Shaughnessy Number: 129001

Date out of EFGWB: FEB 24 1991

To: M. Erumsale-Matzer
Product Manager 23
Registration Division (H7505C)

From: Akiva Abramovitch, Section Head
Environmental Fate Review Section #3
Environmental Fate and Ground Water Branch
Environmental Fate and Effects Division (H7507C)

Thru: Hank Jacoby, Chief
Environmental Fate and Ground Water Branch
Environmental Fate and Effects Division (H7507C)

Attached, please find the EFGWB review of...

Reg./File #: 59639-2

Chemical Name: Clethodim

Type Product: herbicide

Product Name: Select 2-EC

Company Name: Valent U.S.A. Corporation

Purpose: 1) submission of anaerobic aquatic metabolism study

2) request for time extension for spray drift study

Date Received: 10/24/90

Action Code: n.a.

EFGWB#(s): 91-0063

Total Reviewing Time (decimal days): 2

Deferrals to: ___Ecological Effects Branch, EFED

___Science Integration and Policy Staff, EFED

___Non-Dietary Exposure Branch, HED

___Dietary Exposure Branch, HED

___Toxicology Branch

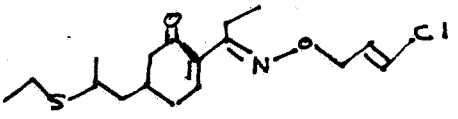
1. CHEMICAL:

chemical name: 2-[1-[[(E-3-chloro-2-propenyl)oxy]-imino]propyl]-5-[2-(ethylthio) propyl]-3-hydroxy-2-cyclohexene-1-one

common name: Clethodim

trade name: Select

structure:



CAS #: not known

Shaughnessy #: 129001

2. TEST MATERIAL: see DER

3. STUDY/ACTION TYPE:

1) submission of anaerobic aquatic metabolism study, *in lieu of* the anaerobic soil study
2) request for time extension for spray drift study

4. STUDY IDENTIFICATION:

Tucker, B.V., **The Anaerobic Aquatic Metabolism of [Ring-4,6-^{14}C] Clethodim**. dated August 29, 1990. performed and submitted by Chevron Chemical Company Agricultural Chemicals Division, Richmond CA. received EPA 10/19/90, under MRID# 416523-01.

5. REVIEWED BY:

Typed Name: E. Brinson Conerly

Title: Chemist, Review Section 3

Organization: EFGWB/EFED/OPP

E. B. Conerly FEB 20 1991

6. APPROVED BY:

Typed Name: Akiva Abramovitch

Title: Section Head, Review Section 3

Organization: EFGWB/EFED/OPP

Akiva Abramovitch FEB 20 1991

7. CONCLUSIONS:

1) The anaerobic aquatic metabolism study will be acceptable to fulfill the requirement for anaerobic aquatic metabolism if some additional information is supplied. If the applicant can supply an acceptable explanation for the choice of Canadian test matrixes, the study will fulfill the requirement for data on anaerobic aquatic metabolism. At that time, it can serve to fulfill the requirement for anaerobic soil metabolism as well. It provides the following information:

Clethodim has a half-life of ca. 150 days (per the applicant) under these conditions. [This reviewer calculates 128 days in the aqueous phase and 214 days in the sediment].

The degradates formed are metabolized approximately as rapidly as they are formed, and do not appear to accumulate.

2) It is general Branch policy to allow the time extension for spray drift data submission which the applicant has requested.

8. RECOMMENDATIONS:

1) The applicant should supply the requested information explaining the choice of Canadian test materials.

2) Sandoz has stated that they are a member of the Spray Drift Task Force and as such have requested a time extension on other spray drift requirements. This time extension should be granted unless there is an immediate need for spray drift exposure information by the human or wildlife toxicologists for clethodim.

