8EHQ-0794-13097

ORIGINAL

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July 1, 1994

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INIT 07/06/94

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Document Processing Center (7407)
(Attention: Section 8(e) Coordinator)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M St., SW
Washington, DC 20460

Dear Section 8(e) Coordinator:

Subject: TSCA 8(e) Notice - Darocur 1173

Ciba-Geigy Corporation (Ciba) claims no information in this letter as Confidential Business Information.

In accordance with EPA's March 16, 1978 policy statement on Section 8(e) reporting under the Toxic Substances Control Act, and EPA's June, 1991 TSCA Section 8(e) Reporting Guide, Ciba wishes to bring to the attention of the Environmental Protection Agency results seen in a 4-week oral toxicity study conducted with Darocur 1173. Darocur 1173 is 2-hydroxy-2-methyl-1-phenyl-1-propanone, having CASRN 7473-98-5. Darocur 1173 is a photo-initiator used in coating applications.

This study was recently obtained from our parent company, Ciba-Geigy Limited of Basel, Switzerland. A copy of the study, entitled *"Preliminary testing for subacute toxicity in a 4-week experiment on rats with oral application"*, report number 4/105/85 is enclosed (English translation of text sections).

Darocur 1173 was administered by oral gavage to rats at dosages of 0, 30, 100, 300 and 1000 mg/kg/day for 28 days. The target organ was the liver with findings of increased weight at the 2 highest doses. Histopathologic examination showed cell enlargement and proliferation only at the highest dose. Hematology and clinical chemistry measurements were not conducted. The NOEL appears to be 100 mg/kg/day. Based upon current EPA guidelines it is felt these results warrant reporting under TSCA 8(e).

As a result of this new information, Ciba will revise its Material Safety Data Sheet (MSDS) to reflect this information.

Please call the undersigned if you have any questions about this submittal.

Very truly yours,

A. Di Battista

Anthony DiBattista

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Enclosure

8EDA1173.DOC

2

MERCK
E. Merck, Darmstadt

EMD DAROCUR 1173

Report No. 4/105/85

Experiment T 12 821

Title
Preliminary Testing for Subacute Toxicity in a 4-Week Experiment on Rats with Oral Application

Abbreviated Report

Authors: Kieser, H; v. Eberstein, M.

Date: 10 Sep 1985

[Confidentiality Statement, in English]

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DAROCUR 1173 Rat - Subacute Preliminary 4 Weeks - Oral

1. Summary

DAROCUR 1173 has been clinically tolerated up to a daily dose of 1000 mg/kg. Pathological anatomy revealed distinct enlargements of the liver at this dosage. The morphological correlate was liver cell enlargements and peripheral liver cell proliferation. Increased liver weight had already been registered for 300 mg/kg/day. The dose of 1000 mg/kg/day is considered to be toxic, based on the pathomorphological finding.

2. Introduction

DAROCUR 1173 is a product of E. Merck, Darmstadt, used as a photoinitiator for the UV hardening of lacquers. The present experiment is a "dose-range-finding" study in preparation for a 3-month toxicity testing on rats, as required by international authorities.

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3. Experimental Material

DAROCUR 1173
Art. No. 1/7005
Liquid
Delivery No. U 472205
Release Date: 8 Nov 1984 - Nov 1986

4. Experimental Layout

The experiment made use of roughly 5-week old male and female Wistar rats of strain Emd: Wi-AF/Han (SPF) at an average weight of 125 g (male) or 114 g (female) in five groups of six animals each (three male, three female), a total of 30 rats. The experiment was conducted in March/April 1985 at the Institute of Toxicology of E. Merck, Darmstadt, Room U9/108.

The animals were kept under conventional conditions in the approximately 60 m^2 experimental room; room temperature 23-26°C, humidity 55-70%. The animals were placed individually in Makrolon cages Type III with soft wood granules as litter. Feed pellets (Altromin TPF N 1324) and drinking water were available ad libitum.

