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FINAL REPORT

MUTAGENIC EFFECT
OF DOTATED POTASSIUM
HUMATE POWDER ITEM
BY MICRONUCLEUS TEST

2001

It's a true copy

Hiteles Másolat

Date/Datum 2001 jún 26

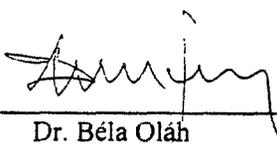
Signature/Aláírás

Teófil Mészáros

STATEMENT OF THE STUDY DIRECTOR

This study has been performed in accordance with the study plan agreed upon by Sponsor, the OECD Guidelines for Testing of Chemicals No.: 474 (1987) and the Principles of Good Laboratory Practice (OECD, Paris 1997).

I declare that this report constitutes a true record of the actions undertaken and the results obtained in this study.

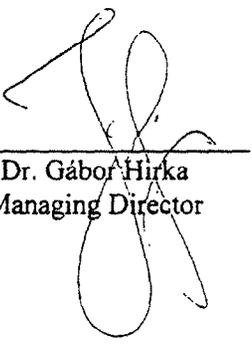
Signature: 
Dr. Béla Oláh
Study Director

Date: 26 Jan 2001

STATEMENT OF THE MANAGEMENT

According to the conditions of the research and development assignment between HUMET Trade, Research and Development Co. (as Sponsor) and Toxicological Research Centre Ltd. (as Testing Facility) " Mutagenic Effect of DOTATED POTASSIUM HUMATE POWDER Test Item by Mironucleus Test." has been performed, insisting on the GLP requirement.

Signature: _____



Dr. Gábor Hirka
Managing Director

Date: 26 Jan 2001

QUALITY ASSURANCE STATEMENT

Study Code: 00/518-013M

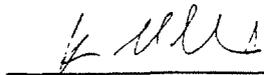
Study Title: Mutagenic Effect of DOTATED POTASSIUM HUMATE POWDER Test Item by Mironucleus Test.

Test Item: DOTATED POTASSIUM HUMATE POWDER

This study has been inspected, and this report audited by the Quality Assurance Unit in compliance with the Principles of Good Laboratory Practice. As far as can be reasonably established the methods described and the results incorporated in this report accurately reflect the raw data produced during this study.

All inspections, data reviews and the report audit were reported in writing to the study director and to management. The dates of such inspections and of the report audit are given below:

Date	Inspection/audit	Date of report to	
		Management	Study Director
13 Oct. 2000	Study Plan	13 Oct. 2000	13 Oct. 2000
08 Dec. 2000	Microscopical evaluation	08 Dec. 2000	08 Dec. 2000
27 Dec. 2000	Draft Report	27 Dec. 2000	27 Dec. 2000
26 Jan. 2001	Final Report	26 Jan. 2001	26 Jan. 2001

Signature: 
Idikó Hermann
Head of QAU

Date: 26 Jan. 2001

STUDY TITLE : Mutagenic Effect of DOTATED POTASSIUM
HUMATE POWDER Test Item by Mironucleus
Test.

SPONSOR : HUMET Trade Research and Development Co.
Address: H-1121 Budapest, Konkoly Thege u. 29-33
HUNGARY
Phone: 36-1-392-2261
Fax: 36-1-392-2265

:
STUDY PERFORMED BY : TOXICOLOGICAL RESEARCH CENTRE Ltd.
Address: H-8201 Veszprém, Szabadságpuszta
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STUDY DIRECTOR : Dr. Béla Oláh
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VETERINARY CONTROL : Zoltán Levente V.M.D.
head veterinarian

STATISTICAL DATA
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deputy head of data processing unit

QUALITY ASSURANCE : Ildikó Hermann
head of QA

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SUMMARY

Potential mutagenic activity of the test item DOTATED POTASSIUM HUMATE POWDER was examined in bone marrow of NMRI mice.

The doses of test item DOTATED POTASSIUM HUMATE POWDER was determined on the basis of the result of acute oral toxicity study.

The acute oral LD₅₀ value of test item DOTATED POTASSIUM HUMATE POWDER in CRL: NMRI BR mice were the following:

Male: >5000mg/kg

Female: >5000mg/kg

The single administration of 5000 mg/kg of test item DOTATED POTASSIUM HUMATE POWDER did not induce any clinical sign and lethality.

