Toxicology Branch/HED (TS-769)

ABK 11/2/84

TO: Timothy A. Gardner, Product Manager #17
Insecticide/Rodenticide Branch
Registration Division (TS-767)

11/6/84

THRU: William L. Burnam, Chief
Toxicology Branch
Hazard Evaluation Division (TS-769)

The Shell Oil Company has applied for registration of Pydrin 4 Insecticide ULV containing the active pesticide chemical cyano(3-phenoxy-phenyl)methyl-4-chloro-alpha-(1-methyl-ethyl) benzeneacetate for use on field corn and cotton.

Pydrin 4 is a formulation of fenvalerate intended specifically for ultra-low volume (ULV) application using vegetable oil as the carrier. This formulation which contains 4 lbs. a.i./gal is essentially the same as the currently registered Pydrin 2.4 EC (EPA Reg. No. 201-401) with the differences being Pydrin 4 ULV does not contain the emulsifying agents found in the EC formulation and contains approximately 18.4% more active ingredient. The inert ingredient(s) is cleared under 40 CFR 1001.

The applicant in support of the registration of this formulation has submitted the following acute toxicology data which has been reviewed by Toxicology Branch and classified as to its scientific acceptability.

Study	Classification	Category of Toxicity
AOLD50 - Rat	Guideline	3
ADL50 - Rabbit	Guideline	3
Primary Eye Irritation - Rabbit	Guideline	3
Primary Dermal Irritation - Rabbit	Guideline	3
Dermal Sensitization - Guinea Pig	Guideline	Not a Sensitizer

10/16

The Toxicology Branch is requesting at this time that the registrant submit an acute inhalation study on this formulation.

The Toxicology Branch is also requesting that the following label changes be made:

Delete from the front panel precautionary labeling the following;

"May be irritating to skin, eyes, nose and throat. Causes moderate eye injury. Harmful if swallowed." Insert instead the following - See precautionary statements on side panel.

Delete the statement (See additional precautionary statements on side panel).

Add the following statement to the Hazards to Humans Caution: Avoid inhalation.

Residue Chemistry Branch consideration permitting, Toxicology Branch has no objection to the registration of this formulation for the intended uses.

Attachment: RCB Review: Propst, 4/24/84

OPP:HED:TOX:A.KOCIALSKI:sb 11/1/84 X73710 #5-D20

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

004076

APR 24 1984

OFFICE OF PESTICIDES AND TOXIC SUBSTA

MEMORANDUM

SUBJECT: EPA Reg. No. 201-URT. PYDRIN® 4 ULV Concentrate on field corn and cotton. Accession Number 252652.

FROM: Linda S. Propst, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Linda S. Propst

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: Timothy Gardner, Product Manager #17
Insecticide-Rodenticide Branch
Registration Division (TS-767)

Inert ingredient information may be entitled to confidential treatment

Shell Oil Company has requested to register a new fenvalerate formulation PYDRIN® 4 for use on field corn and cotton. This formulation is intended specifically for ultra-low volume (ULV) application using vegetable oil as the carrier.

Tolerances have been established for residues of the insecticide cyano(3-phenoxy-phenyl)methyl-4-chloro-alpha-(1-methyl-ethyl) benzeneacetate in or on corn fodder and forage at 50 ppm, corn grain at 0.02 ppm, and cottonseed at 0.2 ppm (40 CFR 180.379). According to our records in PP#'s 1F2430 and 2F2598 these corn tolerances have not received favorable recommendations from RCB and TOX Branch due to the absence of studies indicating the toxicity of the photodegradate (SD 54597) of fenvalerate. This degradate may comprise about 4% of the total residue in corn forage and fodder.

PYDRIN® 4 ULV is a mixture of technical PYDRIN (EPA Reg. No. 201-402) 50.9% and [redacted] This formulation which contains 4 lbs active per gallon is essentially the same as the currently registered PYDRIN 2.4 EC with the differences being PYDRIN 4 ULV does not contain the emulsifying agents found in the EC formulation and contains approximately 18.4% more active.