It should be noted that for all spray drift data requirements, there is no waiver of the requirements with the participation in the Spray Drift Task Force. All spray drift data requirements will remain in effect as requested. Time extensions for submission of the data must be requested on a product by product basis. (A company or task force may request several product extensions at one time, but each product must be individually identified.) If the EPA feels that certain spray drift information must be made available to the EPA before the final Spray Drift Task Force report(s), those data requirements [for a particular chemical] will be identified for submission with an accelerated time schedule.

9. BACKGROUND:

Clethodim is a post-emergent herbicide with a proposed label use rate of 0.125/0.25 lb ai/A (max. appl. 0.5 lb/season) to control weeds in cotton and soybeans. Known available environmental data for Clethodim depict a compound which is stable to hydrolysis, except in acid conditions, but highly susceptible to photolysis and metabolism. It and its degradates are mobile. At exaggerated treatment rates, some uptake of radiocarbon into confined rotational crops occurred, about 1/3 were closely related degradates and 2/3 from the "carbon pool". Clethodim and degradates do not show persistence in field dissipation studies. No significant bioaccumulation occurs in fish. Under present use patterns, it does not appear to threaten ground or surface water.

The following summarizes the data requirements.

NOT FULFILLED --

Metabolism - Anaerobic Soil -- will be fulfilled by the anaerobic aquatic study discussed in this review, MRID # 416523-01, when satisfactory additional information is received. MRID # 410301-36, previously reviewed, while not acceptable to fulfill the data requirement, does provide some supplemental information, as follows: Anaerobic metabolism takes a distinctly different pathway from that under aerobic conditions. Principal degradates at 31 days were clethodim imine (43.5% of applied) and clethodim imine sulfate (14.3% of applied) , and do not include CO_2. Degradates formed by anaerobic means may persist, as indicated by 63 day values. Clethodim imine represented 33.0% of applied material, and the imine sulfate was 11.2%.

Accumulation -- Rotational Crop, Field -- no data submitted

Spray Drift Field Evaluation -- no data submitted

Droplet Size Spectrum -- no data submitted

FULFILLED -- no further information required

Degradation - Hydrolysis -- **MRID # 409745-20** -- Propyl-labeled [14C]-clethodim degraded with half-lives of 26 days (pH 5) and approximately 300 days (pHs 7 and 9). Allyl-labeled clethodim degraded with half-lives of 42 days (pH 5) and 360 days (pH 7). The major degradates were **clethodim oxazole** and **1-chloropropen-3-ol**.

Degradation - Aqueous Photolysis -- **MRID # 410301-34**, done with Ring - labelled compound and **MRID # 410301-33**, with Allyl-labelled compound:

Ring labelled -- First-order half-lives were 1.5, 6.4, and 9.3 days at pH 5, 7, and 9 respectively for irradiated samples. Corresponding dark controls were 12.5, 99.4, and 330.2 days. Major photoproducts were clethodim sulfoxide, imine, imine sulfoxide, and DME sulfoxide. Minor photoproducts were trione sulfoxide, oxazole, oxazole sulfoxide, and imine ketone. After 30 days the major products remaining are imine sulfoxide and DME sulfoxide. Most photoproducts are rapidly formed and then degraded, except DME sulfoxide. Material balance ranged from 88.2% to 108.1%. Very little volatile material was produced.

Allyl labelled -- First-order half-lives were 1.39, 4.05, and 5.43 days at pH 5, 7, and 9 respectively for the irradiated samples. Dark controls were 20.06, 5042.8, and 60.85 days. The major initial photoproducts were clethodim sulfoxide, chloroallyl alcohol, and 3-chloropropenal, with lesser amounts of oxazole, oxazole sulfoxide, imine, imine sulfoxide, and DME sulfoxide. After 30 days the major products remaining are chloroallyl alcohol and 3-chloropropenal. Most of the photoproducts are rapidly formed and then degraded. Total material balance ranged from 86.8% to 103.5%. Very little volatile material was produced.