On the basis of results of acute study we chose 2000mg/kg dose of test item for examination in micronucleus test.

In the main study the animals were treated with 2000mg/kg of test item once, by oral route with stomach tube. The treatment volume: 0.1 ml/10g body weight. Sampling were made twice, in the 24th and 48th hours after the treatment. Five males and five females/dose/sampling time were involved in this study. Vehicle control groups received Aqua destillate pro injectione.

Animals of the positive control group received 60 mg/kg Cyclophosphamide.

Two thousand polychromatic erythrocytes (PCEs) were scored per animal to assess the micronucleated cells.

The single administration of 2000 mg/kg of the test item did not induce significant increases in the frequency of micronucleated polychromatic erythrocytes (MPCEs) in male and female mice at either 24 or 48 hours after the treatment compared to the vehicle control.

The ratio of polychromatic to normochromatic erythrocytes was used to assess the toxicity of the test item. This ratio was calculated on the basis of the number of mature cells encountered while accumulating 200 PCEs.

No biologically important alteration occurred in the treated groups compared to the vehicle control.

Positive control Cyclophosphamide caused significant increase in the number of MPCEs in the 48th hour after the application, thus validates the test.

Under the conditions of this mouse micronucleus test the test item DOTATED POTASSIUM HUMATE POWDER proved to be negative for mutagenicity in NMRI mice.

1. INTRODUCTION

The micronucleus assay is an in vivo test for the detection of chromosomal damage or damage of the mitotic apparatus caused by a test item. The basis of this test is the increase in the number of micronucleated polychromatic erythrocytes in the bone marrow of mice exposed to a clastogen. Micronuclei are believed to be formed from chromosomes or chromosome fragments left behind during anaphase and are scored during interphase because they persist. Thus, the time involved in searching for metaphase spreads in treated cell populations is eliminated. Test items affecting spindle fiber function or formation, as well as clastogenic agents, can be detected through micronucleus induction.

2. OBJECTIVE

The main objective of this study is to determine the chromosomal damage or damage of mitotic apparatus in a mammalian test in vivo. The basis of this assay is an increase of micronuclei in the polychromatic erythrocytes of treated animals versus controls.

3. MATERIALS AND METHODS

The start of treatment: 31 October 2000
End of in life phase 02 November 2000

3.1. TEST ITEM

Name: DOTATED POTASSIUM HUMATE POWDER
Active component: potassium humate (22.5mg/g)
Appearance: dark brown powder with characteristic odour and smell
Storage conditions: 15-25°C
Batch No.: 007DKH0500
Producing date: 19 June 2000
Expiry date: 19 June 2001

Characteristics of the test item was included in the Analytical Certificate. According to this Certificate the test item was free from contaminants that could influence the study.

No special safety procedures was required. The safety rules with organic chemicals had to be taken into consideration.

3.1.1. Identification, Receipt

The test item of a suitable chemical purity was supplied by the Sponsor. All precautions required in the handling and disposal of the test item was outlined by the Sponsor. Analytical certificate was supplied by the Sponsor and archived with the raw data.

3.1.2. Formulation

The test item was administered in form of mixture prepared with vehicle (Aqua destillate). Formulation was prepared freshly.

The necessary amount of the test item was weighed into a calibrated volumetric flask and vehicle was added partially and its was stirred to obtain homogenous mixture. It was diluted to the final volume with vehicle (Aqua destillate).and homogenized with stirring. Cyclophosphamide (positive control) was solved in NaCl pro injectione, for the treatment.

The test item was prepared with vehicle (Aqua destillate) solution) in 20.0 w/v %.