4.2 Treatment and Dosage

The treatment period covered four weeks. Application was done p.o. (rubber mouth probe) as a suspension in 0.25% aqueous Methocel, once a day, 7 times a week. The application volume was 10 ml/kg.

Dosage		Animal No. Male	Female	Concentration, g/l
Daily Dose per kg BW				
Group 1	0 mg	1-3	16-18	Methocel
Group 2	30 mg	4-6	19-21	3
Group 3	100 mg	7-9	22-24	10
Group 4	300 mg	10-12	25-27	30
Group 5	1000 mg	13-15	28-30	100

A 3% suspension in Methocel proved to be stable when kept 14 days in the refrigerator (up to +8°C).

4.3 Investigations

Behavior and appearance were checked every day. The body weight was determined twice and the food consumption once a week.

24 hours after the last treatment, all animals were stunned with CO_2 and bled. Next, the animals' bodies were weighed, dissected, and investigated in terms of pathological anatomy. Twelve organs were weighed: heart, liver, kidneys, spleen, thymus, testicles or ovaries, prostate or uterus, adrenal glands, thyroid gland, hypophysis, brain, eyes. Liver and kidneys were histopathologically examined.

5. Findings

The increase in body weight and food consumption were normal. The liver weight was increased from Group 4 onward (300 mg/kg/day), the kidney weight in females in Group 5 (1000 mg/kg/day).

The histopathological investigations of the liver in Group 5 revealed circumscribed, centrolobular/intermediary hepatic cell enlargement and moderate to significant peripheral hepatic cell proliferation (especially in females). The increase in organ weight therefore has a morphological correlate.

The kidneys revealed only nonspecific alterations.

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MERCK
E. Merck, Darmstadt

EMD DAROCUR® 1173

Bericht Nr. 4/105/85
Report no. / Rapport n° / Informe no.

Experiment T 12 821
Titel / Title / Titre / Título

Orientierende Prüfung auf subakute Toxizität im 4-Wochen-Versuch an Ratten bei oraler Applikation

Kurzbericht

Autor(en) / Author(s) / Auteur(s) / Autor(es)
Kieser, H.
v. Eberstein, M.

Datum / Date / Date / Fecha 10. September 1985

Vertraulich / Confidential / Confidentiel / Confidencial
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T 12821
TOX LOG 5/1 090885

EMD

DAROCUR® 1173

Bericht Nr.
Report no. / Rapport n° / Informe no.
4/105/85

Experiment T 12821

Titel / Title / Titre / Titulo

Orientierende Prüfung auf subakute Toxizität im 4-Wochen-Versuch an Ratten bei oraler Applikation

Kurzbericht

Wir erklären hiermit, daß diese Arbeiten von uns oder unter unserer Aufsicht gemäß den hier beschriebenen Methoden durchgeführt wurden und daß dieser Bericht die Ergebnisse der Arbeiten vollständig und korrekt wiedergibt.

We hereby declare that this study was carried out by us or under our supervision in accordance with the methods described herein and that this report reflects the results obtained fully and faithfully.

Nous certifions que ces travaux ont été effectués par nous ou sous notre direction, selon les méthodes décrites ici, et que ce rapport reproduit intégralement et correctement les résultats obtenus.

Declaramos que estos trabajos se realizaron por nosotros o bajo nuestro control y conforme con los métodos aquí descritos, y que en este informe se reproducen completa y correctamente los resultados de los trabajos.

