HIGH PRODUCTION VOLUME (HPV) CHEMICAL CHALLENGE PROGRAM TEST PLAN

For

2-(hydroxymethyl)-2-nitro-1,3-propanediol
and
2-methyl-2-nitro-1-propanol

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I. INTRODUCTION

ANGUS Chemical Company (ANGUS) committed to provide screening level human health effects, environmental effects and fate, and physiochemical test data on 2-methyl-2-nitro-1-propanol and 2-(hydroxymethyl)-2-nitro-1,3-propandiol under the Environmental Protection Agency's (EPA's) High Production Volume (HPV) Challenge Program (Program). After this commitment was made ANGUS was bought by the Dow Chemical Company (DOW) and is now a wholly owned subsidiary of DOW.

This plan details how both substances can be placed in a single category, nitro alcohols, and identifies existing data of adequate quality for those substances.

II. DESCRIPTION OF THE NITRO ALCOHOL CATEGORY

ANGUS Chemical Company is the largest producer of nitroparaffins in the world. Indeed, of those it manufactures, nitromethane, nitroethane, 1-nitropropane, and 2-nitromethane, only nitromethane is available from another producer. One use for these substances is the production of **nitro alcohols,** which are obtained by the reaction of the nitroparaffin with formaldehyde in the presence of base as a catalyst. The nitro alcohols obtained from each of the nitroparaffins are displayed in Table I.

Table I. Nitro Alcohols from the Niroparaffins*

NITROPARAFFIN Precursor	formaldehydes added	NITRO ALCOHOL Obtained
Nitromethane 75-52-5	2	2-nitro-1,3-propanediol
	3	**2-(hydroxymethyl)-2-nitro-1,3-propanediol**
Nitroethane 79-24-3	2	2-methyl-2-nitro-1,3-propanediol
1-Nitropropane 108-03-2	1	2-nitro-1-butanol
	2	2-ethyl-2-nitro-1,3-propanediol
2-Nitropropane 79-46-9	1	**2-methyl-2-nitro-1-propanol**

- Substances in bold are HPV substances

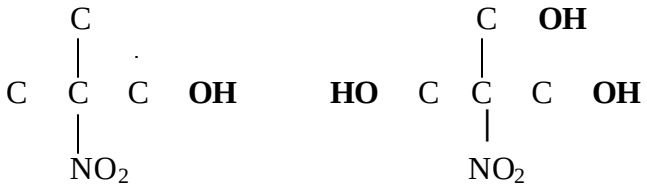
Of these substances only the following are High Production Volume chemicals:

	CAS Reg. No.
2-methyl-2-nitro-1-propanol (MNP)	76-39-1
2-(hydroxymethyl)-2-nitro-1,3-propandiol (TN)	126-11-4

Both are non-volatile crystalline solids. The major use of all nitroalcohols is as closed-system intermediates in the production of alkanolamines. These two, MNP and TN are used to produce 2-amino-2-methyl-1-propanol and 2-amino-2-(hydroxymethyl)-1,3-propanediol. Thus exposure to MNP and TN is only expected to occur under upset

conditions in this application. Suitable protective equipment would be worn during any operation where worker exposure is expected.

In addition, TN is used as a biocide and as a cross-linker in the production of plywood but this represents a relatively small portion of the total amount of TN produced. TN is used as an antimicrobial agent for the control of bacteria in industrial processes such as cooling towers and metalworking fluids. Efficacy as a biocide is obtained by the slow release of formaldehyde from TN in a alkaline environment. A Reregistration Eligibility Decision was published by EPA in 1993. In the case of plywood, TN is used in the resin curing operation releasing formaldehyde and is consumed during the curing process. During plywood production, limited dermal exposure could occur to workers handling the adhesive containing TN. Consumer exposure would be expected to be nil.



MNP (HPV) TN (HPV)

III. TEST PLAN RATIONALE

A. Overview

Due to its use as a biocide, TN is registered under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA). Subsequently, a Reregistration Eligibility Decision (RED) document was published by EPA in 1993. Thus a complete HPV battery of tests are already available.

Only acute data are available for **MNP**; however, it currently is used only as a closed-system intermediate for the production of 2-amino-2-methyl-1-propanol. In the past it did find use as an adhesion promoter in tire production, a use in which the substance is consumed, however, this technology has been replaced and no further production for this use is planned.

At basic pH and/or when exposed to heat, all these nitro alcohols readily hydrolyze to yield formaldehyde and their parent nitroparaffin. The nitroparaffins involved and formaldehyde are all HPV substances which are subject to separate submission.

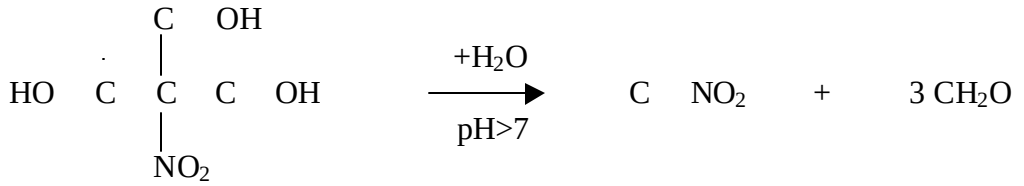
As **TN** is the only nitro alcohol for which there is any appreciable human and environmental exposures, it is the surrogate of choice for all of the nitro alcohols.