The proposed use pattern on both field corn and cotton entails multiple applications of 0.05-0.20 lb ai/A in non-volatile

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once refined vegetable oils in a total spray volume of 1 or more quarts/acre. Apply as necessary to maintain control of various insects, however, do not exceed a total of 2 lbs active/acre/season for a crop of cotton or 1 lb active/acre/season for field corn. All remaining pertinent labelling for PYDRIN® 4 on cotton and field corn is the same as that for PYDRIN® 2.4 EC on these crops. Corn, cottonseed and soybean oils are exempted from the requirement of a tolerance for use on crops under 40 CFR 180.1001 (c).

With this request for product registration, the registrant has submitted data comparing residues of fenvalerate and the photodegradate (SD 54597) resulting on field corn foliage when treated with the currently registered 2.4 EC formulation using water as the carrier with the 2.4 EC formulation using vegetable oil as the diluent applied ultra-low volume (ULV) and with the proposed PYDRIN® 4 ULV formulation. The plots for these studies were located in North Carolina, Texas, and Mississippi. All field corn received one application using 0.2 lb. active/acre. Although up to 5 applications at that rate are permitted on the label, we consider the data appropriate as most of the observed PHI's were much shorter than the requested 21 days. At each location water (2-5 gal/A) and vegetable oil (1 qt-2 gal/A) were used as carriers. Residues in corn foliage are summarized below.

FORMULATION	DILUENT	PHI	ppm of Pydrin	ppm of SD54597
2.4 EC	Water	0	4.8 - 8.7	<0.01 - 0.02
2.4 EC	Oil	0	1.7 - 7.8	<0.01 - 0.02
4 ULV	Oil	0	1.2 - 7.7	<0.01 - 0.02
2.4 EC	Water	3	3.7 -14.0	0.12 - 0.60
2.4 EC	Oil	3	2.4 -13.0	<0.02 - 0.08
4 ULV	Oil	3	1.6 - 8.5	<0.02 - 0.07
2.4 EC	Water	7	2.2 -12.0	0.05 - 0.51
2.4 EC	Oil	7	3.0 -13.0	0.03 - 0.17
4 ULV	Oil	7	3.1 -12.0	0.02 - 0.15
2.4 EC	Water	14	2.4 - 8.4	0.09 - 0.38
2.4 EC	Oil	14	2.9 -13.0	0.05 - 0.27
4 ULV	Oil	14	3.1 -11.0	0.04 - 0.26
2.4 EC	Water	21	1.6 - 6.2	0.08 - 0.60
2.4 EC	Oil	21	1.9 - 7.7	0.08 - 0.38
4 ULV	Oil	21	3.2 - 8.2	0.08 - 0.31

There was no data submitted which compared residues of fenvalerate on cottonseed resulting from the use of PYDRIN® 4 ULV versus residues resulting from the already registered PYDRIN® 2.4 EC.

From the above data we conclude that residues of fenvalerate and the photodegradate resulting on corn from the use of PYDRIN® 4 ULV with vegetable oil as a carrier are not significantly different than those resulting from the use of PYDRIN® 2.4 EC with water or vegetable

oil as a carrier. The 50 ppm tolerance for fenvalerate on corn forage and fodder will be adequate. The corn grain tolerance (0.02 ppm) is also satifactory. We would not expect the carrier to greatly effect residues on the grain as the kernels are protected from the spray by the husks. Since the residue levels resulting on corn foliage are comparable using either the 2.4 EC or the 4 ULV formulation, we have no reason to anticipate higher residues on cottonseed when using the 4 ULV formulation. Therefore, we are willing to transfer residue data from corn foliage to cotton and conclude that the established tolerance of 0.2 ppm on cottonseed is adequate to cover all residues of fenvalerate which may occur when using the 4 ULV formulation on cotton. Regarding the photodegradate, however, the absence of toxicity studies has prevented a final decision by TOX concerning allowable levels of this breakdown product in food items (A. Kocialski, 6/24/83, PP#1F2430). Therefore we recommend against the proposed registration of this new fenvalerate formulation until the photodegradate issue has been resolved.