Darmstadt, 10. September 1985

Versuchsdurchführung — Dr. rer. nat. H. Kieser

Pathologie — Dr. med. vet. M. v. Eberstein

Leiter des Institutes für Toxikologie — Dr. med. vet. A. Hofmann

Durchführung des Versuches: 18.03. - 16.04.1985

T 12821

TOX LOC 5/1 090885

1. Zusammenfassung

DAROCUR® 1173 wurde bis zu einer Tagesdosis von 1000 mg/kg klinisch vertragen. Pathologisch-anatomisch zeigten sich in dieser Dosis deutliche Vergrößerungen der Leber. Das morphologische Korrelat waren Leberzellvergrößerungen und periphere Leberzellproliferation. Erhöhte Lebergewichte wurden bereits bei 300 mg/kg/Tag registriert. Die Dosis 1000 mg/kg/Tag wird aufgrund der pathomorphologischen Befunde als toxisch angesehen.

2. Einleitung

DAROCUR® 1173 ist ein Produkt der E. Merck, Darmstadt, das als Photoinitiator für die UV-Härtung von Lacken eingesetzt wird. Der vorliegende Versuch ist eine "dose-range-finding"-Studie als Vorbereitung für eine 3monatige Toxizitätsprüfung an Ratten, wie sie von internationalen Behörden gefordert wird.

3. Prüfmaterial

DAROCUR® 1173
Art. Nr. 1/7005
Flüssigkeit
Ablieferung Nr. U 472205
Freigabe: 08.11.1984-November 1986

4. Versuchsanordnung

Für den Versuch wurden ca. 5 Wochen alte männliche und weibliche Wistar-Ratten vom Stamm Emd: Wi-AF/Han (SPF) im durchschnittlichen Gewicht von 125 g (♂) resp. 114 g (♀) in 5 Gruppen zu je 6 Tieren (3 ♂, 3 ♀), insgesamt 30 Ratten eingesetzt. Der Versuch wurde im März-April 1985 im Institut für Toxikologie der E. Merck, Darmstadt, Raum U9/108, durchgeführt.

Die Haltungsbedingungen in dem ca. 60 m² großen Versuchsraum waren konventionell; Raumtemperatur 23-26 °C, Luftfeuchtigkeit 55-70 %. Die Tiere saßen einzeln in Makrolonkäfigen Typ III mit Weichholzgranulat als Einstreu. Futterpellets (Altromin TPF®N 1324) und Trinkwasser standen ad libitum zur Verfügung.

4.2 Behandlung und Dosierung

Die Behandlungsperiode umfaßte 4 Wochen. Die Applikation erfolgte p.o. (Gummischlundsonde) als Suspension in 0,25 %igem wäßrigen Methocel®, täglich einmal, 7mal pro Woche. Das Applikationsvolumen betrug 10 ml/kg.

Dosierung		Tier-Nr. ♂	Tier-Nr. ♀	Konzentration in g/l
Tagesdosis pro kg KGW				
Gruppe 1	0 mg	1-3	16-18	Methocel
Gruppe 2	30 mg	4-6	19-21	3
Gruppe 3	100 mg	7-9	22-24	10
Gruppe 4	300 mg	10-12	25-27	30
Gruppe 5	1000 mg	13-15	28-30	100

Eine 3 %ige Suspension in Methocel erwies sich bei 14tägigem Aufenthalt im Kühlschrank (bis +8 °C) als stabil.

4.3 Untersuchungen

Verhalten und Aussehen wurden täglich kontrolliert. Das Körpergewicht wurde zweimal und der Futterverbrauch einmal pro Woche bestimmt.

24 Stunden nach der letzten Behandlung wurden alle Tiere mit CO_2-Gas betäubt und entblutet. Anschließend wurden die Tierkörper gewogen, seziert und pathologisch-anatomisch untersucht. 12 Organe wurden gewogen: Herz, Leber, Nieren, Milz, Thymus, Hoden resp. Ovarien, Prostata resp. Uterus, Nebennieren, Schilddrüse, Hypophyse, Gehirn, Augen. Leber und Nieren wurden histopathologisch befundet.

5. <u>Ergebnisse</u>

Die Körpergewichtszunahme und der Futterverbrauch waren unauffällig. Das Lebergewicht war ab Gruppe 4 (300 mg/kg/Tag), das Nierengewicht bei Weibchen in Gruppe 5 (1000 mg/kg/Tag) erhöht.

