2.2 – Treatment

The animals of Group 2, received an effective dose of 5000 mg/kg body weight of product, administered by force-feeding under a volume of 5mL/kg body weight using a suitable syringe graduated fitted with an oesophageal metal canula.

3 - RESULTS

No mortality occurred during the study.

The clinical observations are shown in the observations data sheet, tables 1 to 2 and those of body weight evolution in tables 3 and 4, hereafter.

No clinical signs related to the administration of the test product were observed. The body weight evolution of the animals remained normal throughout the study, similar between treated and control animals.

The results of the macroscopical examinations are shown in the necropsy data sheet, tables 5 to 8, hereafter.

The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.

4 - CONCLUSION

The LD_{50} of the product **REF.03.749 CENNAMIDE CERO 15** is higher than 5000 mg/kg body weight by oral route in the rat.

According *to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the E.E.C. Directives 67/548, 2001/59 and 99/45*, the product **REF.03.749 CENNAMIDE CERO 15** must not be classified.

5 - ARCHIVES

All original data and the final report related to this study will be stored for a period of 10 years in the company under the reference **TAO423-PH-03/0307**. After this period, the Sponsor's instructions will be applied.

6 - PROTOCOL ADHERENCE

Environmental parameter: A temperature of 18°C was registered during this study instead of 19°C (minimal limit) as planned in the experimental protocol.

This deviation did not, in any case, influence the development and the results of the study.

TOXICITY LEXICON

* Spontaneous Activity :	Normal (N) | Decrease (D) | Increased (A)
* Preyer's Reflex :	Normal (N) | Decrease (D) | Increased (A) | None (0)
*Respiratory Rate :	Normal (N) | Dyspnea (D) | Bradypnea (B) | Polypnea (P)
* Convulsions :	None (N) | Tonic (T) | Clonic (C)
* Tremors :	None (N) | Tremors (Tr)
* Body Temperature :	Normal (N) | Hypothermia (D) | Hyperthermia (A)
* Muscle Tone :	Normal (N) | Decreased (D) | Increased (A)
* Palpebral Opening :	Normal (N) Eyes partly closed (Pc) Eyes completely closed (Cc)
* Pupil Appearance :	Normal (N) | Mydriasis (Md) | Myosis (Ms)
* Salivation :	Normal (N) | Increased (A)
* Lachrymation :	Normal (N) | Increased (A)
* Righting Reflex :	Normal (N) | Limited (D) | None (0)
* Back Hair Appearance :	Normal (N) | Piloerection (Pi)

NOTES :

- *The observations are performed by comparison with the control animals standing in the same environment.*
- *The temperature of animal is evaluated by touch.*

[redacted]

TEST PRODUCT: REF.03.749 CENNAMIDE CERO 15

Treatment: 5000 mg/kg body weight

Opérators: F. Richeux
G. Creste

D0: 10/07/03 (females)
10/10/03 (males)

Number of animals: 6

Table 1

OBSERVATIONS : **T0 + 1 hour** **T0 + 3 hours** **T0 + 5 hours**	MALES			FEMALES		
	Rm 4064	Rm 4065	Rm 4066	Rf 4046	Rf 4047	Rf 4048
Spontaneous activity	N	N	N	N	N	N
Preyer's reflex (noise)	N	N	N	N	N	N
Respiratory rate	N	N	N	N	N	N
Convulsions	N	N	N	N	N	N
Tremors	N	N	N	N	N	N
Body temperature	N	N	N	N	N	N
Muscle tone	N	N	N	N	N	N
Palpebral opening	N	N	N	N	N	N
Pupil appearance	N	N	N	N	N	N
Salivation	N	N	N	N	N	N
Lachrymation	N	N	N	N	N	N
Righting reflex	N	N	N	N	N	N
Back hair appearance	N	N	N	N	N	N
MORTALITY	0	0	0	0	0	0
Remarks	None			None		

OBSERVATION DATA SHEET No. 2 – Group 2 (treated)

TEST PRODUCT: REF.03.749 CENNAMIDE CERO 15

Treatment: 5000 mg/kg body weight

Opérators: F. Richeux
G. Creste & A. Ehanno

D0: 10/07/03 (females)
10/10/03 (males)

