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Safety and Environmental Affairs Department  
Safety Programs  
L. E. Schmaltz  
MANAGER

ORIGINAL

November 7, 1994



INIT 11/16/94

TSCA Section 8(e) Substantial Risk Notice for  
Steam Cracked Petroleum Distillate CASRN 64742-91-2

U. S. Environmental Protection Agency  
Office of Pollution Prevention and Toxics  
Document Processing Center (TS-790)  
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Washington, D. C. 20460

Contains No CBI

ATTN: Section 8(e) Coordinator



88950000047

Dear Sir:

A skin tumor promotion study of materials boiling in the middle distillate range of petroleum products began in May 1994. A product identified as HAN 957 (HAN is an acronym for Heavy Aromatic Naphtha), which is also known as Steam Cracked Aromatic Petroleum Distillate, CASRN 64742-91-2, is one of the various compounds being evaluated.

The study is designed to evaluate the role of irritation on tumor promotion activity. In addition to being applied neat, skin irritation of each test material is reduced or eliminated by dilution in a lubricant base stock.

Preliminary data from week 21 of the study indicates that the Steam Cracked Aromatic Petroleum Distillate may be a weak skin tumor promoter. DMBA initiated mice treated with this test compound had increased tumor incidence as noted on the summary data attached.

Based on previous observations of other middle distillate petroleum fractions, this result is not unexpected; however, this same material was evaluated in an earlier dermal carcinogenic bioassay with a finding of no carcinogenic activity. A copy of that earlier study is enclosed, dated April 9, 1991.

These findings are based on preliminary data. As soon as the study is completed and a final report is issued, we will forward a copy to you. Please contact me at 713-870-6874 if there are additional questions.

Very truly yours,

Harry L. Hunter, Jr.

Attachments

12/15/94

## I. INTRODUCTION

The production of moderate to severe skin irritation by certain middle distillate products and their ability to produce a weak tumorigenic response in the mouse skin bioassay continue to be explored. Previous studies by EBSI and other industry groups have examined the roles of chronic irritation, the refining process, and product composition in tumorigenicity. The objective of this study was to examine the role of dose and continuous chronic irritation in middle distillate-induced skin tumorigenicity. HAN 906 (high aromatic naphtha, a steam cracked gas oil) and Turbo Fuel A (similar to kerosene) were selected as test samples. Both 100% HAN 906 (now branded as HAN 957) and 100% Turbo Fuel A were tested in the mouse skin bioassay using either a continuous or intermittent dosing schedule. The purpose of the intermittent dosing was to determine whether uninterrupted chronic irritation is required to elicit the tumorigenic response. In addition, 50% and 25% dilutions of HAN 906 in 100 Solvent Neutral (S100N, a non-irritating, non-tumorigenic highly refined 100 SUS mineral oil) were applied continuously. A complete record of this study can be found in the EBSI laboratory report 90MRL 210.

## II. METHODS

Male C3H/HeNCr1BR mice, approximately 6 to 8 weeks of age, were obtained from Charles River Breeding Laboratories (Kingston, NY), and randomly assigned to test groups containing 50 mice each. They were housed individually in suspended stainless steel cages and identified by ear tags. Food and water were available on an ad libitum basis. Other matters of animal husbandry were carried out according to standards, promulgated by the U.S. Department of Health, Education and Welfare.

The test materials were applied to the clipped interscapular area of the back of each mouse. Benzo(a)pyrene, diluted to 0.05% in toluene, served as the positive control and was applied as a single 25 microliter dose 3 times a week. Turbo Fuel A and HAN 906 were applied as single 37.5 microliter doses 2 times per week. Turbo Fuel A was administered undiluted while HAN 906 was applied either undiluted or as 50% and 25% dilutions. Solvent 100 Neutral (S100N) served as the vehicle for HAN 906 and as a negative control. In addition, both 100% Turbo Fuel A and 100% HAN were applied using an intermittent dosing schedule in which dosing was suspended when extreme signs of dermal irritation were noted and resumed when irritation disappeared.

The animals were observed twice daily for viability. Observations were made at study initiation and every week thereafter until the study was terminated for signs of the onset and progression of toxicological responses as well as for the presence of dermal growths and irritation. The level of dermal irritation was semiquantitated as an "Irritation Index" as previously described (MR.1400.90). A complete gross necropsy was performed on each animal following death. In addition, the treated

- 2 -

skin was excised and examined histopathologically. The median latency of tumor development was estimated using the Weibull distribution function<sup>1</sup>.