Die histopathologischen Untersuchungen der Leber in Gruppe 5 zeigten herdförmige, zentrolobuläre/intermediäre Leberzellvergrößerung und mäßige bis deutliche periphere Leberzellproliferation (besonders bei ♀). Die Organgewichtserhöhung hat mithin ein morphologisches Korrelat.

Die Nieren zeigten lediglich unspezifische Veränderungen.

DAROCUR® 1173	Ratte - subakut orientierend 4 Wochen - oral	Table 1

Table No.

1

Abbreviations

used in the tables

N	=	number of animals
M	=	mean values
SD	=	standard deviation
SIG	=	significance (compared to control)
*	=	no statement
-	=	no significant difference to control
+	=	significant difference to control $p \leq 0.05$
++	=	significant difference to control $p \leq 0.01$
0	=	not examined

Contents

(mean values)

Body weight 2-5

Food consumption 6-9

Organ weights - male 10-13

Organ weights - female 14-17

T 12821

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TABLE 2

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

BODYWEIGHT IN GRAMS

SPECIES: RAT,EMD: WI-AF/HAN (SPF)

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX	MALE	-1	1	1	2	2	3	3	4	4
GROUP 1	N	3	3	3	3	3	3	3	3	3
0	M	124	146	167	191	216	236	255	265	279
MG/KG	SD	4	4	3	5	1	3	8	8	9
GROUP 2	N	3	3	3	3	3	3	3	3	3
30	M	127	153	176	195	224	244	265	273	289
MG/KG	SD	2	3	2	3	6	10	13	16	17
	SIG	*	*	*	*	*	*	*	*	*
GROUP 3	N	3	3	3	3	3	3	3	3	3
100	M	123	147	170	193	218	238	256	265	282
MG/KG	SD	3	4	4	7	10	11	15	19	18
	SIG	*	*	*	*	*	*	*	*	*
GROUP 4	N	3	3	3	3	3	3	3	3	3
300	M	126	147	171	191	220	237	256	269	283
MG/KG	SD	2	3	2	2	2	2	2	7	8
	SIG	*	*	*	*	*	*	*	*	*

SIGNIFICANCE TEST IS BASED ON DIFFERENCE BETWEEN PRESENT AND INITIAL VALUES

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TABLE 3

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

BODYWEIGHT IN GRAMS

SPECIES: RAT,EMD: WI-AF/HAN (SPF)

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX	MALE	-1	1	1	2	2	3	3	4	4
GROUP 5	N	3	3	3	3	3	3	3	3	3
1000	M	124	144	169	187	215	232	253	265	282
MG/KG	SD	2	3	5	5	3	2	2	3	7
	SIG	*	*	*	*	*	*	*	*	*

SIGNIFICANCE TEST IS BASED ON DIFFERENCE BETWEEN PRESENT AND INITIAL VALUES

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TABLE 4

E.MERCK CARMSTACT
EXPERIMENT T12821

PILOT STUDY

BODYWEIGHT IN GRAMS

SPECIES: RAT, EMD: WI-AF/HAN (SPF)

TEST MATERIAL: CAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX FEMALE

		-1	1	1	2	2	3	3	4	4
GROUP 1	N	3	3	3	3	3	3	3	3	3
0	M	111	125	134	143	155	165	173	177	185
MG/KG	SD	2	4	4	7	7	8	6	6	7
GROUP 2	N	3	3	3	3	3	3	3	3	3
30	M	116	129	138	147	155	166	175	184	191
MG/KG	SD	4	3	2	4	4	1	3	4	3
	SIG	*	*	*	*	*	*	*	*	*
GROUP 3	N	3	3	3	3	3	3	3	3	3
100	M	116	130	140	151	162	169	179	182	190
MG/KG	SD	2	3	4	6	6	8	9	6	9
	SIG	*	*	*	*	*	*	*	*	*
GROUP 4	N	3	3	3	3	3	3	3	3	3
300	M	113	125	139	145	158	166	173	181	189
MG/KG	SD	1	2	5	6	8	6	5	10	9
	SIG	*	*	*	*	*	*	*	*	*