Number of animals: 6

Table 2

OBSERVATIONS : **T0 + 24 hours** **T0 + 48 hours**	MALES			FEMALES		
	Rm 4064	Rm 4065	Rm 4066	Rf 4046	Rf 4047	Rf 4048
Spontaneous activity	N	N	N	N	N	N
Preyer's reflex (noise)	N	N	N	N	N	N
Respiratory rate	N	N	N	N	N	N
Convulsions	N	N	N	N	N	N
Tremors	N	N	N	N	N	N
Body temperature	N	N	N	N	N	N
Muscle tone	N	N	N	N	N	N
Palpebral opening	N	N	N	N	N	N
Pupil appearance	N	N	N	N	N	N
Salivation	N	N	N	N	N	N
Lachrymation	N	N	N	N	N	N
Righting reflex	N	N	N	N	N	N
Back hair appearance	N	N	N	N	N	N
MORTALITY	0	0	0	0	0	0
Remarks	None			None		

BODY WEIGHT EVOLUTION - GROUP 1 (Control)

CONTROL PRODUCT : DISTILLED WATER

Treatment: 10000 mg/kg body weight

Operators: G. Creste
A. Ehanno

D0: 10/07/03 (females)
10/10/03 (males)

Number of animals: 6

Table 3

(Body weight and weight gain in grams)

MALES	D0	D2	D2-D0	D7	D7-D0	D14	D14-D0
Rm 4049	190	252	62	285	95	332	142
Rm 4050	189	249	60	290	101	338	149
Rm 4051	197	255	58	290	93	348	151
MEAN	**192.0**	**252.0**	**60.0**	**288.3**	**96.3**	**339.3**	**147.3**
Standard deviation	**4.4**	**3.0**	**2.0**	**2.9**	**4.2**	**8.1**	**4.7**
FEMALES							
Rf 4031	162	176	14	202	40	218	56
Rf 4032	170	188	18	213	43	237	67
Rf 4033	159	176	17	206	47	225	66
MEAN	**163.7**	**180.0**	**16.3**	**207.0**	**43.3**	**226.7**	**63.0**
Standard deviation	**5.7**	**6.9**	**2.1**	**5.6**	**3.5**	**9.6**	**6.1**

BODY WEIGHT EVOLUTION - GROUP 2 (treated)

TEST PRODUCT: REF.03.749 CENNAMIDE CERO 15

Treatment: 5000 mg/kg body weight

Operators: G. Creste
S. Uteau & A. Ehanno

D0: 10/07/03 (females)
10/10/03 (males)

Number of animals: 6

Table 4

(Body weight and weight gain in grams)

MALES	D0	D2	D2-D0	D7	D7-D0	D14	D14-D0
Rm 4064	184	222	38	261	77	298	114
Rm 4065	184	232	48	270	86	313	129
Rm 4066	191	246	55	280	89	339	148
MEAN	**186.3**	**233.3**	**47.0**	**270.3**	**84.0**	**316.7**	**130.3**
Standard deviation	**4.0**	**12.1**	**8.5**	**9.5**	**6.2**	**20.7**	**17.0**
FEMALES							
Rf 4046	160	178	18	210	50	230	70
Rf 4047	156	166	10	189	33	198	42
Rf 4048	163	179	16	205	42	224	61
MEAN	**159.7**	**174.3**	**14.7**	**201.3**	**41.7**	**217.3**	**57.7**
Standard deviation	**3.5**	**7.2**	**4.2**	**11.0**	**8.5**	**17.0**	**14.3**

NECROPSY DATA SHEET No. 1 Group 1 (Control)

CONTROL PRODUCT : DISTILLED WATER

Dose: 10000 mg/kg body weight

Operator: A. Ehanno

Route: oral

Sex / No. animals: 3 males Rm4049 to Rm4051

Necropsy date: 10/24/2003

Species: Sprague Dawley Rats

Table 5

Spontaneous death : [ ] Euthanasia : [X] At term [X]