### III. RESULTS

The effects of HAN 906 and Turbo Fuel A on tumor incidence, mean survivorship and time to tumor are shown in Table 1. The continuous application of 100% Turbo Fuel A produced tumors in approximately 44% of the animals. When the intermittent dosing schedule was employed, only one animal treated with 100% Turbo Fuel A developed tumors. No tumors were produced in mice receiving 100% HAN 906 either by the continuous or intermittent dosing schedules or following treatment with 25% HAN 906. However, tumors were observed in one animal in the group receiving 50% HAN 906. Continuous application of 100% Turbo Fuel A significantly reduced survival and time to tumor.

A time-related index of irritation (described in MR.1400.90) is provided in Figure 1 for undiluted HAN 906 and Turbo Fuel A. The most severe signs of skin irritation as supported by histopathological evidence, were observed in the animals treated with benzo(a)pyrene, or following continuous dosing with 100% Turbo Fuel A or 100% HAN 906. A dose-related increase in irritation occurred in the groups treated continuously with dilutions of HAN 906. As expected, the intermittent dosing schedule tended to ameliorate (on average) the irritation produced by 100% Turbo Fuel A and 100% HAN 906. The shaved untreated and vehicle control groups showed no consistent evidence of dermal irritation.

### IV. DISCUSSION

These data suggest that with those middle distillate products eliciting a tumorigenic response, 1) there is a requirement for continuous dosing and 2) chronic irritation alone does not explain the tumorigenic effect. Also, the aromatic nature of HAN 906 suggests that aromaticity is not critical for the middle distillate tumorigenic response.

Application of both test materials using the intermittent dosing schedule resulted in reduced irritation during suspension of dosing, and prevented prolonged periods of severe irritation. The requirement for continuous dosing was demonstrated by the fact that the moderate tumorigenic response caused by the continuous application of 100% Turbo Fuel A disappeared when the intermittent dosing schedule was used.

The application of HAN 906 clearly indicates that chronic irritation alone is not sufficient to cause the tumorigenic effect. Although highly irritating, HAN 906 was not a skin carcinogen.

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<sup>1</sup>Whitmore, A. and Keller, J. B., (1978). Quantitative Theories of Carcinogenesis Soc. Ind. Appl. Math. Review 20: 1-30.

- 3 -

These data support previous middle distillate studies and infer that chronic skin irritation may be required but is not, in itself, sufficient for tumor development.

TABLE 1

EVALUATION OF THE CARCINOGENIC POTENTIAL OF TURBO FUEL A  
AND HAN 906 USING THE MOUSE SKIN BIOASSAY

Treatment	Tumor Bearing Animals (TBA) Gross Count	Histologically Confirmed	Weibull Mean Survivorship (Days)	Mean Time to Tumor (Days) <sup>1,2</sup>
Shaved Untreated (Control)	0	0	627	1292 <sup>a</sup>
S100N	0	0	610	1275 <sup>a</sup>
B(a)P (0.05% in Toluene)	49	47(46) <sup>3</sup>	347	324 <sup>b</sup>
100% Turbo A	17	22(19)	561	628 <sup>c</sup>
100% Turbo A (VDS)	1	1	616	1135 <sup>a</sup>
100% HAN 906	0	0	583	1236 <sup>a</sup>
100% HAN 906 (VDS)	0	0	610	1266 <sup>a</sup>
50% HAN 906	0	1	649	1333 <sup>a</sup>
25% HAN 906	0	0	639	1312 <sup>a</sup>

1. Estimated by Weibull Method  
 2. Values with different superscripts are significantly different from each other (p < 0.05).  
 3. The number of TBA with carcinomas indicated in parentheses  
 4. VDS - variable dosing schedule