3.1.3. Vehicle:

Name:	Aqua destillate pro injectione
Batch No.:	20000816-152-153
Source:	Gróf Esterházy Hospital, Pápa, Hungary
Expiry:	16 August 2001

Name:	0.9% NaCl infusion
Batch No.:	20000313-696
Source:	Gróf Esterházy Hospital, Pápa ,Hungary
Expiry:	13 Marc 2001

3.1.4. Positive Control Cyclophosphamide

Batch No.:	44H0486
Supplier:	SIGMA Chemical Company
Expiry:	December 2001

3.2. EXPERIMENTAL ANIMALS

Species and strain:	CRL: NMRI BR mice
Source:	Charles River (Europe) Laboratories Budapest, HUNGARY
Hygienic level at arrival:	SPF
Hygienic level during the study:	good conventional
Justification of strain:	The NMRI mouse is one of the standard animals in mutagenetic tests
Number of animals:	30 males and 30 females
Sex:	male and female
Age of animals:	young adult mice, less than 8 weeks old
Body weight range at start of study:	27.9-33.8 g male 24.9-27.8 g female
Date of receipt:	25 October 2000
Acclimatization time:	5 days

3.2.1. Husbandry

Animal health:	Only animals in acceptable health condition were used for the test. It was certified by the veterinarian.
Room:	241
Housing:	Group caging (5 animals/cage)
Cage type:	II. type polypropylene/polycarbonate
Bedding:	laboratory bedding
Light:	12 hours daily, from 6.00 a.m. to 6.00 p.m.
Temperature:	22 ± 3 °C
Relative humidity:	30 - 70 %

Animal Identification:

The individual animal identification was performed by tattoo numbers on the tail of the mice.

The cages were marked with identity cards, with information about study code, sex, individual animal number and dose group.

Randomization:

The animals were randomized and divided into the control and test item treated groups. The randomization was controlled by computer program according to the actual body weights verifying the homogeneity and deviation between the groups.

3.2.2. Food and Feeding

Animals received SSNIFF R/M-Z+H diet for rats and mice produced by Ssniff Spezialdiäten GmbH, D-59494 Soest Germany. Diet was supplied to the animals, ad libitum.

Contents of standard diet for rats and mice are shown in Appendix 3.

3.2.3. Water Supply

Animals received aqua fontana, as for human consumption, ad libitum, from 500 ml bottles.

3.3. TEST PROCEDURE

3.3.1. Determination of the dose

The doses of test item DOTATED POTASSIUM HUMATE POWDER were determined according to the p.o. LD₅₀ value.

In the preliminary acute oral study the animals were treated with the following dose.

Groups	Dose (mg/kg)	Number of Animals	Mortality
Group I	5000	5 males	0
Group II	5000	5 females	0

The test item did not induce any symptom.

The animals were symptom free during the observation period.

The acute oral LD₅₀ value of test item DOTATED POTASSIUM HUMATE POWDER in CRL: NMRI BR mice were the following:

Male: >5000mg/kg

Female: >5000mg/kg

On the basis of the result of acute oral toxicity study the test item will be applied at 2000 mg/kg dose level.

3.3.2. Dosage

The test item was applied at one dose level.

The Cyclophosphamide (positive control) was administered at 60 mg/kg dose level.

DOSES	No. OF ANIMALS
Test item 2000mg/kg	10 males and 10 females
Cyclophosphamide 60 mg/kg	5 males and 5 females
Vehicle control Aqua destillate pro injectione 0.1 ml/ 10 g b. w.	10 males and 10 females
Untreated control	5 males and 5 females

3.4. APPLICATION AND SAMPLING TIME

Animals were treated with the test item once, by oral route with stomach tube. The treatment volume: 0.1 ml/10g body weight.

Sampling were made twice in the 24th and in the 48th hours after the treatment.

5 male and 5 female animals by dose groups were used for sampling at each occasion.

Cyclophosphamide (positive control) was administered by intraperitoneal route with injection. The treatment volume: 0.1 ml/10g body weight.

The sampling was performed 48 hours after the beginning of the treatment.

As a positive control, five male and female animals were treated with Cyclophosphamide.

The vehicle (Aqua destillate pro injectione) was administered by gavage. Animals were treated once and the sampling was performed 24 and 48 hours after the application. The treatment volume: 0.1 ml/10g body weight.

5 male and 5 female animals were used for sampling at each occasion.

Untreated control groups contained 5 male and 5 female animals.

In case of untreated control the sampling was performed 24 hours after the beginning of the study.

3.5. PREPARATION OF BONE MARROW

Bone marrow was obtained from two femurs of the five surviving freshly sacrificed mice from every dose/sex/timepoint. The bone marrow was flushed with fetal calf serum. The cells were concentrated by a gentle centrifugation, spread on a standard microscopic slide. Slides were fixed and stained with Giemsa. Two slides were prepared from each animal.