GENERAL APPEARANCE BEFORE AUTOPSY : Normal

	Observed Organs	Results	Remarks
* ŒSOPHAGUS	X	N.t.R.	
* STOMACH	X	N.t.R.	
* DUODENUM	X	N.t.R.	
* JEJUNUM	X	N.t.R.	
* ILEON	X	N.t.R.	
* CAECUM	X	N.t.R.	
* COLON	X	N.t.R.	
* RECTUM	X	N.t.R.	
* SPLEEN	X	N.t.R.	
* LIVER	X	N.t.R.	
* THYMUS	X	N.t.R.	
* TRACHEA	X	N.t.R.	
* LUNGS	X	N.t.R.	
* HEART	X	N.t.R.	
* KIDNEYS	X	N.t.R.	
* URINARY BLADDER	X	N.t.R.	
* TESTICLES	X	N.t.R.	
* OVARIES	-	-	
* UTERUS	-	-	
* TREATMENT AREA	-	-	
* ADRENALS	X	N.t.R.	
* PANCREAS	X	N.t.R.	

PARTICULARS : None

N.t.R. : Nothing to report

NECROPSY DATA SHEET No. 2 Group 1 (Control)

CONTROL PRODUCT : DISTILLED WATER

Dose: 10000 mg/kg body weight

Operator: G. Creste

Route: oral

Sex / No. animals: 3 females Rf4031 to Rf4033

Necropsy date: 10/21/2003

Species: Sprague Dawley Rats

Table 6

Spontaneous death : [ ] Euthanasia : [X] At term [X]

GENERAL APPEARANCE BEFORE AUTOPSY : Normal

	Observed Organs	Results	Remarks
* ŒSOPHAGUS	X	N.t.R.	
* STOMACH	X	N.t.R.	
* DUODENUM	X	N.t.R.	
* JEJUNUM	X	N.t.R.	
* ILEON	X	N.t.R.	
* CAECUM	X	N.t.R.	
* COLON	X	N.t.R.	
* RECTUM	X	N.t.R.	
* SPLEEN	X	N.t.R.	
* LIVER	X	N.t.R.	
* THYMUS	X	N.t.R.	
* TRACHEA	X	N.t.R.	
* LUNGS	X	N.t.R.	
* HEART	X	N.t.R.	
* KIDNEYS	X	N.t.R.	
* URINARY BLADDER	X	N.t.R.	
* TESTICLES	-	-	
* OVARIES	X	N.t.R.	
* UTERUS	X	N.t.R.	
* TREATMENT AREA	-	-	
* ADRENALS	X	N.t.R.	
* PANCREAS	X	N.t.R.	

PARTICULARS : None

N.t.R. : Nothing to report

[redacted]

TEST PRODUCT: REF.03.749 CENNAMIDE CERO 15

Dose: 5000 mg/kg body weight

Operator: A. Ehanno

Route: oral

Sex / No. animals: 3 males Rm4064 to Rm4066

Necropsy date: 10/24/2003

Species: Sprague Dawley Rats

Table 7

Spontaneous death : [ ] Euthanasia : [X] At term [X]

GENERAL APPEARANCE BEFORE AUTOPSY : Normal

	Observed Organs	Results	Remarks
* ŒSOPHAGUS	X	N.t.R.	[redacted]
* STOMACH	X	N.t.R.	
* DUODENUM	X	N.t.R.	
* JEJUNUM	X	N.t.R.	
* ILEON	X	N.t.R.	
* CAECUM	X	N.t.R.	
* COLON	X	N.t.R.	
* RECTUM	X	N.t.R.	
* SPLEEN	X	N.t.R.	
* LIVER	X	N.t.R.	
* THYMUS	X	N.t.R.	[redacted]
* TRACHEA	X	N.t.R.	[redacted]
* LUNGS	X	N.t.R.	
* HEART	X	N.t.R.	
* KIDNEYS	X	N.t.R.	[redacted]
* URINARY BLADDER	X	N.t.R.	
* TESTICLES	X	N.t.R.	
* OVARIES	-	-	
* UTERUS	-	-	
* TREATMENT AREA	-	-	[redacted]
* ADRENALS	X	N.t.R.	[redacted]
* PANCREAS	X	N.t.R.	

