ACUTE TOXICITY IN MICE

COMPOUND 3-Hydroxy-3-methylbutanoic acid (Tur 13)

SOURCE Lorillard - Organic Chemistry LORILLARD NO.: OR39-23 LOT NO.: A4

DATE RECEIVED: Unk. TESTED: 12/28/78 REPORTED: 5/3/79 10/6/80, Update

INVESTIGATOR(S): H. S. Tong & M. S. Forte' NOTEBOOK/PAGE: BIO14-23

SIGNATURE(S): H. S. Tong M. S. Forte (by A. Poole)

STRAIN OF MICE: Swiss-Webster MALE: X FEMALE: ____ DATE RECEIVED: Unk.

AVERAGE WEIGHT/RANGE (GM): ____ SOURCE: Camm Research

ROUTE OF COMPOUND ADMINISTRATION: ☒ P.O. ☐ I.P. ☐ I.V. ☐ INHALATION

COMPOUND VEHICLE: ☒ .5 % METHYL CELLULOSE ☐ CORN OIL ☐ SALINE ☐ OTHER ____

GROUP NO.	% SOLUTION	DOSAGE (mg/kg BODY WEIGHT)	RESULTS (NO. DEAD/NO. TESTED)
1	5	1800	1/6
2	10	2160	0/6
3	10	2592	0/6
4	10	3732	3/6
5	10	4479	6/6

REFERENCE FOR CALCULATION: Litchfield, J. T. and Wilcoxin, F., J. of Pharmacol. and Exper. Ther., 90:99, 1948.

LD50 (95% CONFIDENCE LIMITS): 3.5 (3.1 to 3.9) g/kg

CONCLUSION: This compound appears to act as a CNS depressant with symptons of respiratory depression, constriction of blood vessels, and inactivity. Survivors recovered in 48 hours. The recommended safe dose for a single trial by inhalation in man is 0.3 mg.

Copies to the Following: Dr. H. J. Minnemeyer
Ms. L. B. Gray

00040534

Manuscript Review Form

TOBACCO SCIENCE

Registration No. 533 Date March 18, 1968

AUTHORS Andrew G. Kallianos, Richard E. Means, James D. Mold

TITLE "Effect of Nitrates in Tobacco on the Catechol Yield in Cigarette Smoke"

REVIEW COMPLETED 3/29/68 RECOMMENDATION: X APPROVE IN ITS PRESENT FORM; ____ NOT APPROVE (Give reasons below); ____ APPROVE TENTATIVELY, SUBJECT TO THE FOLLOWING SUGGESTED REVISIONS: (itemize below):

Page 4 - Last line should be Mass spectrometric, instead of Mass spectroscopic.

00070353

NOTE—Execute in triplicate using additional sheets if more space is required. Retain the third copy for your file. Return the original (signed) and the first carbon (*unsigned*) along with the manuscript to this office. The unsigned copy and the manuscript will be returned to the author for his consideration.

Date: September 21, 1976

Sample No. 6030

Type of Cigarette 85 mm Filter

Batch Size 50 lbs.

Original Request Made By Dr. A. W. Spears on September 21, 1976

Sample Specifications Written By W. E. Routh

BLEND	CASING	RECASING	FINAL FLAVOR	Additional Spray ~~XXXXXX~~
OGS	OGS	OGS	OGS	3.4% PMO in EtoH

Cigarettes

Maker AMF
Length 85 mm
Circumference 25.0
Weight To be det. (803 mg tobacco)
Pressure Drop To be determined
Filter Length 20 mm
Paper 554
Tipping Paper 30 mm

Filters

Kind 20 mm True plastic rod
Process
Rod Length
Pressure Drop
Circumference
Weight
Plasticizer
Plug Wrap

Capping

Labels White
Closures Blue
Tear Tape White
Cartons "
Markings Sample No. on overwrap

Responsibility

Tobacco Blend Ammons
Filter Production Wicker
Making & Packing Brown/Routh
Shipping Routh
Sample Requisition "
[Form 02:02:06]

Requirements

Laboratory 3 cartons
Other 20,000 cigts.