Slides were coded for blind microscopic analysis.

3.6. EXAMINATION OF SLIDES

The slides were examined in a blind manner. Two thousand PCEs were scored per animal to assess the micronucleated cells. The frequency of micronucleated cells were expressed as percent of micronucleated cells based on the first 2000 PCEs counted in the optic field. Multiple micronuclei was not registered.

The proportion of immature among total (immature+mature) erythrocytes were determined for each animal by counting a total of at least 200 immature erythrocytes.

3.7. EVALUATION OF THE RESULTS

The results are presented in Summary Tables. These tables contain the results of treated, untreated, vehicle and positive control groups. The micronucleated PCEs per 2000 PCE and the ratio of PCE / NCE were listed for each animal (APPENDIX 2).

The frequency of micronuclei of treated male and female groups were compared with those of the vehicle control groups.

Dose and time dependent increase of the number of micronucleated PCEs was evaluated by Kruskal-Wallis Non Parametric ANOVA test at 1 and 5% probability levels.

3.8. CRITERIA OF POSITIVITY

Criteria of positivity is a significant increase (>0.003) at $p<0.05$, $p<0.01$ of the frequency of micronucleated polychromatic erythrocytes at least in two treated groups in one or both sexes.

This increase might be observed:

- at adjacent dose levels: in the same experiment, dose- dependency,
- at adjacent time points: in the same experiment, same dose level, that is time-dependency,
- in two experiments, in the same dose level and time point, that is reproducibility.

3.9. ARCHIVES

The study documents:

- study plan,
- all raw data,
- specimen of the test item,
- study report,
- correspondence.

are stored in the archives of TRC Ltd., Hungary 8201 Veszprém, Szabadságpuszta P.O.B.348. according to the OECD GLP and to the TRC's SOP's. The retained materials will be offered for the Sponsor for further retainment.

4. RESULTS AND DISCUSSION

The test item DOTATED POTASSIUM HUMATE POWDER did not induce significant increases in the number of the micronucleated PCEs at 2000 mg/kg dose level (24, 48 hours after the treatment) in male and female NMRI mice. Considerable differences in the ratio of polychromatic and normochromatic erythrocytes were not found after the treatment. Biologically significant depression of PCE:NCE ratio was not observed in the study.

Cyclophosphamide treated mice (60 mg/kg) showed significantly increased MPCE numbers compared to the control.

The summary of results is shown in APPENDIX 1.

The experimental data of Study are shown in APPENDIX 2.

5. CONCLUSION

Under the conditions of this assay the test item DOTATED POTASSIUM HUMATE POWDER did not induce significant increase in the number of micronucleated polychromatic erythrocytes at 2000 mg/kg dose level after single administration in NMRI mice.

Under the conditions of this mouse micronucleus test DOTATED POTASSIUM HUMATE POWDER proved to be negative for mutagenicity in NMRI mice.

6. REFERENCES

1. Schmid, W.(1976). The micronucleus test for cytogenetic analysis. In Chemical Mutagens. Principles and Methods for their Detections, Vol. 4, ed. A. Hollander, Plenum, Press, New York, pp. 31-53.
2. Salamone, M.F., Heddle, J.A. (1983). The bone marrow micronucleus assay: rationale for a revised protocol
In Chemical Mutagens., Principles and Methods for their Detections, Vol. 8, ed. F.J.Serres. Plenum Press, New York, pp. 11-149.
3. Heddle, J.A., Hite, M. et al. (1983). The induction of micronuclei as a measure of genotoxicity.
A Report of the U.S. Environmental Protection Agency Gene-Tox Program, Mutation Research, 123, 61-118.

7. DEVIATION FROM THE STUDY PLAN

The Batch No. of test item was 007DKH0500 insted of 007DKH0600.

The animals in the vehicle control groups were treated with Aqua destillate pro injectionem insted of. isotonic 0.9% NaCl infusionem.

Date of Final Report is 30 January 2001 instead of 15 Dec. 2000.