PARTICULARS : None

N.t.R. : Nothing to report

[redacted]

TEST PRODUCT: REF.03.749 CENNAMIDE CERO 15

Dose: 5000 mg/kg body weight

Operators: G. Creste

Route: oral

Sex / No. animals: 3 females Rf4046 to Rf4048

Necropsy date: 10/21/2003

Species: Sprague Dawley Rats

Table 8

Spontaneous death : [ ] Euthanasia : [X] At term [X]

GENERAL APPEARANCE BEFORE AUTOPSY : Normal

	Observed Organs	Results	Remarks
* ŒSOPHAGUS	X	N.t.R.	[redacted]
* STOMACH	X	N.t.R.	
* DUODENUM	X	N.t.R.	
* JEJUNUM	X	N.t.R.	
* ILEON	X	N.t.R.	
* CAECUM	X	N.t.R.	
* COLON	X	N.t.R.	
* RECTUM	X	N.t.R.	
* SPLEEN	X	N.t.R.	
* LIVER	X	N.t.R.	
* THYMUS	X	N.t.R.	
* TRACHEA	X	N.t.R.	
* LUNGS	X	N.t.R.	
* HEART	X	N.t.R.	
* KIDNEYS	X	N.t.R.	
* URINARY BLADDER	X	N.t.R.	
* TESTICLES	-	-	
* OVARIES	X	N.t.R.	
* UTERUS	X	N.t.R.	
* TREATMEANT AREA	-	-	
* ADRENALS	X	N.t.R.	
* PANCREAS	X	N.t.R.	

PARTICULARS : None

N.t.R. . Nothing to report

APPENDICES

Appendix 1: Statement of GLP Compliance (1 page)

Appendix 2: Animals diet sheet (1 page r/v)

Appendix 1: Statement of CLP Compliance (1 page)

REPUBLIQUE FRANCAISE

PREMIER MINISTRE

GROUPE INTERMINISTERIEL DES PRODUITS CHIMIQUES

LE PRESIDENT

Tél : 01 53 44 96 82 10

Paris, le 20 JUIN 2003

La correspondance est à adresser au :
Secrétariat du GIPC
Le BERVIL
12 rue Villiot
75572 PARIS CEDEX 12

OBJET : Evaluation de la conformité aux B.P.L. selon la directive 88/320/C.E.E.

Consécutivement à votre engagement vis à vis du GIPC et du COFRAC et en application du décret n° 81-278 du 25 mars 1981 portant création d'un groupe interministériel des produits chimiques, modifié notamment par le décret 90-206 du 7 mars 1990 et par le décret n° 98-1312 du 31 décembre 1998 concernant les bonnes pratiques de laboratoires, je vous confirme que le GIPC, au vu des résultats du contrôle exercé par le Comité français d'accréditation (COFRAC) - Section Essais a décidé pour votre installation du statut suivant :

respect des principes de B.P.L.

Domaines de reconnaissance :

- ☐ 1 - essais physico-chimiques
- ☒ 2 - **études de toxicité**
- ☐ 3 - études de mutagénicité
- ☐ 4 - études écotoxicologiques sur les organismes aquatiques et terrestres
- ☐ 5 - études portant sur le comportement dans l'eau, dans le sol et dans l'air ; bioaccumulation
- ☐ 6 - études portant sur les résidus
- ☐ 7 - études portant sur les effets sur les mésocosmes et les écosystèmes naturels
- ☐ 8 - méthodes de chimie analytique et clinique
- ☐ 9 autres études

Date d'inspection : 19 - 20 mai 2003

- ☐ inspection initiale (i.i)
- ☐ inspection de contrôle périodique (i.p)
- ☐ inspection de contrôle complémentaire (i.c)
- ☐ inspection d'extension (i.e)
- ☒ **inspection de renouvellement (i.r)**

Date de décision du G.I.P.C. : 28 mai 2003
Date de prise d'effet : 20 mai 2003
Année de première conformité : 1998
Date de validité : 28 novembre 2004

Le Conseiller d'Etat h.
Président du Groupe Interministériel des Produits Chimiques

M. Pierre CREYSSEL

PHYCHER BIO DEVELOPPEMENT
18, chemin Lou Tribail
Z.I. de Toctoucau
33611 CESTAS Cedex

[redacted]

