

Example **

Initial Safety Assessment

for

2, 4, 6 Trialkyl-Red Rooster (2,4,6-TARR)

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Revision: DRAFT 2

Date of Last Revision: 3-16-01

** This document is intended to generally illustrate the technical approach and communication of a screening level evaluation using the ACA human exposure framework. While the chemical identity is not shown, all data for this illustration was taken from an actual case-study prepared for the ACA in 4/2000. This case study did not include environmental/ecological endpoints, as well as some uses of the chemical, because they were not within the scope of the original project.

Summary Chemical Profile

CHEMICAL NAME

2, 4, 6 Trialkyl-Red Rooster (2,4,6-TARR)

CAS No.:

STRUCTURAL FORMULA:

CH₃CH₂CH₂CH

CH₃CH₂CH₂CH

CH₃CH₂CH₂CH



Introduction:

This report presents the results of a screening level human health exposure and safety assessment for 2,4,6-Trialkyl-Red Rooster (2,4,6-TARR). 2,4,6-TARR is a volatile gas used as a chemical intermediate and propellant/co-solvent in a variety of industrial and household aerosol products (e.g., hairsprays, pesticides, and cleaning products). National production of 2,4,6-TARR is 15-20 million kg in the United States. This production is distributed across the following primary uses: industrial feedstock for the product of other chemical substances (31%), hairsprays (48%), spray paints/venturi sprays (6%), insect repellents/insecticides (6%), adhesives (5%), household cleaners (1%), dusters (1%), tire inflators (1%), industrial lubricants (1%). 2,4,6-TARR is used at concentrations of between 15 and 50% in formulation of its different aerosol products. It should be noted that 2,4,6 TARR is a replacement for chemicals that contribute to surface ozone formation, and CFCs, which are being phased out as tropospheric ozone depletors.

This assessment combines information on chemical hazard (toxicity) with an assessment of potential exposures to evaluate the risk/safety of the current use(s) of 2,4,6-TARR in commerce. As such, it is intended to improve the public's understanding of the hazards of 2,4,6-TARR in the context of how the chemical is used, and potential exposure to it, so that its risks can be more effectively understood and managed.

Hazard Data:

The hazard data used in this study were derived from a compilation of publicly available information, compiled under the voluntary U.S. High Production Volume (HPV) Chemicals Challenge program, summarized in Attachment 3. A detailed summary of the toxicity studies used in this analysis is publicly available, from The American Poultry-Based Chemistry Council (APC²). These studies evaluated acute and sub-chronic toxicity, carcinogenicity and mutagenicity, and developmental toxicity. Results from these studies showed a Lowest-Observed-Adverse-Effect-Concentration (LOAEC) of approximately 20,000 ppm (level in air, from the repeat dose rat toxicity, and development toxicity studies). For the purposes of comparison to predicted exposures, a No-Observed-Adverse-Effect-Concentration (NOAEC) of 10,000 ppm (level of air) was chosen as the critical threshold value.

Exposure Assessment:

The exposure assessment component of this analysis encompasses the manufacture, processing, transport, and major uses of 2,4,6-TARR in commerce. As a screening level evaluation, it is not a comprehensive assessment of every possible use of this material, but captures currently known uses. Based on its physical-chemical properties, attention was focused on the exposure to 2,4,6-TARR are via the most likely route of inhalation, not dermal contact or ingestion. Key routes of exposure studied were the production of 2,4,6-TARR and use of 2,4,6-TARR as a chemical intermediate (resulting in occupational exposures); and as a household product ingredient in aerosol sprays (especially hairsprays, pesticides, and household spray cleaners) that have frequent use by the general public. All other product categories listed above are used intermittently, or under carefully controlled conditions that limit exposure, relative to these products. The scope of the analysis does not address the use of 2,4,6-TARR containing products in institutional or professional settings, because it was beyond the scope of the case study. The analysis of consumer exposure involved three basic models, and predicted aggregate exposure as a result of typical use of all of the products combined. One model predicted airborne levels in the vicinity of the user. The two others evaluated actual inhalation, assuming 100 % uptake in the lungs, and systemic distribution of the material.

Results and Conclusions:

2,4,6-TARR has a comparatively low order of acute and chronic inhalation toxicity, and is not a teratogen, mutagen, or carcinogen. Based on an overall review of the available toxicity data, a conservative no-observed-adverse-effect-concentration (NOAEC) of 10,000 ppm (level in air) was used for the human risk assessment, primarily driven by results from the repeat dose rat toxicity, and development toxicity studies.