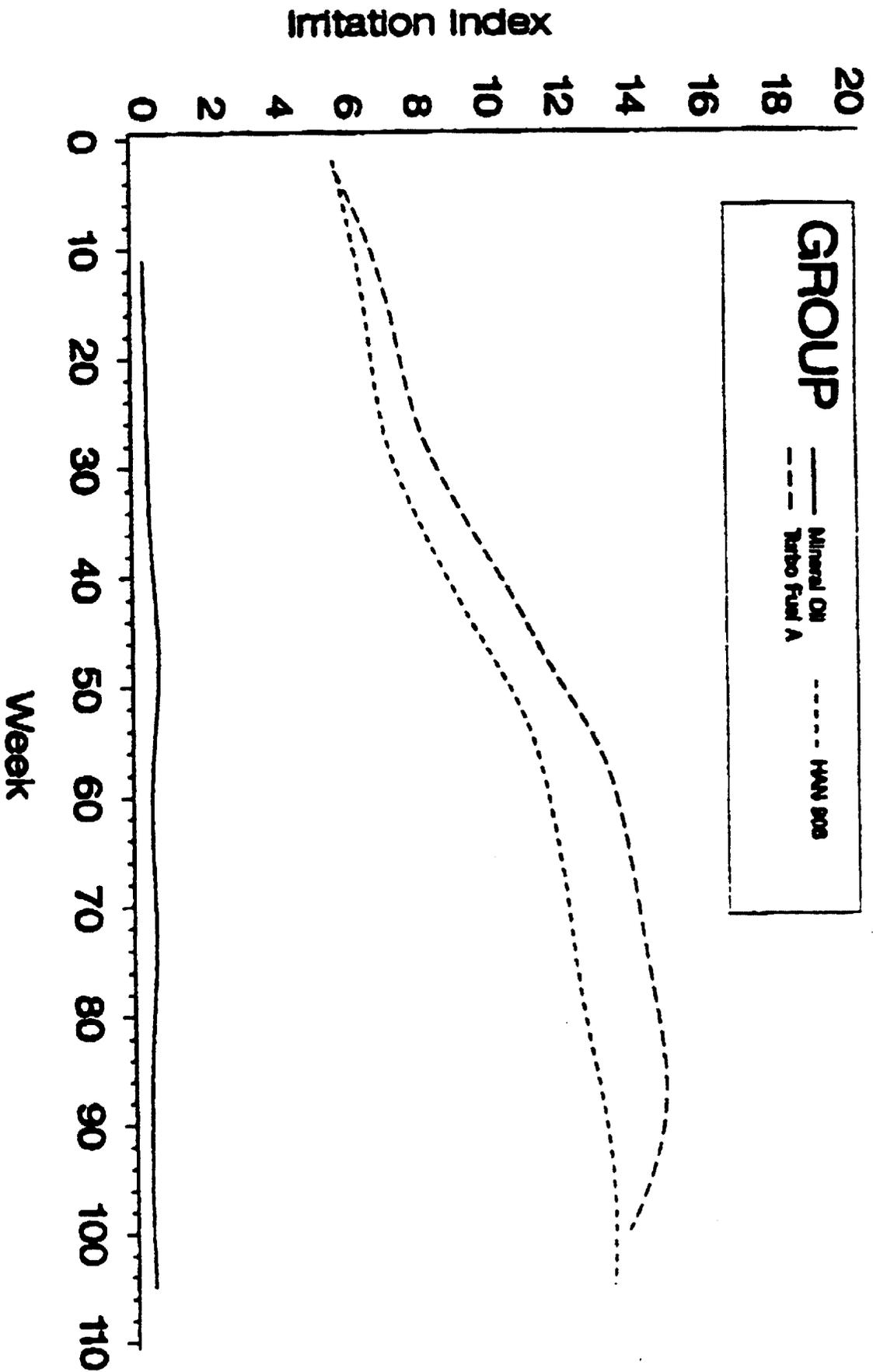


Figure 1. Time-related skin irritation index elicited by undiluted HAN 906 and Turbo Fuel A.

# EXXON BIOMEDICAL SCIENCES, INC.

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**PROPRIETARY INFORMATION**

**TECHNICAL REPORT**

EVALUATION OF HAN 906 AND TURBO FUEL A  
FOR DERMAL CARCINOGENIC POTENTIAL  
USING THE MOUSE SKIN BIOASSAY

C. McGowan  
J. J. Freeman

April 9, 1991  
MR.400.91

**EXXON BIOMEDICAL SCIENCES, INC.****For authorized company use only  
PROPRIETARY INFORMATION****MANAGEMENT DIGEST  
Technical Report**April 9, 1991  
MR.400.91**EVALUATION OF HAN 906 AND TURBO FUEL A  
FOR DERMAL CARCINOGENIC POTENTIAL  
USING THE MOUSE SKIN BIOASSAY**

This study was conducted to further investigate the dermal irritation and tumorigenic response observed with certain middle distillate products. Turbo Fuel A and HAN 906 (currently branded as HAN 957), previously evaluated for chronic skin irritation potential in mice, were tested in the mouse skin bioassay to determine whether middle distillate-induced skin irritation is necessary and/or sufficient to cause skin tumors. This project was sponsored by the Mutualized Technical Program.

HAN 906 is a steam cracked gas oil with a high aromatic content (~95%), and Turbo Fuel A is essentially kerosene with an aromatic content of ~21%. HAN 906 and Turbo Fuel A were tested undiluted under continuous and intermittent dosing schedules. Under the intermittent dosing schedule, dosing was suspended upon the onset of severe skin irritation and resumed when the irritation resolved. HAN 906 was also tested for dose-response using 50% and 25% dilutions in 100 Solvent Neutral, a non-irritating, non-tumorigenic mineral oil.