Laboratory Analysis

Smoke Analysis
PMO Analysis

Special Requirements

Spray 50 lbs. tobacco with solution of 880 g (= 1.94 lbs.) PMO in 1175 ml of denatured alcohol. This should give 3.4% PMO add-on (3.3% PMO contained) assuming 88% spraying efficiency. PMO delivery from 85 mm cigarette smoked to 30 mm butt should be 6.5 mg/cig.

Reports

Written by P. D. Schickedantz
Original to Dr. A. W. Spears
Copies to Dr. F. J. Schultz
Dr. H. J. Minnemeyer

00093726

H. J. Minnemeyer
Manager, ~~Product Development~~ Research

Date: 7/16/68

Sample No. 5031

Original request made by Mr. C. L. Tucker, Jr. on 7/10/68

Sample specifications written by John H. M. Bohlken

BLEND CASING RECASING FINAL FLAVOR MENTHOL FLAVOR

OLD GOLD STRAIGHT Tobacco Blend

Control for Sample No. 5030

Cigarettes:

Brand	OLD GOLD STRAIGHT
Length	85 mm.
Circumference	25.3 mm.
Paper	Ecusta 556
Firmness	OLD GOLD STRAIGHT
Draw	OLD GOLD STRAIGHT
Weight	OLD GOLD STRAIGHT
Tipping Paper	--
Print	OLD GOLD STRAIGHT
Filter Length	--

Wrappings:

Labels	OLD GOLD STRAIGHT
Closures	Standard Blue
Tear Tape	Gold
Cartons	OLD GOLD STRAIGHT
Markings	Sample number on each pack and carton

Requirements:

Laboratory	One Tray
Others	

Laboratory Analysis:

7-16-68 7-16-68 7-16-68

Tars and Nicotine, Taste Panel, Burning Time, Gas Phase Analysis, Benzo (A) Pyrene Analyses — 7-16-68- C. L Assisted

Responsibility:

Tobacco Blend	Manufacturing - A. Kraus
Filter Production	--
Making & Packing	Product Development , John H. M. Bohlken
Shipping	

Reports:

Written by -- John H. M. Bohlken
Original to - Mr. C. L. Tucker, Jr.
Copies to --- Dr. A. W. Spears

Chas. L. Tucker, Jr.

GREY ADVERTISING INC. – MEETING REPORT

FEB 23 1982

CLIENT: Brown & Williamson

PRODUCT: Viceroy

PRESENT: (For the client)
T. Parrack

(For the agency)
P. Hendricks

DATE: 1/19/82 **NO.** V82-2 R1

PLACE: Telephone

DATE OF REPORT: 2/17/82

SUMMARY:

Written by: P. Hendricks

CONFIDENTIAL

Client confirmed agreement for Agency to pay advance to photographer, with official signed estimate to follow, for Viceroy shoot week of 1/25/82. This was agreed to by T. Parrack and A. Forsythe at the January 18 pre-production meeting.

PH:mg

cc: R. Schoenfein
S. Dammers
P. Hendricks

670121460

PU 1020 (1-81)

BROWN & WILLIAMSON TOBACCO CORPORATION

MATERIAL SPECIFICATION OR DESIGN CHANGE AUTHORIZATION

NEW ITEM

DESCRIPTION VICEROY Rich Lights 100's 20's Label

BRAND(S) VICEROY Rich Lights

DESIGN NO. 81-257 UPC NO. 272972 MATERIAL NO. 50-034A

TYPE CHANGE: ☒ OFFICIAL ☐ TEMPORARY

USE: ☒ DOMESTIC ☐ MILITARY EXPORT ☐ GENERAL EXPORT ☐ CUSTOMER SPEC. (GRAVURE)

Is a material or dimensional change also involved? ☐ YES ☒ NO
If yes, supply details:

BRANCH	LOUISVILLE	PETERSBURG	MACON	WINSTON-SALEM
SCHEDULE: DATE OR INVENTORY DEPLETION	10/30/81			
DELIVERY DATE	10/16/81			

REPLACEMENT

DESCRIPTION VICEROY Rich Lights 100's 20's Label

DESIGN NO. 80-15 UPC NO. 272972 MATERIAL NO. 50-034

BRANCH	LOUISVILLE	PETERSBURG	MACON	WINSTON-SALEM
INVENTORY DEPLETION DATE	10/30/81			

COMMENTS: Material #50-034A has been assigned to the VICEROY Rich Lights 100's 20's Label with new bottom panel. Bottom now incorporates shield. On both side and bottom panels, "VICEROY" and "Rich Lights" have been inverted. Cartons and labels must change design simultaneously. The current design cannot be used in production after 10/30/81.