SIGNIFICANCE TEST IS BASED ON DIFFERENCE BETWEEN PRESENT AND INITIAL VALUES

TABLE 5

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

BODYWEIGHT IN GRAMS

SPECIES: RAT,EMD: WI-AF/HAN (SPF)

TEST MATERIAL: DARGOUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX	FEMALE	-1	1	1	2	2	3	3	4	4
GROUP 5	N	3	3	3	3	3	3	3	3	3
1000	M	114	130	141	150	164	168	175	183	190
MG/KG	SD	3	6	5	6	9	6	4	8	8
	SIG	*	*	*	*	*	*	*	*	*

SIGNIFICANCE TEST IS BASED ON DIFFERENCE BETWEEN PRESENT AND INITIAL VALUES

TABLE 6

E.MERCK CARMSTACT
EXPERIMENT T12821

PILCT STUDY

FCOD CCNSLMFTION IN GRAMS

SPECIES: RAT,EMD: WI-AF/HAN (SPF)

TEST MATERIAL: CAROCUR 1173
ADMINISTRATICN: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX	MALE	1	2	3	4
GRCUP 1	N	3	3	3	3
0	M	137	157	171	174
MG/KG	SD	2	2	8	7
GRCUP 2	N	3	3	3	3
30	M	145	161	168	172
MG/KG	SC	4	1	6	1C
	SIG	*	*	*	*
GRCUP 3	N	3	3	3	3
100	M	136	155	163	168
MG/KG	SD	4	3	5	8
	SIG	*	*	*	*
GRCUP 4	N	3	3	3	3
300	M	138	153	165	172
MG/KG	SD	3	3	6	5
	SIG	*	*	*	*

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TABLE 7

E.MERCK CARMSTADT
EXPERIMENT T12821

PILOT STUDY

FOOD CONSUMPTION IN GRAMS

SPECIES: RAT, EMD: WI-AF/HAN (SPF)

TEST MATERIAL: CAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX MALE

		1	2	3	4
GROUP 5	N	3	3	3	3
1000	M	141	152	172	165
MG/KG	SD	9	9	3	5
	SIG	*	*	*	*

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TABLE 8

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

FOOD CONSUMPTION IN GRAMS

SPECIES: RAT, EMD: WI-AF/HAN (SPF)

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX	FEMALE	1	2	3	4
GROUP 1	N	3	3	3	3
0	M	108	111	113	118
MG/KG	SD	5	3	4	3
GROUP 2	N	3	3	3	3
30	M	109	111	116	124
MG/KG	SD	1	1	5	7
	SIG	*	*	*	*
GROUP 3	N	3	3	3	3
100	M	112	114	115	118
MG/KG	SD	11	6	9	9
	SIG	*	*	*	*
GROUP 4	N	3	3	3	3
300	M	115	112	115	120
MG/KG	SD	5	7	9	9
	SIG	*	*	*	*

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TABLE 9

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

FOOD CONSUMPTION IN GRAMS

SPECIES: RAT, EMD: WI-AF/HAN (SPF)

TEST MATERIAL: CARDCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

* MEAN VALUES *

IN WEEK

SEX	FEMALE	1	2	3	4
GROUP 5	N	3	3	3	3
1000	M	112	114	118	124
MG/KG	SD	8	7	2	2
	SIG	*	*	*	*

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TABLE 10

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT, END: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: DARCOUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: MALE