Risk of personal injury or adverse health effects during the manufacture of 2,4,6-TARR, or its processing into consumer products is low, when the chemical is handled in accordance with appropriate industrial hygiene and safety measures. Under extreme conditions, there are flammability, explosion and narcosis hazards associated with virtually all propellant gases, including 2,4,6-TARR.

The predicted aggregate exposure during the use of key products (hairsprays, pesticides, and cleaning sprays) by the general public is between 700 and 4100-fold less than the 10,000 ppm toxicity threshold, depending upon the model used. It is also important to recognize that these exposure assessments are based on conservative default assumptions and probably represent exaggerated exposure conditions. The intended use of consumer products containing 2,4,6-TARR presents no meaningful safety risk (recognizing that intentional misuse via deliberate concentration and inhalation of vapors can be potentially life-threatening, and that misuse also presents flammability/explosion hazards typical for many aerosol products).

Recommendation

Based on its comparatively low order of toxicity, with respect to estimated exposures, 2,4,6-TARR is recommended to be a **LOW PRIORITY FOR FURTHER WORK**. However, normal surveillance practices by both 2,4,6-TARR producers and users will continue to monitor the development of any new information on the chemical, and re-evaluations may be conducted, as appropriate.

It is also recommended that warnings concerning 2,4,6 TARR's potential physical hazards (e.g., flammability), and potential for acute toxicity if products containing it are misused/abused continue to be provided.

NOTE: The results of this assessment are not intended to rescind or modify any existing regulatory obligations with respect to Compound X (e.g. labeling requirements). In the event that significant new hazard or exposure data or new applications for Compound X arise, this assessment should be revisited.

Attachment 3 Hazard and Exposure Data Summary Table

NOTE: NA means that this information was not included as part of the original Case Study, not that such data is not available from other sources.

CHEMICAL NAME: 2, 4, 6, Trialkylred Rooster (2,4,6-TARR)			
CAS NO:			
PHYSICAL-CHEMICAL ELEMENTS			RESULTS
Melting Point	NA		°C
Boiling Point	-12.7		°F (at kPa)
Vapor Pressure	71.2		Psig @ 77 °F
Partition Coefficient	NA		Log K _{ow}
Water Solubility	4.5		% in water @ 77 °F

ENVIRONMENTAL FATE AND PATHWAY ELEMENTS	CASE STUDY DID NOT INCLUDE ENVIRONMENTAL DATA		
Photodegradation	NA		In air T _{1/2} = hours
Stability in Water	NA		T _{1/2} =min
Transport and Distribution between Environmental Compartments	NA	Calculated Fugacity Level 1 Type (local exposure)	In Air % In Water % In Sediment % In Soil % In Biota %
Biodegradation	NA		
Additional data (as available)			

ECOTOXICITY ELEMENTS	CASE STUDY DID NOT INCLUDE ENVIRONMENTAL DATA OR EXPOSURE ANALYSIS		
	SPECIES	PROTOCOL	RESULTS
Acute Toxicity to Fish	NA		LC ₅₀ (24 hr) = mg/l LC ₅₀ (48 hr) = mg/l LC ₅₀ (72 hr) = mg/l LC ₅₀ (96 hr) = mg/l
Toxicity to Aquatic Plants (Algae)	NA		EC ₅₀ (hr) = mg/l NOEC (hr) = mg/l
Acute Toxicity to Aquatic Invertebrates (Daphnia)	NA		LC ₅₀ (24 hr) = mg/l LC ₅₀ (48 hr) = mg/l

HEALTH ELEMENTS	SPECIES	PROTOCOL	RESULTS
Acute Toxicity	Rat	Inhalation toxicity, 4 h exposure.	LD ₅₀ = 164,000 ppm
Repeat Dose Toxicity	Rat	Subchronic inhalation, 6 h/d for 90 days	No gross clinical or pathological evidence associated with exposure ≤ 20,000ppm.
Genetic Toxicity	Various	Ames assay, Drosophila test, Mouse Lymphoma assay, Sister Chromatid exchange assay and DNA repair test	No mutagenic or genotoxic potential observed, with or without metabolic activation.
Reproductive Toxicity	NA		