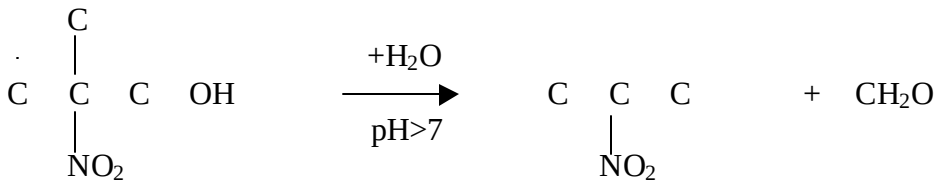
B. Physicochemical Properties

Extensive data already exist for all HPV endpoints (Table 2). All members of this category are crystalline solids at room temperature, and all decompose with a significant release of energy at temperatures only slightly above their melting points. Thus it is very difficult to measure vapor pressure of either material. The vapor pressure is expected to <1.3 hPa for both materials.

C. Environmental Fate

The estimated half-life of photodegradation of TN was 5.6 days and that of MNP was 14 days (AOPWIN model) (Table 2). The nitro alcohols all undergo hydrolysis at pH greater than 7 to yield formaldehyde and the nitroparaffin parent compound as follows:





Level I and level III fugacity-based models were used to evaluate the distribution of TN and MNP between environmental compartments. Based on the level III calculation, 77% of TN and 39.4% of MNP emissions will reside in water and 16.5% of TN and 43.4% of MNP will reside in the soil. Almost none of either substance will migrate to the air. TN was only 13.4% degraded in a ready biodegradation test (OECD 301F).

D. Ecotoxicity

Data on TN are available for all three aquatic toxicity endpoints in the HPV program (Table 2). MNP is site-limited and therefore does not get released to waters. The LC_{50} of TN in the fathead minnow (pimephales promelas) was determined to be 280 mg/L using OTS protocol 797.1400. Using the procedure of OPP 72-2, the 48-hour EC_{50} for daphnia magna was 80 mg/L. An EC_{50} of only

0.656 mg/L for TN was obtained using the OECD 201 "Algae Growth Inhibition Test".

E. Animal Toxicity Testing

A complete battery of HPV animal toxicity studies already are available for TN (Table 2). Only acute toxicological data and an AMES test are available on MNP. The oral LD_{50} for TN is 990-1000 mg/kg bw and that for MNP is 845-1480 mg/kg bw. These data do not indicate that there are differences in toxicity for the nitro alcohols which are great enough to warrant further testing of MNP.

The primary route of exposure to TN is the dermal route. Therefore, the 90-day repeat dose study was done via the dermal route. At 1000 mg/kg/day, a slight yellow discoloration of the skin was observed at the application site which was attributed to repeated application of an impurity. There were no systemic effects evident from the histopathological examination of the rat organs including the gonads. Further, in oral teratology studies in rats and rabbits, no significant effects in fetal mortality, developmental anomalies, malformations, or litter numbers were noted at doses below those which induced maternal toxicological effects.

Neither TN nor MNP were mutagenic in the Ames test either with or without S9 activation. Further negative results were obtained for TN in the Chinese Hamster Ovary (CHO) test and the *in vitro* Unscheduled DNA Synthesis test.

IV. TEST PLAN SUMMARY

Due to the closed system intermediate use for MNP, the use of protective equipment whenever worker exposure could occur to MNP and the lack of any effect observed in the 90-day dermal study with TN, additional studies are not considered to be necessary for MNP. A complete data set exists for TN. Thus no additional studies are needed. All data required for the HPV program are summarized in the IUCLID data sets which accompany this report. The two teratology studies conducted on TN and the 90-day dermal study suffice to satisfy the reproductive toxicity requirement.

Robust summaries for the nitro alcohol data as required for the HPV program as well as for addition studies follow in the IUCLID data sets. The references for the cited studies are found in them.

Table 2
Test Plan for 2-(hydroxymethyl)-2-nitro-1,3-propanediol
and 2-methyl-2-nitro-1-propanol

	2-Methyl-2-nitro-1-propanol CAS Reg. No. 76-39-1	**2-(Hydroxymethyl)-2-nitro-1,3-propanediol CAS Reg. No. 126-11-4**
Melting Point	D 90 C	D 175 C
Boiling Point	D 94 C @ 19.5hPa	D decomposes at mp
Vapor Pressure	D nil at normal pres.	D nil
Partition Coefficient	Estimate	D 1.06
Water Solubility	D 350g/100 mL water	D 220g/100g water
Stability in Water	CA	D 2.4 day @25 C
Photodegradation	$t_{1/2}$=14 days (Estimate)	$t_{1/2}$=5.6 days (Estimate)
Fugacity Level III 1000 kg/hr each to air, water and soil	39.4% water 43.4% soil 17.1% sediment <0.1% air	77% water 16.5% soil 6.5% sediment <0.1% air
Biodegradation	CA	D 13.4% in 28 days
Acute Toxicity - Fish	CA	D 96 hr LC50=280mg/L
Acute Toxicity - Daphnia	CA	D 48 hr EC50=80 mg/L
Acute Toxicity - Algae	CA	D 96 hr EC50=0.656 mg/L
Acute Toxicity - Mammalian	D LD50 rat, 845-1480mg/kg	D LD50 rat, 990-1000 mg/kg
Mutagenicity - invitro	D negative Ames	D negative Ames
Mutagenicity - invitro	CA	D negative CHO chrom aberr.
Repeat Dose Toxicity	CA	D NOAEL >1000mg/kg in dermal study with rats
Reproductive Toxicity	CA	Data available from exam of reproductive organs in 13 week repeated dose toxicitystudy.
Developmental Toxicity	Not Required	D Data avilable from studies in two mammalian species

CA - Analog
D - Data