APPENDICES

STUDY CODE : 00/518-013M
 TEST ITEM : DOTATED POTASSIUM HUMATE POWDER
 TEST SYSTEM : CRL:NMRI BR MICE

EXPERIMENTAL DATA OF MICRONUCLEUS STUDY

SEX: MALE

SAMPLING TIME: 24th hours

GROUPS	ANIMAL No.	BODY WEIGHT (g)	APPL. VOLUME (ml)	MPCE	PCE	NCE	PCE/NCE RATE
Untreated	1	30.3	0.00	3	200	162	1.23
Control	2	31.1	0.00	3	200	135	1.48
	3	33.3	0.00	4	200	154	1.30
	4	33.2	0.00	4	200	140	1.43
	5	30.0	0.00	2	200	152	1.32
	MEAN	31.58		3.20			1.35
	±SD	1.58		0.84			0.10
Vehicle	6	33.8	0.34	4	200	178	1.12
Control	7	29.8	0.30	3	200	171	1.17
Aqua destillate	8	31.8	0.32	5	200	142	1.41
	9	31.9	0.32	3	200	152	1.32
	10	28.8	0.29	4	200	139	1.44
	MEAN	31.22		3.80			1.29
	±SD	1.96		0.84			0.14
TEST ITEM	11	29.4	0.29	4	200	169	1.18
2000	12	28.7	0.29	4	200	144	1.39
mg/kg	13	30.3	0.30	3	200	152	1.32
	14	33.4	0.33	6	200	172	1.16
	15	31.8	0.32	4	200	176	1.14
	MEAN	30.72		4.20			1.24
	±SD	1.89		1.10			0.11

REMARKS:

PCE = Polychromatic Erythrocyte

NCE = Normochromatic Erythrocyte

MPCE = Number of Micronucleated Polychromatic Erythrocytes per 2000 PCE

STUDY CODE . 00/518-013M
 TEST ITEM : DOTATED POTASSIUM HUMATE POWDER
 TEST SYSTEM : CRL:NMRI BR MICE

 EXPERIMENTAL DATA OF MICRONUCLEUS STUDY

SEX: MALE

SAMPLING TIME: 48th hours

GROUPS	ANIMAL No.	BODY WEIGHT (g)	APPL. VOLUME (ml)	MPCE	PCE	NCE	PCE/NCE RATE
Vehicle	16	33.4	0.33	4	200	158	1.27
Control	17	29.5	0.30	3	200	150	1.33
Aqua destillate	18	31.2	0.31	4	200	144	1.39
	19	31.8	0.32	3	200	146	1.37
	20	29.8	0.30	5	200	178	1.12
	MEAN	31.14		3.80			1.30
	±SD	1.58		0.84			0.11
TEST ITEM	21	32.7	0.33	4	200	186	1.08
2000	22	27.9	0.28	3	200	178	1.12
mg/kg	23	30.6	0.31	5	200	157	1.27
	24	29.9	0.30	5	200	190	1.05
	25	32.2	0.32	4	200	167	1.20
	MEAN	30.66		4.20			1.14
	±SD	1.92		0.84			0.09
Positive	26	29.6	0.30	42	200	582	0.34
Control	27	30.9	0.31	35	200	608	0.33
(Cyclophosphamid)	28	30.4	0.30	40	200	580	0.34
60 mg/kg	29	31.7	0.32	32	200	597	0.34
	30	32.8	0.33	43	200	649	0.31
	MEAN	31.08		38.40			0.33
	±SD	1.23		4.72			0.01

REMARKS:

PCE = Polychromatic Erythrocyte

NCE = Normochromatic Erythrocyte

MPCE = Number of Micronucleated Polychromatic Erythrocytes per 2000 PCE

STUDY CODE . 00/518-013M
 TEST ITEM : DOTATED POTASSIUM HUMATE POWDER
 TEST SYSTEM : CRL:NMRI BR MICE

EXPERIMENTAL DATA OF MICRONUCLEUS STUDY

SEX: FEMALE

SAMPLING TIME: 24th hours

GROUPS	ANIMAL No.	BODY WEIGHT (g)	APPL. VOLUME (ml)	MPCE	PCE	NCE	PCE/NCE RATE
Untreated	31	25.6	0.00	3	200	156	1.28
Control	32	25.4	0.00	3	200	138	1.45
	33	26.8	0.00	3	200	152	1.32
	34	27.2	0.00	3	200	154	1.30
	35	26.1	0.00	3	200	147	1.36
	MEAN	26.22		3.00			1.34
	±SD	0.77		0.00			0.07
Vehicle	36	25.8	0.26	4	200	161	1.24
Control	37	26.4	0.26	4	200	184	1.09
Aqua destillate	38	27.8	0.28	3	200	177	1.13
	39	25.9	0.26	3	200	146	1.37
	40	25.4	0.25	4	200	122	1.64
	MEAN	26.26		3.60			1.29
	±SD	0.93		0.55			0.22
TEST ITEM	41	27.6	0.28	5	200	166	1.20
2000	42	25.4	0.25	3	200	160	1.25
mg/kg	43	24.9	0.25	6	200	146	1.37
	44	27.2	0.27	4	200	162	1.23
	45	25.4	0.25	3	200	244	0.82
	MEAN	26.10		4.20			1.18
	±SD	1.21		1.30			0.21

REMARKS:

PCE = Polychromatic Erythrocyte

NCE = Normochromatic Erythrocyte

MPCE = Number of Micronucleated Polychromatic Erythrocytes per 2000 PCE

STUDY CODE : 00/518-013M
 TEST ITEM : DOTATED POTASSIUM HUMATE POWDER
 TEST SYSTEM : CRL:NMRI BR MICE

 EXPERIMENTAL DATA OF MICRONUCLEUS STUDY

SEX: FEMALE

SAMPLING TIME: 48th hours

GROUPS	ANIMAL No.	BODY WEIGHT (g)	APPL. VOLUME (ml)	MPCE	PCE	NCE	PCE/NCE RATE
Vehicle	46	27.3	0.27	5	200	142	1.41
Control	47	25.9	0.26	3	200	141	1.42
Aqua destillate	48	27.7	0.28	4	200	129	1.55
	49	25.1	0.25	4	200	164	1.22
	50	25.3	0.25	4	200	175	1.14
	MEAN	26.26		4.00			1.35
	±SD	1.18		0.71			0.16
TEST ITEM	51	26.4	0.26	4	200	137	1.46
2000	52	25.8	0.26	4	200	173	1.16
mg/kg	53	25.3	0.25	4	200	160	1.25
	54	27.4	0.27	6	200	168	1.19
	55	25.8	0.26	5	200	146	1.37
	MEAN	26.14		4.60			1.29
	±SD	0.80		0.89			0.13
Positive	56	26.3	0.26	38	200	626	0.32
Control	57	25.5	0.26	32	200	596	0.34
(Cyclophosphamid)	58	26.1	0.26	32	200	574	0.35
60 mg/kg	59	25.3	0.25	39	200	542	0.37
	60	27.2	0.27	32	200	596	0.34
	MEAN	26.08		34.60			0.34
	±SD	0.75		3.58			0.02

REMARKS:

PCE = Polychromatic Erythrocyte

NCE = Normochromatic Erythrocyte

MPCE = Number of Micronucleated Polychromatic Erythrocytes per 2000 PCE

**CONTENTS OF SSNIFF R/M-Z+H EXTRUDED COMPLETE DIET FOR
RATS AND MICE**

Crude protein	19.00 %
Crude fat	3.50 %
Crude fiber	4.90 %
Crude Ash	6.00 %
Lysine	1.10 %
Methionine	0.60 %
Calcium	1.00 %
Sodium	0.20 %
Magnesium	0.20 %
Phosphorus	0.80 %
Vitamin A	22000 IU
Vitamin D ₃	1000 IU
Vitamin E	120 mg/kg

These data are standard and guaranteed values provided by the supplier.

CERTIFICATE OF TEST ITEM

HUMET Kereskedelmi, Kutatási és Fejlesztési Részvénytársaság
1121 Budapest, Konkoly Thege u. 29-33.
1525 Budapest, 114. Pf. 49.