CONCLUSIONS AND RECOMMENDATIONS

1. The established fenvalerate tolerances of 0.02 ppm and 50 ppm for corn grain and corn forage/fodder are adequate to cover any residues which might occur from the use of this new formlation.

2. By translating residue data from corn foliage to cottonseed, we conclude that the established fenvalerate tolerance (0.2 ppm) is adequate to cover all residues which might occur from the use of this new formulation on cotton.

3. Due to the absence of toxicity studies for the photodegradate the Residue Chemistry and Toxicology Branches have not given final approval of the fenvalerate tolerances for corn (grain, forage, fodder)

For the reason stated in Conclusion 3 we recommend against the registration of this new fenvalerate formulation PYDRIN® 4 ULV. However, if TOX concludes that the photodegradate is not toxicologically significant, we would have no objection to registering this formulation on field corn and cotton.

cc: R.F., Circu, Linda S. Propst, Subject File, Amended Use File
RDI: A.R.Rathman, 4/24/84; R.D.Schmitt, 4/24/84
TS-769:RCB:LSP:lsp:CM#2:Rm 810:2/24/84

SUBJECT: (AOLD50- Rat). Rat Acute Oral Toxicity of Pydrin 4 0S

TEST COMPOUND: Pydrin 4 Insecticide ULV Concentrate

SYNONYMS: Pydrin 4 0S
SD-43775 4 0S

EPA REG. No. 201-URT
201-417

ACCESSION No. 252652

FORMULATION: Active Ingredient
(Technical Pydrin) 50.9%

CONFIDENTIAL

Inert Ingredient

CBI removed

CONFIDENTIAL

TESTING FACILITY: Stillmeadow, Inc., Houston, Texas

PROJECT No. 2968-83

REPORT SUBMITTED TO SPONSOR: May 10, 1983

CLASSIFICATION: Guideline

TOXICITY CATEGORY: Category III

Materials and Methods:

Thirty male and 30 female young adult rats, in good health, of the Blu (SD) strain were obtained from the Blue Spruce Farms of Altamont, New York. Animals were housed one per cage, received food and water ad libitum and were acclimated to laboratory conditions. Prior to the day of dosing the animals were weighed, randomly allocated to six treatment groups and fasted for 16-20 hours. Food was again made available ad libitum at 1.0 hour post-dosing. Control animals received 5.0 ml/kg of deionized water and test animals were administered the test material undiluted.

Observations for mortality and pharmacologic/toxicologic effects were made hourly for the first 6 hours post-treatment and twice daily thereafter for 14 days. Individual body weights were recorded prior to fasting, at dosing, on days 7 and 14 or at the time of discovery after death.

A gross necropsy examination was conducted on each animal at sacrifice or at the time of discovery after death.

Results:

Dose levels and deaths were as follows:

Dose (ml/kg)*	Number Dead/Number Treated Males	Females	Combined
0.00	0/5	0/5	0/10
0.56	1/5	2/5	3/10
1.00	1/5	0/5	1/10
1.80	3/5	1/5	4/10
3.20	3/5	2/5	5/10
5.60	5/5	4/5	9/10

* (Density approximately 1.0 gm = 1.0 ml)

Signs in males were generally manifested within 1-3 hours post-dosing, depending upon dose, and were still evident 2-5 days post dosing. Signs in females were generally manifested within 1-3 hours post-dosing, depending upon dose and persisted 3-6 days post-dosing. Prominent in life signs observed in either sex consisted of activity decrease, ataxia, body tremors, chromodacryorrhea, convulsions, diarrhea, difficulty walking, dilated pupils, lacrimation, piloerection, polyuria, salivation, sensitivity to touch, squirming and unusual hind limb extention. Test animals that died generally expired within 1-4 days of receiving the test compound. Males died within 1-2 days with females dying later. Signs, severity of signs and deaths increased with dose.