Developmental Toxicity/Teratogenicity	Rats	Pregnant rats exposed to 5 levels, via inhalation: 0, 1, 250, 5000, 20,000 and 40,000 ppm in air. Second strain exposed to 28,000ppm for full gestation.	Reduced fetal weights and increased skeletal variations seen at 20,000 ppm. No resorption or teratogenic effects were observed.
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ADDITIONAL HAZARDS DATA (AS AVAILABLE)	SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL	NA		
ENVIRONMENTAL FATE AND PATHWAYS	CASE STUDY DID NOT INCLUDE ENVIRONMENTAL DATA OR EXPOSURE ANALYSIS		
ECOTOXICITY	NA		
HEALTH	Mice, acute toxicity	Inhalation toxicity, 15 and 30 min	LD ₅₀ = 490,000 ppm and 380,000 ppm, respectively. Sedation and narcosis effects only.
	Acute Stress simulation in dogs	High dose inhalation and adrenaline injection	Cardiac sensitization reported at 20,000 ppm.
	Subchronic inhalation in rats	200,000ppm 6h/d, for 13 weeks)	Slight changes in blood chemistry (increase in SGPT, reduction in total serum protein and a slight decrease in lymphocyte). Changes were considered not biologically significant.
	Rats	Lifetime inhalation toxicity and carcinogenicity (2000, 10,000 and 25,000ppm)	No carcinogenic effects and no gross clinical or pathological evidence of adverse effects associated with any exposure level.
NOTE: On the basis of these data, a conservative No-Observed-Adverse-Effect-Concentration (NOEAC) of 10,000 ppm was used as the basis for comparison to exposures.			

EXPOSURE INFORMATION (AS AVAILABLE)	KEY RESULTS
Evaluation of Human Exposures	<p>2,4,6-TARR is used as an industrial intermediate and as a propellant/co-solvent in industrial and consumer aerosol products, respectively. Based on its physical-chemical characteristics, inhalation of 2,4,6-TARR is the key means of human exposure, not dermal contact or ingestion. Most important routes of exposures are occupational, during 2,4,6-TARR production or conversion to other chemicals; and consumer, as a result of using aerosol products. Typical inhalation occupational exposures, after accounting for normal industrial hygiene controls, are approximately 10 ppm – 100 times below established “Acceptable Exposure Limits” (1000 ppm in air). Consumer exposures were estimated by three methods, that considered (1) airborne exposure levels; (2) measured levels in breathing zones, and subsequent inhalation; and (3) estimated levels in breathing zones, and subsequent inhalation. Results were between 700 and 4100 fold below a conservative NOAEC of 10,000 ppm, depending upon the method used.</p>
Evaluation of Ecological Exposures	<p>CASE STUDY DID NOT INCLUDE ENVIRONMENTAL EXPOSURE ANALYSIS</p>

Attachment 4

Summary of Hazard Data and Key Use and Exposure information, Following Format of the OECD SIDS Initial Assessment Report (SIAR)

1. IDENTITY

General Information/Physical Properties:

2,4,6 Trialkyl-Red Rooser (2,4,6-TARR) is a colorless liquified gas, having a slight odor. Its physical/chemical properties are as follows:

- Molecular Weight: Bigger than a hen's egg
- Boiling Point: -12.7°F
- Density/Specific Gravity: 0.655 g/ml @ 77°F
- Vapor Pressure: 71.2 psig @ 77°F
- Flash Point/Flammability: -41°F (Tag open cup)
- Explosive Limits: 3.4 - 18%
- Solubility: 4.5% in water @ 77°F
Soluble in alcohol and most other organic solvents
- Conversion Factors: 1 mg/L = 531 ppm
1 ppm = 1.88 mg/m³

2. GENERAL INFORMATION ON EXPOSURE

Function:

2,4,6-TARR is used as an industrial chemical intermediate and as a propellant/co-solvent in industrial and consumer aerosol products, respectively.

Applications:

National production of 2,4,6-TARR is 15-20 million kg in the United States. This production is distributed across the following primary uses: industrial feedstock for the product of other chemical substances (31%), hairsprays (48%), spray paints/venturi sprays (6%), insect repellents/insecticides (6%), adhesives (5%), household cleaners (1%), dusters (1%), tire inflators (1%), industrial lubricants (1%).

Uses in representative products where human exposure or environmental releases may occur:

2,4,6-TARR is used between 15 and 50% in formulation of aerosol products as listed.