RAT AND MOUSE MAINTENANCE DIETS

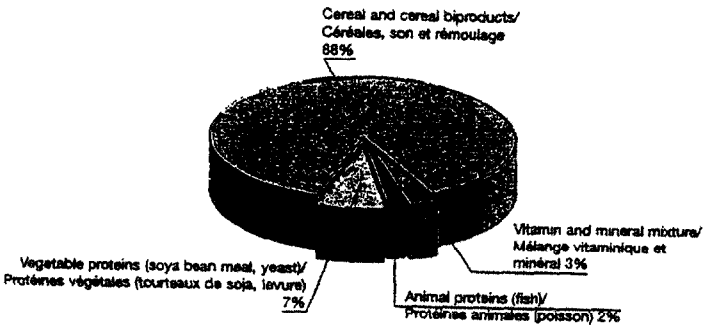
RATS - SOURIS ENTRETIEN

Certified	*: A04*
Irradiated Certified	*: A04-10*
Control	*: A04C*
Control Irradiated	*: A04C-10*
Form	*: Pellets ø 15 mm*
Standard pack	
- Certified	*: 20 Kg paper bag*
- Control or Irradiated	*: 20 kg double paper bag with aluminium on the outside*
Rate per day	*rat 15 to 25 g, mouse 5 to 10 g.*

Certifié	: A04
Certifié irradié	: A04-10
Contrôle	: A04C
Contrôle irradié	: A04C-10
Présentation	: Pellets ø 15 mm
Conditionnement	
- Certifié	: 20 Kg en sac papier
- Contrôle ou irradié	: 20 Kg double sac papier avec feuille alumisée externe
Ration journalière	: rat de 15 à 25 g, souris de 5 à 10 g.

Formula

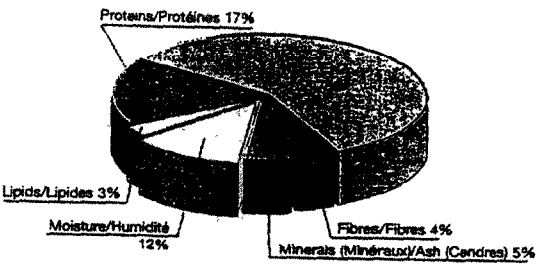
Formule



Average analysis

Analyse moyenne

Calorific value/Apport calorique (kcal/kg) 2 900



Amino acid values (calculated/kg)

Apport en acides aminés (calculé/kg)

9 800 mg	Arginine
2 300 mg	Cystine
8 500 mg	Lysine
3 200 mg	Methionine
1 900 mg	Tryptophan
8 100 mg	Glycine

Fatty acid values (calculated/kg)

Apport en acides gras (calculé/kg)

2 600 mg	palmitic ac.
Traces	palmitoleic ac.
500 mg	stearic ac.
8 000 mg	oleic ac.
14 500 mg	linoleic ac.
Traces	linolenic ac.

Mineral and vitamin content

Contenu minéral et vitaminique

MINERALS calculated/kg **MINERAUX calculés/kg**		Nat. val.	CMV val.	TOTAL
P	mg	5 900	-	5 900
Ca	mg	3 300	5 000	8 300
Na	mg	300	1 600	1 900
K	mg	6 700	-	6 700
Mg	mg	1 900	100	2 000
Mn	mg	50	40	90
Fe	mg	90	150	240
Cu	mg	15	15	30
Zn	mg	40	45	85
Co	mg	Traces	1,5	1,5
I	mg	0,3	-	0,3

VITAMINS calculated/kg **VITAMINES calculées/kg**		Nat. val.	CMV val.	TOTAL
Vitam. A	UI	Traces	7 500	7 500
Vitam. D3	UI	Traces	1 500	1 500
Vitam. B1	mg	6	1	7
Vitam. B2	mg	2	4,5	6,5
Vitam. B3	mg	10	6,5	16,5
Vitam. B6	mg	1,3	1,3	2,6
Vitam. B12	mg	0,01	0,01	0,02
Vitam. E	mg	15	15	30
Vitam. K3	mg	0,25	2,25	2,5
Vitam. PP	mg	60	15	75
Ac. Folic	mg	0,5	0	0,5
Biotine	mg	0,04	0	0,04
Choline	mg	1 200	400	1 600

FICHE QUALITE A04

		Moyenne		Déviation standard	Limites de conformité
Quantité moyenne par lot	(en tonnes)	20	±	13	
Contrôle de la composition centésimale	(en %)	100 02	±	0,04	(99 5 à 100,5)