Degradation - Soil Photolysis -- **MRID # 410301- 35** -- Photolysis of clethodim on soil will not be a major pathway of degradation, since metabolism is so rapid. Less than 6.8% of parent remained after 7 days. Little or no volatile material, organic or CO_2, was produced. The single major product was clethodim sulfoxide. Minor products ranged from 0.2 to 2.6%. Half-lives of 1.87 and 1.96 days for the dark samples (agreeing with the independent soil metabolism study), and 1.53 and 1.82 days for light samples in two runs were statistically identical. Therefore, the degradates detected were probably metabolites, not photoproducts.

Metabolism - Aerobic Soil -- **MRID # 413768-01** (**ring** and **allyl** labelled) and **MRID # 409745-22** (**propyl** labelled)

Ring and allyl[^{14}C]-labeled incubated at 25°C at initial concentrations of 10 ppm in sandy loam soil degraded with half-lives of ca. 1 day. Degradates at the end of 4 months incubation were: **CO_2** -- 57% of the ring labeled and 45% of the allyl labeled applied radioactivity; **Clethodim sulfoxide** Peaked at 62-72% of applied radioactivity at 3-7 days post-treatment and then declined (half-life approximately 30 days) to 0.2-0.5% of applied at 121 days post-treatment; **Clethodim sulfone**, formed by oxidation of sulfoxide, peaked at 15% of applied at 30 days post-treatment and then declined to 5-7% of applied at 121 days post-treatment.

Propyl-labeled [^{14}C]-clethodim incubated at 25°C at an initial concentration of 10.3-10.7 ppm in a sandy loam soil degraded with half-life of approximately 2.6 days. Degradates were: CO_2 -- 54.4% of the applied radioactivity at the end of the 380 day incubation period; **Clethodim sulfoxide** peaked at 60.7-64.6% of the applied at 7 days post-treatment, decreased to 12.8-16.5% at 62 days, and was ≤0.3% at 120-380 days; **Clethodim sulfone**, formed from the oxidation of the sulfoxide peaked at 10.1-11.7% of the applied at 62 days post-treatment, declined to 3.7-5.0% at 90 days post-treatment, and was ≤ 0.6% at 180-380 days post-treatment.

Mobility - Leaching and Adsorption/Desorption -- **MRID # 409745-23** -- Clethodim and its sulfoxide, sulfone, and oxazole sulfone degradates were weakly adsorbed onto 2 sandy loam soils, a clay loam, a sandy clay loam, and a sandy soil. The following ranges of Freundlich K_{ads} values were reported for the 5 test soils at 25°C: clethodim (0.08-1.6), clethodim sulfoxide (≤ 0.2), clethodim sulfone (≤ 0.1), and clethodim oxazole sulfone (0.3-7.0).

Field Dissipation -- fulfilled -- **MRID # 410302-08** (cotton in California) and **MRID # 410302-07** (cotton in Mississippi) -- Clethodim and its degradates do not persist in California. The parent clethodim was only found at or near the 0.02 ppm limit of quantitation (loq). Both parent and metabolites disappeared rapidly. 21 day samples showed no residues of any kind. No vertical movement of the residues was observed as all measurable residues were confined to the top 20 cm of the soil. Results in Mississippi were similar to those in California. In all cases, the 28 day samples showed no residues of any kind. All measurable residues were confined to the top 20 cm of the soil.

Accumulation -- Confined Rotational Crop -- **MRID # 410302-11** -- lettuce, carrots, and wheat grown as confined rotational crops. Some uptake and concentration were detected at an exaggerated rate of application (4 x the maximum single application). Closely related metabolites accounted for around 1/3 of the total radioactivity observed in the plants. The remaining labelled material may derive from the soil "carbon pool". EGWB understands at this time that the residues which could be expected from use at legal label rates would not be of concern to TOX or Dietary Exposure Branches.

Laboratory Accumulation - Fish -- **MRID #s 409745-31 and 409745-24** taken together -- Maximum bioconcentration factors reported for total[^{14}C]-in bluegill sunfish exposed to 0.06 ppm [^{14}C]clethodim for 28 days at 21°C were 0.7-2.1X for edible tissues, 3.0-4.0X for non-edible tissues, and 2.3-3.6X for whole fish.

