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September 26, 2006

Document Control Office (7407W)  
U. S. Environmental Protection Agency  
ATTN: TSCA Section 8(e) Coordinator  
Office of Pollution Prevention and Toxics  
1200 Pennsylvania Avenue, NW  
Washington, D.C. 20460

**COMPANY SANITIZED**

**Re: 8EHQ-06-16539 [3-Aminopentanenitrile; CAS # 75405-06-0]**

Dear 8(e) Coordinator:

This letter is a follow-up to our one dated July 25, 2006, in which we informed you of the results of a 28-day repeated dose oral toxicity study in the rat with the above referenced test material.

Enclosed are two copies of the final report. The thicker of the two is the final study report in its entirety and contains Confidential Business Information (CBI). The thinner document is the full summary of the report with the details redacted. INVISTA claims of CBI are substantiated in the enclosed document. If you have any questions or need additional information, please contact me at (316) 828-1342.

Sincerely,

James D. Jernigan, Ph.D.  
Product Safety Manager  
Environmental, Health and Safety

Enclosures



299030

**SafePharm  
Laboratories**

*Company Sanitized*

**DYTEC ® 3APN**

**TWENTY-EIGHT DAY REPEATED DOSE ORAL (GAVAGE) TOXICITY STUDY IN  
THE RAT**

**SPL PROJECT NUMBER: 1058-0083**

**AUTHORS:**

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**STUDY SPONSOR:**

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**TEST SITE:**

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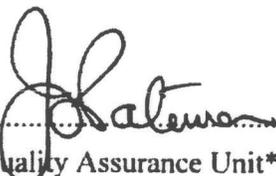
## QUALITY ASSURANCE REPORT

Inspection of the routine and repetitive procedures that constitute the study is carried out as a continuous process designed to encompass the major phases at or about the time this study was in progress.

This report has been audited by Safeparm Quality Assurance Unit, and is considered to be an accurate account of the data generated and of the procedures followed.

Unless otherwise indicated, the outcome of QA evaluation is reported to the Study Director and Management on the day of evaluation. Audits of study documentation, and process inspections appropriate to the type and schedule of this study were as follows:

08 November 2005	Protocol Compliance Audit
24 November 2005	Range-Finder
20 November 2005	Test Material Preparation
25 November 2005	Animal Preparation
17 November 2005	Dosing
06 November 2005	Assessment of Response
11 November 2005	Chemical Analysis
11 November 2005	Post Mortem
ϕ 23 December 2005	Histology (reported to management on 10 January 2006)
§ 23 May 2006	Draft Report Audit
§ Date of QA Signature	Final Report Audit
§	Evaluation specific to this study
ϕ	Audit by Propath UK QAU Ltd


 ..... DATE: ..... **15 AUG 2006**

For Safeparm Quality Assurance Unit\*

**\*Authorised QA Signatures:**

Head of Department:

JR Pateman CBiol MIBiol DipRQA FRQA

Deputy Head of Department:

JM Crowther MIScT MRQA

Senior Audit Staff:

JV Johnson BSc MRQA; G Wren ONC MRQA



### GLP COMPLIANCE STATEMENT

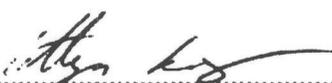
The work described was performed in compliance with UK GLP standards (Schedule 1, Good Laboratory Practice Regulations (SI 1999/3106 as amended by SI 2004/0994)). These Regulations are in accordance with GLP standards published as OECD Principles on Good Laboratory Practice (revised 1997, ENV/MC/CHEM(98)17); and are in accordance with, and implement, the requirements of Directives 2004/9/EC and 2004/10/EC.

These international standards are acceptable to the Regulatory agencies of the following countries: Australia, Austria, Belgium, Canada, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Republic of Korea, Luxembourg, Mexico, The Netherlands, New Zealand, Norway, Poland, Portugal, Slovenia, Spain, South Africa, Sweden, Switzerland, Turkey, the United Kingdom, and the United States of America.

This report fully and accurately reflects the procedures used and data generated.

Exception to GLP Compliance:

The protocol was not reviewed for compliance prior to the start of the study.

 ..... DATE: **10 AUG 2006** .....

K Knox BSc (Hons)

Study Director

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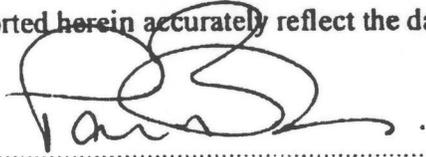
The following scientific and supervisory personnel were involved in the study under the overall supervision of the Study Director:

N Szysler HNC  
M Trussell HNC  
J Kemp



## AUTHENTICATION

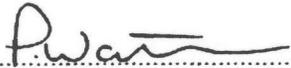
The microscopic pathology data presented in this report were compiled by me and the results reported herein accurately reflect the data obtained.



DATE: 10 AUG 2006

P N Brooks MSc BSc EurProBiol CBiol MIBiol  
EUROTOX Registered Toxicologist  
Study Pathologist

The analytical data presented in this report were compiled by me or under my supervision and the results reported herein accurately reflect the data obtained.