TECHNOLOGIE DES PELLETS

Diamètre	(en mm)	16,46	±	0,44	(15,5 à 17,0)
Résistance à l'écrasement	(en Kgf/cm²)	22,2	±	3,6	(12 à 32)
Résistance à l'abrasion	(en %)	96,9	±	0,6	(>96)
Masse Spécifique	(en g/l)	635.5	±	36,9	
Poids	(en g)	5,118	±	0,480	
Longueur	(en mm)	22,13	±	1,31	
Longueur < Diamètre	(en %)	1,1	±	1,6	(<4)
Nombre de pellets chauffés par kg	(/kg)	0	±	0	(<1)

CONTROLE DE LA QUALITE NUTRITIVE

Témoin incorporation mélange minéral	(Na)	positif			
Témoin incorporation pré-mélange oligo-éléments	(Mn et Cu)	positif			
Témoin incorporation pré-mélange vitamines	(Vit A et C)	positif			
Eau	(en %)	12,3	±	0,7	(9 à 14)
Protéines	(en %)	16,0	±	0,6	(14,5 à 18)
Lipides	(en %)	2,7	±	0,4	(1,7 - 3,7)
Glucides E.N.A.	(en %)	59,6	±	0,7	(37 à 63)
dont Amidon	(en %)	44,9	±	2,5	(35 à 53)
* Sucres totaux	(en %)	2,4	±	1,0	
Cellulose WEENDE	(en %)	4,4	±	0,3	(3 à 5,5)
Hémicellulose	(en %)		±		
Cellulose vraie	(en %)		±		
Lignine	(en %)		±		
Minéraux totaux	(en %)	5,0	±	0,2	(4 à 6)
dont Calcium	(en mg/kg)	7900	±	300	(6000 à 10000)
* Phosphore	(en mg/kg)	5800	±	300	(4500 à 7000)
* Sodium	(en mg/kg)	2500	±	200	(1500 à 3500)
* Potassium	(en mg/kg)	6900	±	500	(5500 à 8500)
* Manganèse	(en mg/kg)	63	±	8	(40 à 100)
* Cuivre	(en mg/kg)	16	±	4	(8 à 35)
* Vitamine A	(en UI/kg)	6500	±	1000	(4000 à 11000)
* Vitamine C	(en mg/kg)		±		
* Vitamine D3	(en UI/kg)	800	±	400	(≤3000)
* Vitamine E	(en mg/kg)	30	±	10	

CONTROLE DES CONTAMINANTS

BACTERIOLOGIQUES

Germes revivifiables	(/g)	2300 ± 4000		(<100000)
Moisissures & levures	(/g)	<10		(1000)
Coliformes totaux	(/g)	0		(<5)
Coliformes fécaux	(/g)	0 ± 0		(0)
Anaérobies S.R.	(/g)	<10		(<100)
Salmonelles	(/25 g)	0		(0)

METAUX LOURDS

Plomb	(en µg/kg)	280 ± 90		(<1500)
Mercure	(en µg/kg)	26 ± 15		(<100)
Arsenic	(en µg/kg)	200 ± 140		(<1000)
Cadmium	(en µg/kg)	51 ± 23		(<250)
Sélénium	(en µg/kg)	150 ± 30		(<600)

MYCOTOXIQUES (en µg/kg)

Aflatoxines	<1		(<5)
Ochratoxines	<12		(<200)
Zéaralénone	<50		(<1000)
Stérigmatocystine	<30		(<300)
Patuline			
Toxine T2			

DERIVES NITROSES

NO2	(en mg/kg)	4 ± 3		(Σ<500)
NO3	(en mg/kg)	60 ± 40		(Σ<500)
NDMA	(en µg/kg)	0,57 ± 0,25		(<10)
NDEA	(en µg/kg)	<0,1		(<10)
NDPA	(en µg/kg)	<0,15		(<10)
NDBA	(en µg/kg)	<0,15		(<10)
NPIP	(en µg/kg)	<0,15		(<10)
NPYR	(en µg/kg)	<0,25		(<10)
NMOR	(en µg/kg)	<0,3		(<10)

PESTICIDES ORGANOS-CHLORES
(en µg/kg) (Total <200)