10. DISCUSSION OF INDIVIDUAL TESTS OR STUDIES: See individual DERs.

11. COMPLETION OF ONE-LINER: new information added

12. CBI APPENDIX: attached to individual DERs

DATA EVALUATION REVIEW

I. Study Type: 162-3 -- Anaerobic Aquatic Metabolism

II. Citation:

Tucker, B.V., The Anaerobic Aquatic Metabolism of [Ring-4,6-^{14}C] Clethodim. dated August 29, 1990. performed and submitted by Chevron Chemical Company Agricultural Chemicals Division, Richmond CA. received EPA 10/19/90, under MRID# 416523-01.

III. Reviewer:

Typed Name: E. Brinson Conerly E.B. Conerly 2/20/91
Title: Chemist, Review Section 3
Organization: EFGWB/EFED/OPP

IV. Conclusions:

The study is scientifically sound, but, to be acceptable, it requires additional information satisfactorily explaining the choice of Canadian (instead of American) test matrixes. If the applicant can supply the requested information, the study will fulfill the requirement for data on anaerobic aquatic metabolism. At that time, it can serve to fulfill the requirement for anaerobic soil metabolism as well. Clethodim has a half-life of ca. 150 days (per the applicant) under these conditions. [*This reviewer calculates 128 days in the aqueous phase and 214 days in the sediment*]. The degradates formed are metabolized approximately as rapidly as they are formed, and do not appear to accumulate.

V. Materials and Methods:

test compound -- [ring-4,6-^{14}C] clethodim, sp. act. 56.5 mCi/mMol, radiochemical purity 98.4%

analytical methods

LSC

TLC

system A -- chloroform/acetic acid (9/1)
system B -- hexane-acetone-acetic acid

HPLC -- in a water/glacial acetic acid/acetonitrile gradient solvent system

MS

test media

water -- collected from a slough, a "Shallow Open Water Wetland" at a depth of 8 cm below the water surface, approximately 15 m from shore [in Saskatchewan -- EBC]

sediment -- the top 2 - 3 cm of sediment taken from a different location, but at the same distance (15 m) from the shore. Excess water in the sediment was removed by decantation and filtration. Moisture was determined by overnight drying at 110 ^{o}C.

test conditions -- Incubations were run at 5 °C and 25 °C in flow through systems which were flushed with nitrogen throughout. Volatile products (on polyurethane plugs) and $^{14}CO_2$ (in 0.5 n NaOH traps) were collected from the 25 °C samples, and ^{14}C remaining in the water and sediment was determined. Volatiles were not collected from the 5 °C incubations. Each sample (6.1 gm sediment and 75 ml slough water) was fortified at 1 ppm in the water (95 µl of a 0.793 µg/µl solution in methanol).

extraction methods

polyurethane plugs -- extracted with 3 x 50 ml methanol with sonication.

supernatant -- the water/sediment mixture was centrifuged and the supernatant decanted through glass wool. Aliquots of supernatant were acidified to pH 2 to 3 with $NaHSO_4$, then saturated with $(NH_4)_2SO_4$ and extracted 3 x 25 ml methylene chloride. Average recovery was 74%. The methylene chloride was dried over Na_2SO_4, evaporated to dryness and the residue dissolved in methanol. The methanol was concentrated to 1 ml under a stream of nitrogen and filtered. Aliquots of the methanol extracts were analyzed by TLC and MS. Aliquots of representative supernatants were also lyophilized, the residue dissolved in methanol and counted. Average ^{14}C recovered was 79%. Aliquots of the methanol preparation were analyzed by TLC.