MŰBIZONYLAT

Termék neve	DOTÁLT KÁLIUM-HUMÁT POR	
Nyilvántartási szám:	-	
Gyártóhely:	HUMET Kereskedelmi, Kutatási és Fejlesztési Részvénytársaság 1121 Budapest, Konkoly Thege u. 29-33. 1525 Budapest, 114. Pf. 49.	
Gyártási sorozat száma:	005DKH0500	
Gyártási idő:	05.julius.2000.	
Kiszerezési egység:	200 g laminált alumínium fóliás zacskó	
Tárolása:	15-25 °C	
Dátum: Budapest 2000.julius 20.	Mínőségbiztosító: <i>Dr. Király Árpád</i> Dr. Király Árpád	Mínőreítés: Megfelel

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Date/Dátum 2000. július 20.
Signature/Aláírás *Dr. Király Árpád*

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CERTIFICATE OF TEST ITEM

Gyártási sorozat száma	005DKH0500				
Vizsgálatok	Követelmény	Eredmény			
1. Sajátságok					
1.1. Leírás	Sötétbarna laza por	Megfelel			
2. Gyógyszerforma vizsgálat					
2.1. Nedvesség tartalom	105 °C-on szárítva 10 % min.: 5 % - max.: 15 %	11,2			
2.2. Mechanikai szennyezések	A por vizes szuszpenziója makroszkóposan észlelhető idegen részecskéket nem tartalmaz	Megfelel			
2.3. Szemcseméret	Lineáris méret < 200 µm	Megfelel			
2.4. pH	4,5-6,0	4,7			
3. Összetétel vizsgálat					
3.1. Tisztasági vizsgálat					
3.1.1. Mikrobiológiai tisztaság	Max. 1000 mikroorganizmus /g ebből legfeljebb 100 gomba /g Kizárt: Enterobacteriaceae Pseudomonas aeruginosa Staphylococcus aureus Bacillus subtilis Candida albicans Aspergillus niger	Megfelel			
3.1.2. Nehézfém tartalom					
3.1.2.1. Ólom tartalom	Max. 0,15 g/kg	Megfelel			
3.1.2.2. Arzén tartalom	Max. 0,15 g/kg	Megfelel			
3.1.2.3. Alumínium	Max. 3,0 g/kg	Megfelel			
3.2. Tartalmi meghatározás					
3.3.1. Fémtartalom AAS, vagy ICP analízissel	Vizsgált elem	Néveleges tartalom mg/300ml	Min. mg/300ml	Max. mg/300ml	Analitikai érték mg/300ml
	K	116,4	98,9	133,9	89,1
	Mg	52,4	44,5	60,3	44,1
	Fe	48,9	41,6	56,2	44,0
	Zn	34,9	29,7	40,1	30,5
	Mn	10,5	8,9	12,1	8,6
	Cu	7,0	6,0	8,1	6,0
	V	1,75	1,5	2,0	1,4
	Co	0,7	0,49	0,91	0,6
	Mo	0,61	0,43	0,79	0,55
	Se	0,44	0,31	0,57	0,54

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Signature/Aláírás *[Signature]*

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CERTIFICATE OF TEST ITEM

ANEX_6_1

TOXICOLOGICAL RESEARCH CENTRE
TEST ITEM DATA-SHEET

To be prepared by the sponsor as complete as possible.
This data-sheet may be substituted or completed by a company-own analytical report.

Sponsor: *HUMET RT 1121 Bp. Kőbánya Tere 29-31.*

Product: *Dobaked Potassium Iodate powder* Batch - No.: *005DU0300*
(common name, code): *powder* Quantity: *005DU0300*

Chemical name: *-*
Structural formula: *-*

Purpose of use: *Long term tox on drugs*

Dose of use: *.*
(anticipated)

Active component: *-*
(in %)

Other components: *-*
(qualitative and quantitative)

Analytical method for test item concerning identity, homogeneity, concentration and stability:
JCP-OES, IR

Physical properties:
colour, odour, state: *brown = grey powder, special odour*
melting-point/boiling point: *-*
solubility: *partly soluble in water*
best stability: *60 °C*

Date of production: *-*
Expiration date: *-*

Storage cond.: *ambient 22 °C ± 3* (humidity 50% ± 10)
(please mark with x): *protected from light*
refrigerator, 4 °C ± 2
deep frozen, -22 °C ± 2

other storage cond.: *-*

Hazards and precautions:
(safety handling)

Any additional informations:

Signature of sponsor: *Álvarez Amiel* Date: *2000. Jan 27*

After completion of the study unused test item will be returned to the study sponsor.
TRC will retain a reference sample of the compound.

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Signature/Alíráás *[Signature]*

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