680115980

Copies to: J. F. Banks
C. Lamb
C. L. Domeck
J. W. Webb
L. C. Lanham
Branch QC
Branch Supply

SIGNED: S T Beasley (MRS.) /jlf

S. T. BEASLEY (MRS.)/jlf

DATE: 9/17/81

A-27

AMES ASSAY FOR MUTAGENICITY

COMPOUND: 2,4-Dihydroxypyridine

SOURCE: Lorillard - Organic Chemistry LORILLARD NO.: OR61-2 LOT NO.:

DATE RECEIVED: 9/3/80 TESTED: 9/10/80-10/10/80 REPORTED: 10/10/80

INVESTIGATOR(S): H. S. Tong & A. A. Poole NOTEBOOK/PAGE: BIO7-24

SIGNATURE(S): H. S. Tong A. A. Poole

TOXICITY (% SURVIVAL)		50	80	100
CONCENTRATION (mg/ml)			.5	

SOLVENT: ☒ DMSO; ☐ WATER ☐ OTHER

S. TYPHIMURIUM	TA1535		TA100		TA98			
	(−)S-9	(+)S-9	(−)S-9	(+)S-9	(−)S-9	(+)S-9	(−)S-9	(+)S-9
CONTROL REVERTANTS PER PLATE (0.05 ml SOLVENT)	4.67	8.00	123.00	135.33	3.33	16.00		
COMPOUND (ug/plate)	REVERSION RATE (TEST REVERTANTS/CONTROL REVERTANTS PER PLATE)							
500		.92		.88		.96		
250	1.00	.79	.97	.97	.90	.92		
125		.83		.92		.85		
POSTIVE CONTROL (ug/plate)								
2-AMINOANTHRACENE								
4	1.20	8.63	1.39	7.26	1.80	27.69		
2	.86	4.75	1.24	6.07	.30	24.13		

CONCLUSION: This compound is judged non-mutagenic in this test system.

Copies to the Following: Dr. H. J. Minnemeyer
Ms. L. B. Gray

00836244

COMPOUND PHYSICAL PARAMETERS

LRC FILE NUMBER
A30

LOT NUMBER

PHYSICAL STATE
Clear Colorless liquid

pH
The pH of a 50% concentration of A30 in (52.6% dioxane/)water was calculated to be 8.13 at 24°C according to the extrapolation procedures by Dr. P. D. Schickedantz, Lorillard Research Center Accession Number 1662, Reference OR 83-81.

SOLUBILITY (See SOP for Biological Solutions)

ORAL

Reference OR 100-32

.5g A30 soluble in .5 mL corn oil at room temperature.

ACUTE CARDIOVASCULAR

(See SOP for Determination of Solubility of Materials for Acute Cardiovascular and Respiratory Effects Study in Beagle Dogs)

Reference OR 100-32

.2 mg A30 soluble in .5 mL 10% propylene glycol solution at 38°C. Add A30 to warm (38°C) propylene glycol; add warm water to make 10% propylene glycol solution.

STORAGE RECOMMENDATIONS:
Refrigerate in amber bottle at no more than 8°C.

COMPOUND SENSITIVE TO

☐ AIR ☐ HEAT ☐ MOISTURE ☐ OTHER _____

SAFETY COMMENTS (SUGGESTED HANDLING PROCEDURE)

00836016

SIGNATURE W. A. Long

DATE 8/10/82

LORILLARD RESEARCH CENTER

FORM 8 (7-82)