DATE: 16 AUG 2006

P Watson  
Laboratory Supervisor  
Analytical Services

Approved for issue:



DATE: 10 AUG 2006

E Wood CBiol MIBiol  
Head of Toxicology



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**PART 1: TWENTY-EIGHT DAY REPEATED DOSE ORAL (GAVAGE)  
TOXICITY STUDY IN THE RAT**



**DYTEC ® 3APN:**  
**TWENTY-EIGHT DAY REPEATED DOSE ORAL (GAVAGE) TOXICITY STUDY IN  
THE RAT**

**SUMMARY**

**Introduction.** The study was designed to investigate the systemic toxicity of the test material. It complies with the requirements for notification of a new chemical substance in the EC and follows the testing method described in Commission Directive 96/54/EC (Method B7) and OECD Guidelines for Testing of Chemicals No. 407 "Repeated Dose 28 Day Oral Toxicity Study in Rodents" (Adopted 27 July 1995).

**Methods.** The test material was administered by gavage to three groups, each of five male and five female Sprague-Dawley CrI:CD<sup>®</sup> (SD) IGS BR strain rats, for twenty-eight consecutive days, at dose levels of 15, 150 and 300 mg/kg/day. A control group of five males and five females was dosed with vehicle alone (distilled water).

Clinical signs, functional observations, bodyweight development and food and water consumption were monitored during the study. Haematology and blood chemistry were evaluated for all animals at the end of the study.

All animals were subjected to gross necropsy examination and histopathological evaluation of selected tissues was performed.

**Results.**

**Mortality.** There were no unscheduled deaths.

**Clinical Observations.** Increased salivation immediately after dosing and staining around the eyes, mouth and/or snout were observed on occasion for animals treated with 300 or 150 mg/kg/day.

**Behavioural Assessment.** There were no treatment-related changes in the behavioural parameters measured.

**Functional Performance Tests.** There were no treatment-related changes in the functional performance parameters measured.

**Sensory Reactivity Assessments.** There were no treatment-related changes in sensory reactivity.

**Bodyweight.** A reduction in bodyweight gain was noted for animals of both sexes treated with 300 or 150 mg/kg/day during the first week of treatment. Bodyweight gain recovered thereafter with females treated with 300 or 150 mg/kg/day showing an increase in bodyweight gain during the second week of treatment. A statistically significant reduction in bodyweight gain was also evident for males treated with 300 mg/kg/day during the final week of treatment.

**Food Consumption.** Males and females treated with 300 mg/kg/day and males treated with 150 mg/kg/day showed a reduction in dietary intake with corresponding reduction in food efficiency during the first week of treatment. Males treated with 150 mg/kg/day continued to show a reduction in dietary intake during the second week of treatment. Food consumption and efficiency in females at 150 mg/kg/day were unaffected and, together with both sexes treated with 15 mg/kg/day, remained similar to controls throughout the study.

**Water Consumption.** No intergroup differences were detected.

**Haematology.** No treatment-related changes were detected.

**Blood Chemistry.** A reduction in plasma glucose levels and an increase in plasma creatinine was observed in both sexes at 300 mg/kg/day and 150 mg/kg/day in comparison with controls. In addition, males at these dose levels showed reductions in total protein and females showed lowered cholesterol levels. Males treated with 300 mg/kg/day also showed low albumin levels and females at this time showed an increase in aspartate aminotransferase.

The remaining changes were considered to be incidental and of no toxicological significance.

**Organ Weights.** An increase in absolute adrenal weight was noted for males treated with 300 mg/kg/day. An increase in relative liver weight was noted for animals of both sexes treated with 300 or 150 mg/kg/day.

**Necropsy.** No treatment-related macroscopic abnormalities were detected.

**Histopathology.** The following treatment-related microscopic changes were detected:

**LIVER:** Centrilobular changes characterised by single cell hepatocyte necrosis, accumulations of Perl's positive pigment, probably haemosiderin, and mononuclear cell infiltrates were observed in relation to treatment for rats of both sexes dosed at 300 mg/kg/day, or at 150 mg/kg/day. In addition, and for female rats only, lipid vacuolation of hepatocytes was observed as a consequence of treatment at all dose levels. Isolated instances of hepatocyte enlargement were seen for male rats dosed at 300 mg/kg/day.

**THYROID GLAND:** Hypertrophy of follicle lining cells was seen in relation to treatment for rats of both sexes dosed at 300 mg/kg/day, and for male rats dosed at 150 mg/kg/day.

**Conclusion.** The oral administration of Dytec 3APN to rats for a period of twenty-eight consecutive days at dose levels of 300, 150, and 30 mg/kg/day resulted in toxicologically important histopathological treatment-related effects in animals of both sexes treated with 300 or 150 mg/kg/day. As minor treatment-related findings involving a slight disruption of blood chemical parameters was detected in animals of both sexes treated with 15 mg/kg/day a clear "No Observed Effect Level" (NOEL) in this study was therefore not obtained. The effects detected at 15 mg/kg/day were minimal in nature with no supporting histopathological correlates. On this basis the "No Observed Adverse Effect Level" (NOAEL) was therefore considered to be 15 mg/kg/day.

**Pages 19 – 278 of this Study Report are redacted as  
Confidential Business Information**