Lindane	4 ± 11		(<100)
α HCH	<1		(<20)
b HCH	<5		(<10)
d HCH	<5		(<100)
HCB	<1		(<10)
PCB	<50		(<50)
Aldrine	<1		(<10)
Dieldrine	<1		(<20)
Endosulfan	<1		(<100)

Heptachlore	<1		(<10)
Heptachlore Epoxyde	<1		(<10)
Endrine	<1		(<10)
o,p'DDD	<5		(Σ<50)
p,p'DDD	<5		(Σ<50)
o,p'DDE	<1		(Σ<50)
p,p'DDE	<1		(Σ<50)
o,p'DDT	<5		(Σ<50)
p,p'DDT	<5		(Σ<50)

PESTICIDES ORGANOS-PHOSPHORES
(en µg/kg) (Total <7000)

Acéphate	<45		(<5000)
Azinphos éthyl	<50		(<5000)
Azinphos méthyl	<50		(<5000)
Bromophos éthyl	<10		(<5000)
Bromophos méthyl	<20		(<5000)
Carbophénothion éthyl	<50		(<5000)
Carbophénothion méthyl	<20		(<5000)
Chlorfenvinphos	<25		(<5000)
Chlorméphos	<10		(<5000)
Chlorpyriphos éthyl	<15		(<5000)
Chlorpyriphos méthyl	23 ± 23		(<1500)
Chlorthiophos	<100		(<5000)
Diazinon	<15		(<5000)
Dichlofenthion	<10		(<5000)
Dichlorvos	<22		(<5000)
Diéthion	<15		(<5000)
Dimefox	<10		(<5000)
Diméthoate	<30		(<1000)
Dioxathion	<15		(<5000)
Disulfoton	<30		(<5000)
Ethoprophos	<20		(<5000)
Fenchlorphos	<20		(<5000)
Fénitrothion	<15		(<5000)
Fenthion	<30		(<5000)
Fonofos	<20		(<5000)
Formothion	<15		(<5000)
Heptenophos	<30		(<5000)

Iodofenphos	<25		(<5000)
Malathion	94 ± 49		(<5000)
Méthamidophos	<10		(<5000)
Méthidathion	<20		(<5000)
Mévinphos	<10		(<5000)
Monocrotophos	<90		(<5000)
Naled	<15		(<5000)
Ométhoate	<20		(<5000)
Oxydéméton méthyl	<400		(<5000)
Parathion éthyl	<20		(<5000)
Parathion méthyl	<20		(<5000)
Phosalone	<20		(<5000)
Phosmet	<20		(<5000)
Phosphamidon	<25		(<5000)
Profénofos	<20		(<5000)
Prothoate	<20		(<5000)
Pyridaphenthion	<15		(<5000)
Pyrimiphos éthyl	<20		(<5000)
Pyrimiphos méthyl	75 ± 184		(<2500)
Sulfotep	<20		(<5000)
Téméphos	<15		(<5000)
Tétrachlorvinphos	<30		(<5000)
Thiométon	<40		(<5000)
Triazophos	<30		(<5000)
Trichloron	<10		(<5000)
Trichloronate	<25		(<5000)

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QUALITY ASSURANCE ATTESTATION

I, the undersigned Bernard Benech, Quality Assurance unit of PHYCHER *Bio développement*, attest that the study **TAO423-PH-03/0307** was submitted to the inspection of Quality Assurance.

The routine inspections of the toxicity tests performed within the laboratory of PHYCHER *Bio développement*, are carried out as a control process of different main technical phases concerning at least one similar test. The frequency is once a term or more. The date(s) of technical phases inspections relating to this test are given below:

Date (s) of inspection (s)	: October, 17th , 2003 *Clinical examinations at 48 hours (males)*
Date of reporting to Study Director	: October, 20th , 2003
Date of reporting to Management	: October, 20th , 2003

This report has been audited by PHYCHER *Bio développement* Quality Assurance unit. It is considered to be an accurate account of the data generated and the application of the operating procedures in use within the laboratory.