Gross necropsy revealed no observable abnormalities for those animals which survived the 14 day observation period. However, of those animals dying during the course of the experiment the following findings were considered compound related - chromodacryorrhea, diarrhea, epistaxis, lacrimation, polyuria and salivation; discolorations of the adrenal glands and liver, discoloration of the contents of the stomach and the intestine, adrenal gland encased in a sac of red liquid,

small intestine distended with gas, urinary bladder completely full, testes drawn into abdominal cavity, discoloration of the contents of the urinary bladder.

Body weight gains for males in treated groups, with the exception of the high dose group were comparable to controls. Body weight gains for females were comparable for the low and low-mid dose tested but then decreased 10-15 grams at the higher doses.

Conclusions: Males:

LD_{50} = 1.6 ml/kg 95% CL = 0.83-3.25 ml/kg

Slope = 1.05

Females:

LD_{50} = 3.5 ml/kg 95% CL = 1.17-10.72 ml/kg

Slope = 0.56

Combined Sexes:

LD_{50} = 2.21 ml/kg 95% CL = 1.25-3.92 ml/kg

Slope = 0.76

Classification: Guideline

Toxicity Category: Category III

NOTE: 1.0 ml/kg equivalent ot 1.0 gm/kg.

SUBJECT: ($ADLD_{50}$-Rabbit). Acute Dermal Toxicity of Pydrin 4 OS

TEST COMPOUND: Pydrin 4 Insecticide ULV Concentrate

SYNONYMS: Pydrin 4 OS
SD-43775 4 OS

EPA REG. No. 201-URT
201-417

ACCESSION No. 252652

FORMULATION: Active Ingredient ----- 50.9%
Inert Ingredient

CONFIDENTIAL CONFIDENTIAL

CBI removed

TESTING FACILITY: Stillmeadow, Inc.

PROJECT No. 2857-83

REPORT SUBMITTED TO SPONSOR: February 11, 1983

CLASSIFICATION: Guideline

TOXICITY CATEGORY: Category III

MATERIALS AND METHODS: Male and female albino rabbits of the New Zealand White strain, in good health, were individually housed and acclimated to laboratory conditions prior to testing. The back of the trunk of each animal was then clipped free of hair to expose an area 12 x 17 centimeters. Sixteen males and 16 females were then divided into 4 groups of 4 males and 4 females per group. Eight males and 8 females were given epidermal abrasions deep enough to penetrate the stratum corneum but not deep enough to penetrate the underlying derma or cause bleeding. The remaining animals remained unabraded.

Group II animals (Test Group 8 males and 8 females) were treated with 2.0 ml/kg (equivalent to 2.0 grams/kg) of actual undiluted test material. The test material was applied to a surgical gauze patch and then placed on the skin of the exposure area. The trunk of each animal was then wrapped with polyethylene film and secured in place with an ACE bandage. Group I animals (controls) were treated in the same manner but received only 2.0 ml/kg of deionized water.

Twenty-four hours after treatment all material was removed and the exposure areas gently wiped to remove the remaining test material.

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Observations for pharmacologic/toxicologic effects and mortality were made at 1, 2, 4, 6 and 24 hours post-treatment and twice daily thereafter through Day 14. Individual body weights were recorded on Days 0, 7 and 14. A gross necropsy examination was conducted on each animal at termination.

Observations for erythema and eschar formation, edema formation or other dermal effects were recorded immediately after the 24 hour exposure period and at 14 days post-treatment. Scoring was done according to the method of Draize.

RESULTS:

No animals died prior to the time of terminal sacrifice. There were also no observable abnormalities at the time of necropsy. All control animals appeared normal during the 14 day observation period.

The prominent in life sign manifested was poor hind limb co-ordination for both sexes in abraded and intact groups. The majority of animals were affected in both groups with a longer duration observed in animals whose skin was abraded. The number of animals affected in all groups decreased with time with effects being absent by day 14. Decreased defecation and diarrhea were also observed but generally appeared to be minor effects, and may not have been compound related even though these effects were not observed in controls.

The combined erythema and edema scores in controls at 24 hours for intact and abraded skin was 1.06 (0.88 and 1.25) and 1.19 (1.25 and 1.13) respectively. Recorded scores at 14 days were zero.