ABSOLUTE ORGAN WEIGHTS -VALUES IN G/ANIMAL-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	TESTES	PROSTATE	ADRENALS	THYROIDS	PITUITARY	BRAIN	EYES
GROUP 1	N	3	3	3	3	3	3	3	3	3	3	3	3	3
0	M	275	.724	13.51	2.008	.551	.580	3.178	.452	.0623	.0117	.0100	2.075	.217
MG/KG	SD	7	.014	.63	.052	.032	.120	.427	.046	.0035	.0015	.0026	.039	.005
METHOCEL	SIG													
GROUP 2	N	3	3	3	3	3	3	3	3	3	3	3	3	3
30	M	285	.786	13.27	1.571	.606	.601	2.828	.475	.0570	.0130	.0063	2.154	.223
MG/KG	SD	18	.104	1.13	.255	.010	.037	.101	.030	.0056	.0026	.0005	.044	.015
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 3	N	3	3	3	3	3	3	3	3	3	3	3	3	3
100	M	281	.772	13.37	2.003	.577	.464	3.271	.457	.0566	.0123	.0056	2.087	.216
MG/KG	SD	20	.032	1.10	.270	.130	.118	.398	.130	.0091	.0023	.0021	.060	.004
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 4	N	3	3	3	3	3	3	3	3	3	3	3	3	3
300	M	281	.805	14.71	1.937	.611	.537	3.048	.507	.0713	.0123	.0053	2.105	.222
MG/KG	SD	10	.055	1.14	.084	.035	.043	.500	.060	.0097	.0015	.0006	.037	.011
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

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TABLE 11

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT,EMD: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: MALE

ABSOLUTE ORGAN WEIGHTS -VALUES IN G/ANIMAL-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	TESTES	PROSTATE	ADRE NALS	THYROIDS	PITU ITARY	BRAIN	EYES
GROUP 5	N	3	3	3	3	3	3	3	3	3	3	3	3	3
1000	M	275	.764	16.62	2.026	.595	.513	2.805	.440	.0780	.0123	.0100	2.143	.235
MG/KG	SD	9	.032	.55	.110	.045	.102	.107	.026	.0175	.0015	.0020	.015	.003
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

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CX508 /3 07.85/ 7.21/016

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TABLE 12

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT, END: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: MALE

RELATIVE ORGAN WEIGHTS -VALUES IN G/100G BODYWEIGHT-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	TESTES	PROSTATE	ADRENALS	THYROIDS	PITUITARY	BRAIN	EYES
GROUP 1	N	3	3	3	3	3	3	3	3	3	3	3	3	3
0	M	275	.263	4.91	.730	.200	.211	1.157	.164	.0226	.0042	.0037	.754	.079
MG/KG	SD	7	.006	.26	.045	.010	.048	.180	.013	.0019	.0006	.0010	.032	.002
METHOCEL	SIG													
GROUP 2	N	3	3	3	3	3	3	3	3	3	3	3	3	3
30	M	285	.275	4.66	.693	.214	.211	.995	.167	.0200	.0046	.0029	.759	.078
MG/KG	SD	18	.020	.12	.083	.011	.002	.044	.002	.0025	.0013	.0002	.064	.007
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 3	N	3	3	3	3	3	3	3	3	3	3	3	3	3
100	M	281	.276	4.76	.711	.206	.165	1.163	.162	.0201	.0044	.0034	.745	.077
MG/KG	SD	20	.019	.05	.046	.046	.035	.072	.042	.0020	.0009	.0005	.034	.006
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 4	N	3	3	3	3	3	3	3	3	3	3	3	3	3
300	M	281	.287	5.24	.691	.218	.191	1.089	.181	.0254	.0044	.0033	.752	.079
MG/KG	SD	10	.014	.24	.050	.014	.010	.204	.027	.0036	.0004	.0003	.033	.001
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

CX508 /3(07.85/ 7.21/017

TABLE 13

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT,EMD: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: MALE