COMPOUND PHYSICAL PARAMETERS

LRC COMPOUND CODE: A32

DATE: 11/13/81

MOLECULAR WEIGHT: 200.29

SOLUBILITY ☐ MEASURED ☐ ESTIMATED
☐ WATER ☐ OTHER AMOUNT g/100ml

CLASS ☐ ACID ☐ BASE ☐ SALT ☐ OTHER

REACTIVITY — DESCRIPTION OF REACTIVITY

	WITHOUT HEATING		WITH HEATING (80°C)	
1) WATER or BRINE:	☐ UNCHANGED	☐ DECOMPOSITION	☐ UNCHANGED	☐ DECOMPOSITION
2) 5% HCL:	☐ UNCHANGED	☐ DECOMPOSITION	☐ UNCHANGED	☐ DECOMPOSITION
3) 5% NaOH:	☐ UNCHANGED	☐ DECOMPOSITION	☐ UNCHANGED	☐ DECOMPOSITION
4) ALCOHOLS:	☐ UNCHANGED	☐ DECOMPOSITION	☐ UNCHANGED	☐ DECOMPOSITION
5) OXYGEN:	☐ UNCHANGED	☐ DECOMPOSITION	☐ UNCHANGED	☐ DECOMPOSITION
6) LIGHT:	☐ UNCHANGED	☐ DECOMPOSITION	☐ UNCHANGED	☐ DECOMPOSITION

SAFETY COMMENTS (SUGGESTED HANDLING PROCEDURE)

00837265

CHEMICAL PURITY

ANALYTICAL METHOD(S)

STORAGE RECOMMENDATIONS ☐ NORMAL STORAGE ☒ SPECIAL STORAGE Refrigerate in amber bottle at no more than 8°C

COMPOUND SENSITIVE TO:
☐ AIR ☐ HEAT ☐ LIGHT ☐ MOISTURE ☐ OTHER

COMMENTS

pH - The pH of a 50% concentration of A32 in a 52.6% dioxane/water solution was calculated to be 2.92 at 22°C according to the extrapolation procedures by Dr. P. D. Schickedantz, Lorillard Research Center Accession No. 1662, Reference OR 83-125.

Solubility (See SOP for Biological Solutions)

Oral - 5g A32 forms a suspension with stirring in 10 ml 1% Tween 80 at room temperature. Reference OR 72-151.

Acute Cardiovascular - Mix 2 mg A32 with 0.2 ml 80% propylene glycol and grind lightly. Add 0.8 ml saline solution. A32 is a suspension in this mixture at room temperature. Reference OR 72-152.

SIGNATURE Wm F. Johnson DATE 1/6/82

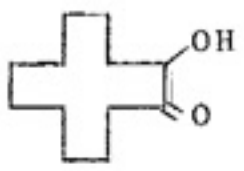
DECISION TREE ESTIMATION OF TOXIC RISK

NAME	DATE
Paul Schickedantz, Jack Reid	12-4-80

COMPOUND NAME

2-Hydroxycyclododecanone

STRUCTURE



ESTIMATED TOXICITY CLASS	LORILLARD COMPOUND CODE NUMBER
II	A41

COMMENTS

This carbocyclic keto alcohol was placed in estimated toxicity class II due to the direct attachment of the ketone to the cyclic nucleus.

00838511

INFORMATION SEARCH SUMMARY

TYPE
CHEMICAL ☐ BIOLOGICAL ☐ COMBINED ☒

NAME Jimmy Bell

DATE May 27, 1982

COMPOUND NAME
Valerian Fluid Extract

LORILLARD COMPOUND CODE
B73

REGISTRY NUMBER (if applicable)
N/A

LITERATURE SURVEYED

DATES REVIEWED

II. (cont'd)

Toxline	1974-Jan. 1982
Registry of the Toxic Effects of Chemicals	to Dec. 1981

Ann C. Stringfield, M.L.S.
Literature Chemist

III. SUPPLEMENTAL LITERATURE SEARCH

Chemical Abstracts Vol. 23 - Vol. 65	1929-1966
Arctander's Perfume and Flavor Materials of Natural Origin (1960)	
Guenther's Monographs on Fragrance Raw Materials (1979)	
Tobacco Abstracts	1957-Dec. 1981
U. S. Dispensatory 23rd edition (1943)	

Jimmy H. Bell B. Sc.
Scientist

00851722

ADDENDUM I

DAWSON RESEARCH CORPORATION

Protocol Change Order No. 1

Protocol LRC-5A

Date 5-13-81

Subject Change in the time of the Pre-dose Biomicroscopic Examination

Authorized by Dr. Connie Stone Date 5-13-81 Method Verbal-Phone
(Means of communication)

Authorized to Mr. Charles Burns

Estimated cost of the study will be:

[X] increased [ ] decreased [ ] not affected

Description of change order:

Section III. A. 2nd paragraph - the first sentence is to be changed to read as follows:

> Twenty-four to 30 hours prior to dosing, both eyes of each rabbit will be examined by an experienced investigator using a slit lamp biomicroscope.