The combined erythema and edema scores in treated animals at 24 hours for intact and abraded skin was 1.81 (1.63 and 2.00) and 2.94 (3.00 and 2.88) respectively. Recorded scores at 14 days were zero.

Body weights were comparable between all groups at termination.

CONCLUSIONS: ADLD$_{50}$ is greater than 2.0 gms/kg.

The compound is considered a mild to moderate irritant under the test conditions.

CATEGORY OF TOXICITY: Category III

CLASSIFICATION: Guideline

D

SUBJECT: Primary Skin (Rabbit) Irritation of Pydrin 4 OS

TEST COMPOUND: Pydrin 4 Insecticide ULV Concentrate

SYNONYMS: Pydrin 4 OS
SD-43775 4 OS

EPA REG. No. 201-URT
201-417

ACCESSION No. 252652

CONFIDENTIAL

FORMULATION: Active Ingredient ----- 50.9%
Inert Ingredient

CONFIDENTIAL

CBI removed

TESTING FACILITY: Stillmeadow, Inc.

PROJECT No. 2859-83

REPORT SUBMITTED TO SPONSOR: January 20, 1983

CLASSIFICATION: Guideline

TOXICITY CATEGORY: Category III

MATERIALS AND METHODS: Three male and 3 female rabbits of the New Zealand White strain, were obtained from the Ray Nichols Rabbitry in good health and acclimated to laboratory conditions for 14 days. Twenty-four hours prior to treatment the back of each animal was clipped free of hair to expose an area 12 x 17 centimeters. Each animal was then abraded by making 2 longitudimal and 2 intersecting lateral epidermal abrasions 2 centimeters apart on 2 of the 4 skin sites selected for testing. The incisions made with a needle were deep enough to penetrate the stratum corneum but not deep enough to penetrate into the derma.

Each test site was treated with 0.5 ml of undiluted test material and covered with a surgical gauze patch. The gauze was then covered with polyethylene film and secured with an ACE bandage.

Twenty-four hours later any remaining residue was removed and the test sites scored according to the method of Draize. Test sites were again scored at 72 hours and on Day 7.

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RESULTS: Tabulation of scores for 24 and 72 hours resulted in a value of 2.92.

CONCLUSIONS: The formulation is considered mildly irritating under test conditions.

CLASSIFICATION: Guideline

CATEGORY OF TOXICITY: Category III

004076

SUBJECT: Rabbit Eye Irritation of Pydrin 4 OS

TEST COMPOUND: Pydrin 4 Insecticide ULV Concentrate

SYNONYMS: Pydrin 4 OS
SD-43775 4 OS

EPA REG. No. 201-URT
201-417

ACCESSION No. 252652

FORMULATION: Active Ingredient ----- 50.9%
Inert Ingredient

CONFIDENTIAL

CBI removed

CONFIDENTIAL

TESTING FACILITY: Stillmeadow, Inc.

PROJECT No. 2858-83

REPORT SUBMITTED TO SPONSOR: January 26, 1983

CLASSIFICATION: Guideline

TOXICITY CATEGORY: Category III

MATERIALS AND METHODS: Nine New Zealand White rabbits in good health were obtained from the Ray Nichol Rabbitry housed individually and acclimated to laboratory conditions for 2 weeks prior to testing. Eyes of all animals were examined using a 0.2% fluorescein sodium opthalmic solution. Only those animals without eye defects or irritation were selected for testing. One tenth of one millimeter (0.1 ml) of actual undiluted test material was placed into the conjunctival sac of the right eye of each animal and the lids then gently held together to allow for dispersion of the compound. Three of the 9 treated eyes were each washed with 300 mls. of tap water beginning 30 seconds post-treatment. The untreated left eye served as the comparative control. The treated eyes of all animals were examined and evaluated for irritation at 1, 24, 48 and 72 hours and at 7 and 14 days post-treatment. The corneas of all treated eyes were re-examined immediately after the 24, 48 and 72 hour and Day 7 and 14 observations with 0.2% fluorescein sodium opthalmic solution and rinsing with 20 milliliters of tap water after 5 seconds. Corneas were then re-evaluated using a hand-held black light.