RELATIVE ORGAN WEIGHTS -VALUES IN G/100G BODYWEIGHT-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	TESTES	PROSTATE	ADRE NALS	THYROIDS	PITU ITARY	BRAIN	EYES
GROUP 5	N	3	3	3	3	3	3	3	3	3	3	3	3	3
1000	M	275	.278	6.04	.736	.216	.186	1.020	.160	.0282	.0045	.0036	.779	.085
MG/KG	SD	9	.009	.15	.043	.013	.036	.051	.014	.0055	.0006	.0007	.021	.002
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

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TABLE 14

E.MERCK CARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT, EMD: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: CAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: FEMALE

ABSOLUTE ORGAN WEIGHTS -VALUES IN G/ANIMAL-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	OVARIES	UTERUS	ADRENALS	THYROIDS	PITUITARY	BRAIN	EYES
GROUP 1	N	3	3	3	3	3	3	3	3	3	3	3	3	3
0	M	180	.522	7.65	1.213	.467	.480	.069	.425	.0637	.0116	.0117	1.951	.216
MG/KG	SD	8	.019	.28	.101	.043	.067	.007	.054	.0078	.0038	.0015	.098	.023
METHOCEL	SIG													
GROUP 2	N	3	3	3	3	3	3	3	3	3	3	3	3	3
30	M	184	.493	7.55	1.343	.421	.406	.075	.466	.0747	.0090	.0127	1.567	.214
MG/KG	SD	3	.010	.35	.080	.024	.070	.012	.088	.0060	.0050	.0006	.080	.004
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 3	N	3	3	3	3	3	3	3	3	3	3	3	3	3
100	M	185	.501	7.67	1.189	.415	.364	.078	.384	.0737	.0117	.0113	1.976	.204
MG/KG	SD	8	.045	.43	.087	.028	.015	.025	.198	.0097	.0029	.0006	.063	.014
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 4	N	3	3	3	3	3	3	3	3	3	3	3	3	3
300	M	179	.479	8.33	1.377	.492	.431	.087	.403	.0740	.0110	.0113	1.922	.216
MG/KG	SD	9	.055	.50	.136	.035	.037	.009	.231	.0151	.0010	.0040	.075	.019
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

TABLE 15

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT, EMD: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: FEMALE

ABSOLUTE ORGAN WEIGHTS -VALUES IN G/ANIMAL-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	OVARIES	UTERUS	ADRENALS	THYROIDS	PITUITARY	BRAIN	EYES
GROUP 5	N	3	3	3	3	3	3	3	3	3	3	3	3	3
1000	M	185	.560	11.05	1.486	.423	.384	.086	.282	.0797	.0123	.0120	2.029	.221
MG/KG	SD	9	.050	1.05	.095	.044	.034	.023	.015	.0076	.0006	.0040	.031	.007
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

170038 - 271085

CX508 /3(07.85/ 7.23/C16

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TABLE 16

E.MERCK DARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT, EMD: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: DAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: FEMALE

RELATIVE ORGAN WEIGHTS -VALUES IN G/100G BODYWEIGHT-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	OVARIES	UTERUS	ADRENALS	THYROIDS	PITUITARY	BRAIN	EYES
GROUP 1	N	3	3	3	3	3	3	3	3	3	3	3	3	3
0	M	180	.290	4.27	.673	.260	.266	.038	.236	.0353	.0065	.0065	1.085	.121
MG/KG	SD	8	.003	.04	.030	.027	.036	.004	.024	.0030	.0023	.0006	.068	.009
METHOCEL	SIG													
GROUP 2	N	3	3	3	3	3	3	3	3	3	3	3	3	3
30	M	184	.268	4.10	.730	.229	.220	.041	.253	.0405	.0049	.0069	1.065	.116
MG/KG	SD	3	.010	.12	.044	.010	.037	.007	.047	.0026	.0028	.0004	.040	.002
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 3	N	3	3	3	3	3	3	3	3	3	3	3	3	3
100	M	185	.271	4.26	.644	.225	.197	.042	.211	.0399	.0063	.0061	1.070	.111
MG/KG	SD	8	.014	.14	.034	.009	.014	.012	.117	.0050	.0016	.0004	.010	.006
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****
GROUP 4	N	3	3	3	3	3	3	3	3	3	3	3	3	3
300	M	179	.267	4.65	.768	.274	.242	.049	.230	.0413	.0062	.0063	1.076	.121
MG/KG	SD	9	.019	.07	.038	.007	.030	.003	.142	.0078	.0005	.0022	.070	.017
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