sediment

The sediment was extracted for 10" with 100 ml methanol. Unlabelled clethodim was added to the 0, 1, and 3 day samples to minimize degradation during extraction; samples with no additional clethodim were run in parallel. The mixture was centrifuged, decanted through filter paper, and the extraction repeated 2 x (without unlabelled clethodim added to any sample). The methanol extracts were combined, their volumes measured, and duplicate aliquots counted. These extracts were evaporated to a small volume by rotary evaporation; solvent vapors were condensed and collected. The remaining unevaporated liquid was then transferred to conical test tubes and concentrated in a stream of nitrogen. Aliquots of both concentrated pot residues and distillates were counted. Distillates did not contain any radioactivity, and were not examined further. Pot residues were analyzed by HPLC. The sediment from the methanol extraction was then extracted with 3 x 100 ml 10 mM $CaSO_4$, using the same technique as for the methanol extraction, but without unlabelled clethodim. These extracts were combined and counted. The extracted sediment residue following both the above procedures was air dried, then ground to a fine powder. Unextracted ^{14}C was determined by combustion.

VI. Study Author's Results and/or Conclusions:

Clethodim degraded with a half-life of 152 days at 25 °C and 559 days at 5 °C. This degradation was primarily due to microbial action rather than hydrolysis. The total ^{14}C accountability ranged from 89.6 to 107.0 %, with an average of 97.5 %, over the 6 month study interval. Less than 1.0 % of the initial ^{14}C treatment evolved as volatile organic molecules or as $^{14}CO_2$. After 6 months, 55.8 % of the initial ^{14}C treatment was in the aqueous supernatant, 28.3 and 1.3 % were extractable from the sediment by methanol and 10 mM $CaSO_4$,

respectively; and 10.7% was unextracted from the sediment.

The aqueous supernatants and methanol extracts of the sediment were qualitatively and quantitatively analyzed using HPLC with an ultraviolet detector and a radioactive detector in series. Representative samples were analyzed by LC/MS and TLC/autoradiography to confirm the metabolite identifications. The major metabolites were clethodim imine in the sediment and clethodim sulfoxide in the aqueous supernatant. While clethodim decreases from 50 % at 70 days to 30% at 120 days, the sum of the two major metabolites plateaus at about 30%. Thus, the two major metabolites don't accumulate, but are degraded at about the same rate as they form.

These results are in good agreement with an unacceptable previous anaerobic soil metabolism study, where soil was not flooded, but maintained under nitrogen. The soil contained clethodim and clethodim sulfoxide, which were metabolized to clethodim imine and clethodim sulfoxide imine under anaerobic conditions.

Total recovery of ^{14}C ranged from 89.6 to 107.0% with an average of 97.5% over the 6 month study interval. Preliminary studies showed that clethodim can be repidly oxidized to clethodim sulfoxide in the extraction procedure; therefore an excess of unlabelled clethodim was added to a duplicate set of 0, 1, and 3 day samples to minimize the effect on the ^{14}C-clethodim. However, the results show that samples with and without unlabelled clethodim give similar amounts of ^{14}C-clethodim; therefore, the extraction technique was performed in such a manner that clethodim oxidation was minimized.

VII. Reviewer's Comments:

1) The sample matrixes were collected in Saskatchewan, not the United States. EFGWB strongly encourages the use of United States samples for these studies. At minimum, the applicant should indicate what areas of the United States were intended to be represented by this study, and provide a discussion of the rationale for using these matrixes.

