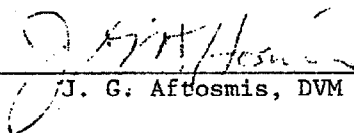


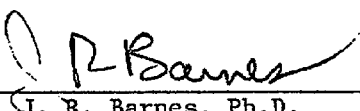
P R O T O C O L

CHRONIC INHALATION TOXICITY STUDIES ON
TiO₂ AND TiCl₄

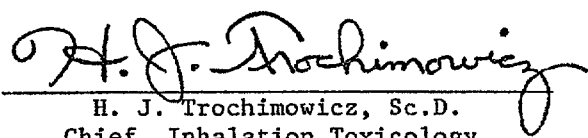
Approved for Pathology: _____

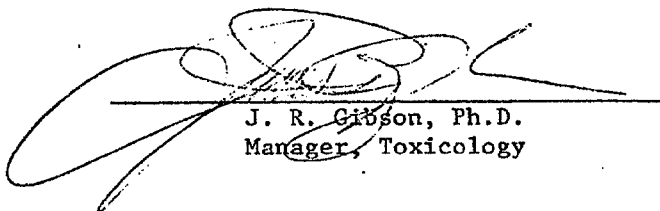

J. G. Aftosmis, DVM

Approved for Biochemistry: _____


J. R. Barnes, Ph.D.

Approved for Toxicology: _____


H. J. Trochimowicz, Sc.D.
Chief, Inhalation Toxicology


J. R. Gibson, Ph.D.
Manager, Toxicology

D R A F T

PRELIMINARY PROTOCOL*
FOR TWO YEAR INHALATION STUDY
FOR TITANIUM DIOXIDE AND TITANIUM TETRACHLORIDE

INTRODUCTION

This study is designed to evaluate the potential chronic toxicity and carcinogenicity of titanium dioxide and titanium tetrachloride, respectively, in rats, by inhalation. The two test compounds will be started simultaneously utilizing one common control.

MATERIALS TO BE TESTED

Titanium dioxide (TiO_2 , Titanium Oxide) is a crystalline and amorphous powder with the following properties:

Form:	White solid, Median Particle Size $\sim 1.0\mu$
Molecular Weight:	79.9
Melting Point:	Decomposes at 1640°C
Specific Gravity (water = 1):	3.8-4.2
Solubility:	Insoluble in water; soluble in sulfuric acid or alkali

Titanium tetrachloride (TiCl_4) is a liquid at room temperature and has the following properties:

Specific Density	1.7 g/cc
Molecular Weight	189.73
Boiling Point at 760 mm Hg	137°C
Color	APHA-40
Vapor Pressure at 25°C	15 mm Hg
Solubility	> 10% in water; reacts with acetone, ethanol, dimethylsulfoxide and vegetable oil

CENTRAL RESEARCH & DEVELOPMENT DEPARTMENT
HASKELL LABORATORY FOR TOXICOLOGY AND INDUSTRIAL MEDICINE

DATE March 5, 1979

CFR/BCM
JGA
FAB
JRG
DNH
INFO

TO: W. H. DARNELL
CHEMICALS, DYES & PIGMENTS DEPARTMENT
B-17366

R E V I S E D

MEDICAL RESEARCH PROJECT MR-2929 PART I

TITLE: CHRONIC INHALATION TOXICITY STUDIES ON TiO_2 AND $TiCl_4$

Authority is requested to undertake the investigation identified above and described as follows:

This revised proposal is written to cover the costs of chronic inhalation toxicity studies on TiO_2 and $TiCl_4$ in rats. A detailed protocol and cost estimate is attached.

The cost estimate below is based on 3 test concentrations/compound with shared control group exposed for 24 months.

This estimate reflects operating cost increases sustained since submittal of the preliminary proposal and includes an allowance for projected cost increases through 1982.

.....
Amount requested \$588,205
Previously authorized \$667,179
Expended to date 0
Account to be charged ~~8225-066~~

Work to be started 2nd Quarter 1979
Request for study made by discussions
between R. Salemi and Haskell personnel,
June, 1977.

7025-000900-000595
.....

If this request meets with your approval, please enter the account to be charged, have two copies authorized and return them to Haskell Laboratory, Control Section. The additional copies may be retained for your information and distribution.

Proposed by Phillip W. Schneider, Jr.
Chief, Chronic Investigations

Approved by Blm Kucuk

PWS/cgs

Authorized R. J. Blain - 5/25/79
date

DUP050447992

N 30820.01

CENTRAL RESEARCH & DEVELOPMENT DEPARTMENT

HASKELL LABORATORY FOR TOXICOLOGY AND INDUSTRIAL MEDICINE

DATE August 17, 1977

TO: DR. ROBERT SALEMI

PIGMENTS DEPARTMENT

MEDICAL RESEARCH PROJECT MR- 2929 PART I

TITLE: CHRONIC INHALATION TOXICITY STUDIES ON TiO_2 AND $TiCl_4$

Authority is requested to undertake the investigation identified above and described as follows:

This proposal is written to cover the costs of chronic inhalation toxicity studies on TiO_2 and $TiCl_4$ in rats. A detailed protocol and cost estimate is attached.

The cost estimate below is based on 3 test levels/compound and a common control group exposed for approximately 18 months (followed by a 6-month holding period). If exposure beyond 18 months is necessary, a Part II to this project will be written. A cost estimate for an additional six months' exposure is included in the attachment.

Amount requested \$667,170

Previously authorized 0

Expended to date _____

Account to be charged 8225-066

Work to be started 1st Quarter 1979

Request for study made by discussions
between R. Salemi and Haskell personnel,
June 1977.

If this request meets with your approval, please enter the account to be charged, have two copies authorized and return them to Haskell Laboratory, Control Section. The additional copies may be retained for your information and distribution.

Proposed by

A. Hochmowicz

Approved by

B. M. Knaack

J. M. Hsu

R. Salemi 9/14/77

Stombaro 9/17/77

Smith 9/19/77

Chen 9/20/77

Authorized

J. H. Baird

9/28/77
date