All eyes were scored using the method of Draize.

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RESULTS: Corneal damage was not observed in any rabbit, and the iris (one rabbit showed very mild iritis) for all practical purposes was also unaffected. Conjunctivitis was the primary response elicited. The maximum average score for unwashed eyes was 13.0 and the maximum average score for washed eyes was 8.0.

CONCLUSIONS:

(1) Corneal damage was not observed.

(2) The iris was for all practical purposes unaffected.

(3) Conjunctivitis was evident.

a) Non-washed eye-maximum average score was 13.0
b) Washed eye-maximum average score was 8.0

(4) The formulation can be considered a mild to moderate irritant.

CATEGORY OF TOXICITY: Category III

CLASSIFICATION: Guideline

004076

SUBJECT: Guinea Pig Skin Sensitization of Pyrdrin 4 OS

TEST COMPOUND: Pydrin 4 Insecticide ULV Concentrate

SYNONYMS: Pydrin 4 OS
SD-43775 4 OS

EPA REG. No. 201-URT
201-417

ACCESSION No. 252652

FORMULATION: Active Ingredient ----- 50.9%
Inert Ingredient

CONFIDENTIAL

CONFIDENTIAL

CBI removed

TESTING FACILITY: Stillmeadow, Inc.

PROJECT No. 2860-83

REPORT SUBMITTED TO SPONSOR: February 22, 1983

CLASSIFICATION: Guideline

TOXICITY CATEGORY: Not a sensitizer.

MATERIALS AND METHODS: Forty short-haired young albino guinea pigs, in good health of the Hartley-Albino strain were received from the Cannon Research Laboratory of Wayne, New Jersey. Animals were acclimated to laboratory conditions and had free access to food and water. Animals were housed 5 per cage and segregated by sex.

Four treatment groups were formed with 5 animals per sex per dose. Group 1 served as control and was administered deionized water. Group 2 was treated with 0.1% w/v solution of 2,4-dinitrochlorobenzene in diethyl ether and served as the positive control group. Group 3 animals were treated with undiluted test material. Group 4 animals were treated with undiluted test material and served as an irritation control group. (The undiluted test material was selected from a previous screening study as the highest non-irritating level of test material.)

The animals in Groups 1, 2, and 3 were treated on Days 2, 9, 16 and all groups were treated on Day 30.

Individual body weights were recorded on Days 0, 7, 14, 21, 28 and 35.

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Forty-eight hours prior to each treatment the backs of the animals were clipped free of hair exposing an area 8 x 10 centimeters. Animals were further depilatated 24 hours prior to treatment with Neet® lotion hair remover.

Groups 1, 2 and 3 were treated on Days 2, 9 and 16 by introducing 0.50 mls of the appropriate material beneath a 1.5 x 2.0 inch dressing. The trunk of each animal was then wrapped with clear polyethylene film to secure the patches. Each animal was then placed in a restrainer for approximately 6 hours.

At the end of the exposure period, the animals were removed from the restrainers, the wrappings and patches were removed, and the animals were returned to their cages. The same test site location was used on each animal on all treatment days. On Day 30, all animals (including Group IV animals) were treated in an identical manner as on the previous three treatment days with the addition of a second test site (also receiving 0.5 ml of the appropriate material) placed laterally on the right rear quadrant of the exposure areas.

Observations for skin reactions were made approximately twenty-four and forty-eight hours after each treatment for each test site. A marked increase in positive skin reactions after the Day 30 treatment (final treatment) above those observed after the Day 2 treatment (initial treatment) was indicative of a sensitizing reaction.

RESULTS: The positive control produced the expected sensitizing reaction. The test material did not mainfest a positive sensitizing response under the test conditions. The control and the irritation control groups produced numerically equivalent responses of zero.

Body weights for all groups were comparable.

CONCLUSIONS: Pydrin 4 OS is not a sensitizer under the test conditions.

CATEGORY OF TOXICITY: Not a sensitizer.

CLASSIFICATION: Guideline