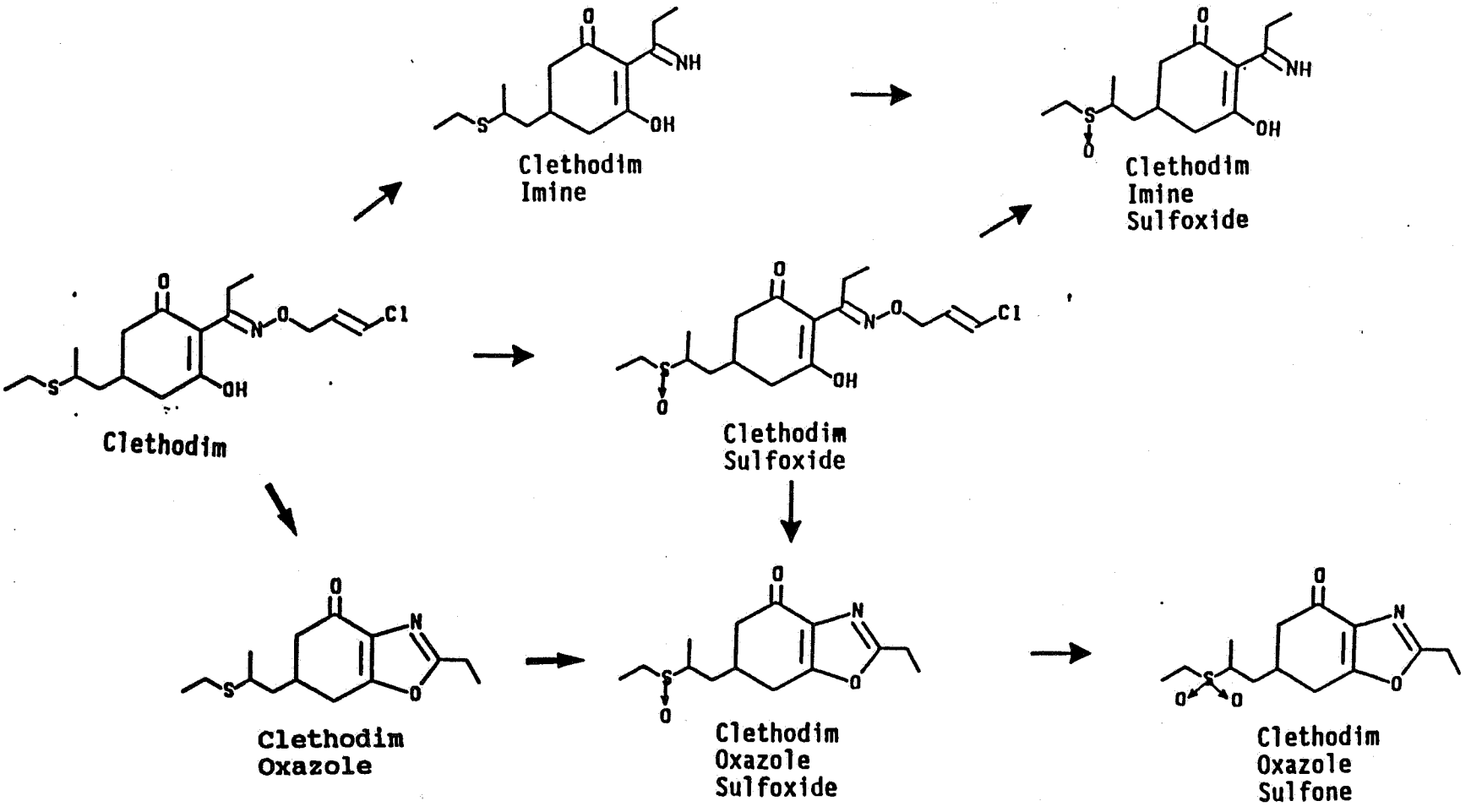
2) This reviewer calculates somewhat different half-lives for supernatant (128 days) and sediment (214 days), but clearly, clethodim is persistent under anaerobic conditions. We note that the decrease in concentration follows a similar time course in both media, and the ratios between aqueous and soil concentrations remain relatively constant (i.e. there is no apparent time-trend evident, indicating that adsorption/desorption is at a steady state and that there is no preferential metabolism favoring one medium over the other). The majority of the clethodim present is found in the aqueous phase at all times.

3) As the applicant has stated, degradates do not appear to accumulate.

4) Aerobic metabolism was studied using propyl and allyl labelled material as well as ring labelled. Although this was not done in the subject study, the metabolic pathway seems to have been sufficiently elucidated.

VIII. CBI Information Addendum: attached

Figure 11. Clethodim Anaerobic Metabolism Pathways



Clethodim environmental fate review

Page _____ is not included in this copy.

Pages 10 through 26 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

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