The change was made so the protocol more closely conforms with the proposed regulations as stated in the Federal Register, Vol. 44, No. 145, 772.112-24 Primary Eye Irritation Study.

00851879

Connie L. Stone 5/19/81

Sponsor Signature

Charles L. Burns 5/14/81

Study Director Signature

PROJECT SHEET

HAZLETON LABORATORIES AMERICA, INC.

9200 LEESBURG TURNPIKE
VIENNA, VIRGINIA 22180
U.S.A.

DATE ISSUED: December 13, 1983 | PROJECT SHEET NO.: 4 | PROJECT NO.: 642-149

STUDY TITLE & PROPOSAL NUMBER: 14-Day Single Dose Subacute Toxicity Study 3212

PROJECT COORDINATOR: D. Serata
SIGNATURE: D. Serata

TEST MATERIAL(s): B121

LOT NO.(s)	RECEIPT DATE(s)	LH-NUMBER(s)
	11/18/83	21,017

PERFORMING DEPARTMENTS (4 COPIES EACH DIRECTOR)
Acute/Dermal Toxicology

ORIGINAL SIGNED PROJECT SHEETS TO PSO

FIXED DISTRIBUTION: (1 COPY TO EACH)

DIR. OF LIFE SCIENCES
HEALTH SERVICES
COMPOUND PREP (TOX)
SCIENTIFIC RES (TOX)
LAB ANIMAL MEDICINE
QUALITY ASSURANCE
CONTRACTS
Sponsor

PROTECTIVE PRECAUTIONS REQUIRED:
HAZARDOUS COMPOUND

EXPLOSIVE ____ CARCINOGEN (OSHA) ____
FLAMMABLE ____ CARCINOGEN (OTHER) ____
RADIOACTIVE ____ ____ ____

FOLLOW DEPARTMENT AND COMPANY SAFETY MANUALS [X]

PHYSICAL DESCRIPTION:

SOLID X
LIQUID ____
PRESSURIZED ____
Brown COLOR

STORAGE CONDITIONS

- [ ] STORE IN DARK
- [X] REFRIGERATOR 8°C
- [ ] ROOM TEMPERATURE
- [ ] SPECIAL INSTRUCTIONS WHILE DOSING
- [ ] DESSICATOR
- [ ] FREEZER
- [ ] OTHER ____

EXPERIMENTAL PROCEDURES to be performed in Acute/Dermal Toxicology, building 18.

This project sheet is issued to correct Project Sheet which was issued on December 6, 1983 to Project Sheet No. 3 instead of 2.

Material Safety Data Sheet is attached to Project Sheet 1.

00860012

COMPOUND PHYSICAL PARAMETERS

LRC FILE NUMBER	LOT NUMBER
B164	

PHYSICAL STATE

Brownish-gray powder

pH

The pH of a 50% concentration of B164 in water was calculated to be 4.82 at 25°C according to the extrapolation procedures by Dr. P. D. Schickedantz, Lorillard Research Center Accession Number 1662.

SOLUBILITY

(See SOP for Biological Solutions)

ORAL

Reference: BC20-48

B164 forms a suspension in corn oil at 0.5 g/1.5 ml

Triple dosing is required

ACUTE CARDIOVASCULAR

(See SOP for Determination of Solubility of Materials for Acute Cardiovascular and Respiratory Effects Study in Beagle Dogs)

Reference: BC20-48

B164 is insoluble according to this procedure

STORAGE RECOMMENDATIONS

Refrigerate in amber glass bottle at no more than 8°C

00865872

COMPOUND SENSITIVE TO

[X] AIR [ ] HEAT [ ] MOISTURE [ ] OTHER

SAFETY COMMENTS (SUGGESTED HANDLING PROCEDURE)

SIGNATURE	DATE
Amelia Poole	8/22/83

B166

PROJECT SHEET

HAZLETON LABORATORIES AMERICA, INC.