	Final report
Date (s) of inspection (s)	: December, 2nd, 2003
Date of reporting to Study Director	: December, 2nd, 2003
Date of reporting to Management	: December, 2nd, 2003

Date : December 2nd , 2003

AUTHENTICATION

I, the undersigned, François Richeux, Study director, certify that the study **TAO423-PH-03/0307** was performed on the premises of the Laboratory PHYCHER *Bio développement.*

I, certify that the objectives laid down in the technical protocol were achieved and no undesirable event occurred to affect the quality or the integrity of the study. I consider the data generated to be valid. This report fully and accurately reflects the operating procedures used in the laboratory and data generated.

The entire work was devised and performed in compliance with the principles of the Good Laboratory Practice (G.L.P.), as defined in *the O.E.C.D. ruling relative to the mutual acceptance of data in the evaluation of chemical substances (C(81) 30 (final) Appendix 2 - May 12th, 1981; C (97) 186, November 26th, 1997)*, and transcribed in the *decree n° 98-1312 dated December 31st, 1998 of the Journal Officiel de la République Française.*

Date : December 2nd , 2003

Dr. François RICHEUX (PhD)
Study Director

SUMMARY AND CONCLUSION OF THE STUDY

The product **REF.03.749 CENNAMIDE CERO 15** was administered to a group of 6 Sprague Dawley rats (3 males and 3 females) at the single dose of 5000 mg/kg body weight according to the experimental protocol established on the basis of the official method as defined in the *O.E.C.D. guideline N° 423 dated March 22nd, 1996 and the test method B.1ter of the Directive N° 96/54/EC dated July 30th, 1996.*

No mortality occurred during the study.

No clinical signs related to the administration of the test product were observed. The body weight evolution of the animals remained normal throughout the study, similar between treated and control animals.

The macroscopical examination of the animals at the end of the study did not reveal treatment-related changes.

In conclusion, the LD_{50} of the product **REF.03.749 CENNAMIDE CERO 15** is higher than 5000 mg/kg body weight by oral route in the rat.

According *to the criteria for classification, packaging and labelling of dangerous substances and preparations in accordance with the E.E.C. Directives 67/548, 2001/59 and 99/45*, the product **REF.03.749 CENNAMIDE CERO 15** must not be classified.

Date : December 2nd , 2003

Scientific Direction PHYCHER *Bio développement*

Dr Christian TOUSSAINT
Pharmacologist
(Hdr)

TEST REPORT

1 - TEST PRODUCT

The product **REF.03.749 CENNAMIDE CERO 15**, sent by BIO-HC – Parc d'activités de Canteranne – Bât 3 – Avenue de Canteranne - 33600 PESSAC, was received on 09/27/2003. Its characteristics were :

- Container : plastic pot
- Quantity : 83.32 (container + contents)
- Batch : 030824
- CAS N° : -
- Form : liquid
- Colour : brown
- Storage : room temperature
- Purity : -

It was identified under the code number: **PH-03/0307**.

Information concerning the identity, purity and stability of the product to be studied are the responsibility of the Sponsor of the study. No information concerning the product was provided by the sponsor.

2 – STUDY DEVELOPMENT

The study was carried out between 10/07/2003 and 10/24/2003, in *PHYCHER Bio développement* - 18 chemin Lou Tribail - Z.I. de Toctoucau - 33611 Cestas cedex, according to the experimental protocol *Ref. TAO423-version December 2000,* established according to *the O.E.C.D. guideline N° 423 dated 03.22.1996 concerning acute oral toxicity and the test method B.1ter of the Directive N° 96/54/EC dated 07.30.1996.*
The animal control group was performed between 10/07/2003 and 10/21/2003 according to the same experimental conditions, with administration of the control product (Distilled water), under a volume of 10mL/kg body weight.

2.1 - Animals

12 Sprague Dawley rats (SPF Caw) originating from Elevage Janvier (53940 Le Genest-St-Isle – France), were used after a 5 to 6-day acclimatisation period. At the beginning of the study, the animals weighted between 184g and 197g (males) and between 156g and 170g (females).

Group 1 (control) :	3 male rats	Rm4049 à Rm4051
	and 3 female rats	Rf4031 to Rf4033
Group 2 (treated) :	3 male rats	Rm4064 to Rm4066
	and 3 female rats	Rf4046 to Rf4048

Environmental parameters for the treated group :
- temperature : between 18°C and 22°C
- relative humidity : between 40% and 67%