Histologic evidence of moderate to severe irritation was produced in mice treated with 100% Turbo Fuel A and 100% HAN 906 using both the continuous and intermittent dosing schedule. A dose-related increase in dermal irritation was noted for the HAN 906 treated groups. The level of irritation observed with these treatments was judged to be similar to that previously observed with Mentor 28 and dilutions of Mentor 28 in toluene (MR.1400.90). In the Mentor 28 study, only undiluted Mentor was carcinogenic to mouse skin. Undiluted Turbo Fuel A, applied continuously, caused a moderate tumorigenic response when evaluated on the basis of tumor latency and tumor count. None of the other treatments produced tumor incidences different from what is routinely observed in control animals.

These data suggest that irritancy alone does not explain the tumorigenic properties of these middle distillate products. However, continuous exposure to some middle distillate products may be required for the manifestation of the tumorigenic response. In addition, the aromatic nature of HAN 906 suggests that aromaticity is not critical for the middle distillate tumorigenic response. Further studies are planned to investigate the importance of hydrocarbon structure to middle distillate carcinogenicity.

C. MCGOWAN & J. J. FREEMAN  
TOXICOLOGY DIVISIONTo: Exxon Biomedical Sciences, Inc.  
Information Services Section  
Proprietary Resources  
Metlars Road, CN 2350  
East Millstone, N.J. 08875-2350

Name, Company, &amp; Mailing Address:

Please send me a copy of Report No. MR.400.91

Signed: \_\_\_\_\_

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**TABLE 1**

**SURVIVORSHIP AND TUMOR INCIDENCE  
IN EBSI PROMOTION STUDY: 21 WEEKS**

DMBA/DMBA (INITIATOR/PROMOTOR)	SURVIVAL (%)	TUMOR INCIDENCE (%)
MINERAL OIL/MINERAL OIL - NEGATIVE CONTROL	100	0
DMBA/PMA - POSITIVE CONTROL	93	93
DMBA/MINERAL OIL - NEGATIVE CONTROL	100	0
DMBA/HAN 957 (100%)	100	13
DMBA/HAN 957 (28.6%)	100	7

**TABLE 2**  
**MOUSE SKIN TUMOR STUDY DATA ON VARIOUS PETROLEUM PRODUCTS**

ESTERIFIED	STEAM CRACKED GAS OIL
Processing History	Steam cracked gas oil
Compositional Information	95% Aromatics -20% 1-Ring -63% 2-Ring 5% olefins
IBP°C (°F)	181 (350)
FBP°C (°F)	266 (511)
Mouse skin cancer bioassay: tumor incidence	0/50
Dermal Bioassay	4/30* high dose
Skin Tumor Promotion: tumor incidence	2/30 low dose
References	EBSI Report 91 MRL 77

\*Preliminary data.



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

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Senior Environmental Associate  
Exxon Chemical Company  
P.O. Box 3272  
Houston, Texas 77253-3272

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

JAN 12 1995

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".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)  
Attn: TSCA Section 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
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

13257 A



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contains at least 50% recycled fiber

17

### Triage of 8(e) Submissions

Date sent to triage: APR 26 1995

NON-CAP

CAP

Submission number: 13257A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO                  AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX                  SBTOX                  SEN                  w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX                  CTOX                  EPI                  RTOX                  GTOX  
STOX/ONCO                  CTOX/ONCO                  IMMUNO                  CYTO                  NEUR

Other (FATE, EXPO, MET, etc.): \_\_\_\_\_

Notes:

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entire document:	0 <u>1</u> 2	pages _____	pages <u>1, tabs</u>
Notes:			
Contractor reviewer:	<u>LPS</u>	Date:	<u>1/30/95</u>

CECATS DATA:

Submission # BEHO-1194-13257 SEQ. A

TYPE: INT/SUPP FLWP

SUBMITTER NAME: Exxon Chemical Americas

INFORMATION REQUESTED: FLWP DATE:

- 0501 NO INFO REQUESTED
  - 0502 INFO REQUESTED (TECH)
  - 0503 INFO REQUESTED (VOL. ACTIONS)
  - 0504 INFO REQUESTED (REPORTING RATIONALE)
- DISPOSITION:  
 0505 REFER TO CHEMICAL SCREENING  
 0578 CAP NOTICE

VOLUNTARY ACTIONS:

- 0401 ACTION REPORTED
- 0402 STUDIES PLANNED/IN PROGRESS
- 0403 NOTIFICATION IN WORK/NOTIFIED
- 0404 LABELS/MSDS (TANGIBLE)
- 0405 PROCESS/AND/OR: (TANGIBLE)
- 0406 APPEASE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

SUB. DATE: 11/07/94 OTS DATE: 11/16/94 CERAD DATE: 12/15/94

CHEMICAL NAME:

HAN 957  
Turbo Fuel A

CASE

64742-91-2  
8008-20-6

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
<input checked="" type="checkbox"/> 0202 ONCO (ANIMAL)	<input checked="" type="checkbox"/> 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 CHEMPHYS PROF	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 BIOAQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI 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 PRODUCE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	<input checked="" type="checkbox"/> 0224 PRODCOMP/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	0229 METAPHARMACO (ANIMAL)	01 02 04		
<input checked="" type="checkbox"/> 0215 CHRONIC TOX (ANIMAL)	<input checked="" type="checkbox"/> 01 02 04	0230 METAPHARMACO (HUMAN)	01 02 04		

IRIS/DATA: NON-CBI INVENTORY YES  
 ONGOING REVIEW: YES (DROP/PREFER)  
 CAS SR: NO  
 SPECIES: MUS  
 TOXICOLOGICAL CONCERN: LOW  
 USE: MED  
 PRODUCTION: HIGH

226 is Interim report.  
 Mouse skin bioassay 2 applications/week for weeks (21 weeks, interim report) at 100%  
 & dilution of 50% and 25% of middle distillate products, HAN 906 and Turbo Fuel A. The treat-  
 ment showed the these products produced severe irritation, and suggested that  
 harmonize properties are not limited only due irritancy.

8 (E) -13257A

L/H

HAN 906: DERMAL ONCOGENICITY IN MALE C3H/HENCR1BR MICE IS OF LOW CONCERN. DOSING (37.5 UL OF TEST SUBSTANCE APPLIED TWO TIMES/WEEK TO CLIPPED SKIN FOR APPROXIMATELY 18 MONTHS, 50 ANIMALS/GROUP) WAS EITHER CONTINUOUS (SEPARATE GROUPS FOR NEAT TEST SUBSTANCE AND 50 OR 25% DILUTIONS IN SOLVENT 100 NEUTRAL), WHICH PRODUCED DOSE-RELATED SEVERITY OF SKIN IRRITATION, OR INTERMITTENT (NEAT TEST SUBSTANCE ONLY) IN WHICH DOSING WAS SUSPENDED WHEN EXTREME SIGNS OF DERMAL IRRITATION WERE NOTED AND RESUMED WHEN IRRITATION DISAPPEARED. ANIMALS WERE SUBJECTED TO COMPLETE GROSS NECROPSY, BUT ONLY THE SKIN WAS EXAMINED MICROSCOPICALLY. SKIN TUMOR INCIDENCES WERE 0/50 FOR EVERY TEST GROUP EXCEPT THE 50% DILUTION (1/50, HISTOLOGICAL CLASSIFICATION NOT GIVEN, BUT NOT CLASSIFIED AS A CARCINOMA). SKIN TUMOR INCIDENCES WERE 0/50 FOR THE UNTREATED CONTROLS AND 0/50 FOR THE SOLVENT (SOLVENT 100 NEUTRAL) CONTROLS.

TURBO FUEL A: DERMAL ONCOGENICITY IN MALE C3H/HENCR1BR MICE IS OF HIGH CONCERN. DOSING (37.5 UL NEAT TEST SUBSTANCE APPLIED TWO TIMES/WEEK TO CLIPPED SKIN FOR APPROXIMATELY 18 MONTHS, 50 ANIMALS/GROUP) WAS EITHER CONTINUOUS, WHICH PRODUCED MODERATE TO SEVERE SKIN IRRITATION, OR INTERMITTENT, IN WHICH DOSING WAS SUSPENDED WHEN EXTREME SIGNS OF DERMAL IRRITATION WERE NOTED AND RESUMED WHEN IRRITATION DISAPPEARED. ANIMALS WERE SUBJECTED TO COMPLETE GROSS NECROPSY, BUT ONLY THE SKIN WAS EXAMINED MICROSCOPICALLY. SKIN TUMOR INCIDENCES WERE 22/50 (19/50 CLASSIFIED AS CARCINOMAS) WITH CONTINUOUS DOSING, 1/50 (0/50 CARCINOMAS) WITH INTERMITTENT DOSING, AND 0/50 FOR THE UNTREATED AND SOLVENT (SOLVENT 100 NEUTRAL) CONTROLS.