x508 /30 7.85/ 7.23/C17

TABLE 17

E.MERCK CARMSTADT
EXPERIMENT T12821

PILOT STUDY

SPECIES: RAT,EMD: WI-AF/HAN (SPF)
WEEK 5

TEST MATERIAL: CAROCUR 1173
ADMINISTRATION: ORAL, BY GAVAGE

SEX: FEMALE

RELATIVE ORGAN WEIGHTS -VALUES IN G/100G BODYWEIGHT-

DOSE		BODY WEIGHT	HEART	LIVER	KIDNEYS	SPLEEN	THYMUS	OVARIES	UTERUS	ADRE NALS	THYROIDS	PITU ITARY	BRAIN	EYES
GROUP 5	N	3	3	3	3	3	3	3	3	3	3	3	3	3
1000	M	185	.303	5.97	.806	.229	.209	.046	.153	.0432	.0067	.0066	1.100	.119
MG/KG	SD	9	.017	.25	.071	.013	.029	.010	.004	.0041	.0002	.0025	.043	.006
	SIG	****	****	****	****	****	****	****	****	****	****	****	****	****

170050 1 221085

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

Anthony Di Battista
Manager, Regulatory Affairs & Toxic Substances Compliance
Toxicology, Regulatory Auditing & Compliance
CIBA-GEIGY Corporation
444 Saw Mill River Road
Ardsley, New York 10502-2699

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

NOV 04 1994

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

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U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

13097 A

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Printed with Soy/Canola Ink on paper that contains at least 50% recycled fiber

Triage of 8(e) Submissions

Date sent to triage: OCT 14 1994

NON-CAP CAP

Submission number: 13097A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

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ATOX SBTOX SEN w/NEUR

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entire document: 0 1 2 **pages** 1 **pages** 1,3

Notes:

Contractor reviewer : NEB **Date:** 9/7/94

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0794-13097 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Ciba-Geigy Corporation

SUB. DATE: 07/01/94 OTS DATE: 07/06/94 CSRAD DATE: 08/01/94

CHEMICAL NAME: Darocur 1173

CAS# 7473-98-5

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/USERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INC. OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YES	YES (DROP/REFER)	RAT	LOW	photo initiator used	
CAS SR	NO	NO (CONTINUE)		MED	[redacted]	
	DETERMINE	REFER:		HIGH		

COMMENTS:

8(e) 8(E)-13097A	TRIAGE ASSESSMENT
TOX CONCERN ~~M~~ L	Low

SUBACUTE ORAL TOXICITY IN RATS IS ~~MEDIUM~~ CONCERN. ANIMALS WERE DOSED WITH 0, 30, 100, 300, OR 1000 MG/KG OF THE TEST MATERIAL FOR 4 WEEKS. THERE WERE NO MORTALITIES. THERE WAS AN INCREASE IN LIVER WEIGHT IN THE 300 AND 1000 MG/KG GROUPS AND AN INCREASE IN THE KIDNEY WEIGHT OF THE FEMALES OF THE 1000 MG/KG GROUP. THE LIVERS SHOWED CIRCUMSCRIBED, CENTROLOBULAR/INTERMEDIARY HEPATIC CELL ENLARGEMENT AND MODERATE TO SIGNIFICANT PERIPHERAL HEPATIC CELL PROLIFERATION. THE NOEL WAS 100 MG/KG.