9200 LEESBURG TURNPIKE
VIENNA, VIRGINIA 22180
U.S.A.

DATE ISSUED Oct. 11, 1983 | PROJECT SHEET NO. 1 | PROJECT NO. 642-138

STUDY TITLE & PROPOSAL NUMBER 3212
Acute Intraperitoneal Toxicity Study in Rats

PROJECT COORDINATOR D. Serata
SIGNATURE: D. Serata

TEST MATERIAL(s)

B166

LOT NO.(s)	RECEIPT DATE(s)	LH-NUMBER(s)
	9/28/83	20,845

PERFORMING DEPARTMENTS (4 COPIES EACH DIRECTOR)
Acute/Dermal Toxicology

ORIGINAL SIGNED PROJECT SHEETS TO PSO

FIXED DISTRIBUTION: (1 COPY TO EACH)

DIR. OF LIFE SCIENCES
HEALTH SERVICES
COMPOUND PREP (TOX)
SCIENTIFIC RES (TOX)
LAB ANIMAL MEDICINE
QUALITY ASSURANCE
CONTRACTS
✓Sponsor

PROTECTIVE PRECAUTIONS REQUIRED:
HAZARDOUS COMPOUND

EXPLOSIVE ____ CARCINOGEN (OSHA) ____
FLAMMABLE ____ CARCINOGEN (OTHER) ____
RADIOACTIVE ____ ____ ____

FOLLOW DEPARTMENT AND COMPANY SAFETY MANUALS [X]

PHYSICAL DESCRIPTION:

SOLID ____
LIQUID X — Colorless COLOR
PRESSURIZED ____

STORAGE CONDITIONS

- [ ] STORE IN DARK
- [X] REFRIGERATOR 8°C
- [ ] ROOM TEMPERATURE
- [ ] SPECIAL INSTRUCTIONS WHILE DOSING
- [ ] DESSICATOR
- [ ] FREEZER
- [ ] OTHER ____

EXPERIMENTAL PROCEDURES to performed in Acute/Dermal Toxicology, building 18.

The protocol for this study is attached.

The protocol was approved in sponsor letter of June 6, 1983.

The anticipated initiation date of this study is October 1983.

The anticipated completion date of this study is November 1983.

00860842

HL FORM NO. 5
REVISED 1-81

☐ PURCHASING
☐ STATIONARY

PURCHASE REQUISITION

P.O. 1534 REV.10/79
LT-10-79

PLEASE INCLUDE ONLY ONE TYPE OF MATERIAL ON THIS REQUISITION

DATE: March 27, 1984

VENDOR — FOR PURCHASING DEPARTMENT USE ONLY
Borriston Laboratories, Inc., 5050 Beech Place Temple Hills, MD 20748

ORDER NO.

Prev. or Recommended Supplier

TERMS: NET 15 F.O.B.: N/A VIA: N/A

SHIP TO (DEPT., BRANCH)
Lorillard Research Center Attn: Dr. Connie Stone

DATE WANTED: As required

420 English Street Greensboro, NC 27405

QUANTITY	CODE	DESCRIPTION	UNIT PRICE
	This is your a	uthorization to perform the "Acute Oral Toxicity Study in the Rat"	
	tests on mater	ials D13 and D23 supplied by Lorillard. The fixed price for each	
	test is $2050	for each material, for a total price of $4100. Studies are to be	
	conducted in a	ccordance with the October 17, 1980 formal agreement between	
	Borriston and	Lorillard. All work is to be coordinated with our Dr.	Connie Stone
	(919) 373-6663.		

00920222

FOLLOW UP DATE	REQUISITION NO.		ISSUED BY
BUDGET NO.	**ACCT. NO.**	**DEPT. NO.**	**APPROVED BY**
	4111	9590	H. J. Zimmermeyer

RJR Mailfile Table Update Sheet

Alert Number 970220

To: RJR IR - Suzi/Art
From: Drew Huyett
Date: 3/7/97

Program Group 102-Eclipse
System Corp/Multibrand

Mailfile ID: 3,984 *(Completed by IR)*
Mailfile Description Mail Order - Indy Responders
Dataset Name *(Completed by IR)*

Quantity: 273
Maildate: 3/17/97
Program #: 700418

BRC Codes w81-carton order form

T Codes NA

Seeds .....25.....
Suppression ....5....

Mailfile Cells

1	HD	home delivery
2	SP	sneak preview
3		
4		
5		
6		
7		
8		
9		
10		

Notes

This is for notes

51673 4300

970220.XLS Mailfile