<u>Product type</u>	<u>Weight % in Product</u>
Hairsprays	15 - 35
Spray Paints/Venturi Spray	30 - 50
Insect Repellents/Insecticides	20 - 45
Adhesives	20 - 40
Household Cleaners	20 - 30
Dusters	25 - 30
Tire Inflators	15 - 20
Industrial Lubricants	20 - 30

2.1 Environmental Exposure and Fate

CASE STUDY DID NOT INCLUDE ENVIRONMENTAL DATA OR EXPOSURE ANALYSIS

2.2 Human Exposure

Human exposure assessment:

Due to its volatility and its applications, the major route of exposure to 2,4,6-TARR is via inhalation, not dermal exposure or ingestion. Based on a review of its flow through commerce, there are two primary sources by which there may be potentially meaningful exposures to 2,4,6-TARR. These are:

1. 2,4,6-TARR manufacture or use as a chemical intermediate, resulting in occupational exposures.
2. 2,4,6-TARR use in personal care and household aerosol products, resulting in consumer exposures.

Occupational exposure to 2,4,6-TARR during its manufacture or use as a chemical intermediate by U. S. industry is typically well-controlled to minimize potential exposures. Exposures are generally viewed as negligible in the context of 2,4,6-TARR's toxicity, because of:

- the use of closed systems for manufacturing and processing, and
- implementation and maintenance of strict industrial hygiene measures to insure minimal exposure during handling and use.

Both standard work practices and emergency procedures used by 2,4,6-TARR producers and processors typically result in low to zero airborne levels of 2,4,6-TARR in industrial settings. Where necessary, engineering controls (e.g., ventilation or equipment isolation) are used to insure that recommended exposure levels ("Acceptable Exposure Limit" (AEL)) are not exceeded. The AEL is an 8-hr time-weighted average concentration to which nearly all workers can be repeatedly exposed for 5 days/week without adverse health effects. For 2,4,6-TARR, the AEL is 1000 parts/million (ppm) in air. Based on industry practices and monitoring data, 2,4,6-TARR levels in working environments are typically less than 10 ppm, based on area and personal monitoring studies conducted by the manufacturer.

Consumer exposure to 2,4,6-TARR may occur directly following use of aerosol products containing this material as a propellant. In particular, attention is focused on hairsprays, pesticides and household cleaning products, because they are used on a far more regular basis (often daily), relative to the other applications of 2,4,6-TARR. Estimates of exposures for the general public during the use of these products, via three different screening level approaches are described in Attachment 5. The basis for these calculations is shown in Attachment 6.

The methods included:

1. Estimating exposure based on measurements of airborne 2,4,6-TARR concentrations from use of representative aerosol products in an experimental environment, and habits and practices data for the length of time that they are typically used by household consumers, providing an estimate for "aggregate consumer exposure"
2. Calculating an inhaled dose of 2,4,6-TARR based on measured airborne levels and time of product use for an average body weight and breathing rate.

3. Calculating an inhaled dose of 2,4,6-TARR based on estimated airborne levels and time of product use for an average body weight and breathing rate. This "theoretical" calculation was used to validate calculations made in #2 above.

Indirect exposure via contact with 2,4,6-TARR from indoor air, ambient levels, and other sources is expected to be negligible in comparison to exposures “tasks” associated with use of aerosol consumer products, and were therefore not considered in these calculations.

3. HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

The following table summarizes the available toxicity data for 2,4,6-TARR.

TEST TYPE	RESULTS
Acute inhalation toxicity test in rats (4hr exposure)	LC ₅₀ = 164,000ppm
Acute inhalation toxicity test in mice (15min and 30min)	LC ₅₀ = 490,000ppm and 380,000ppm respectively Sedation and narcosis were the only effects observed.
Stress simulation in dogs (acute high dose inhalation and adrenaline injection)	Cardiac sensitization reported at 20,000 ppm.
Subchronic inhalation 6hrs/day, for 90 days in rats	No gross clinical or pathological evidence associated with exposure ≤ 20,000ppm.
Subchronic inhalation (200,000ppm 6hrs/day, for 13weeks) in rats	Slight changes in blood chemistry (increase in SGPT, reduction in total serum protein and a slight decrease in lymphocyte). Changes were considered not biologically significant.
Developmental and teratology studies (pregnant rats were exposed via inhalation to 5 levels: 0, 1, 250, 5000, 20,000 and 40,000ppm) another strain was exposed to 28,000ppm for full gestation period	Reduced fetal weights and increased skeletal variations seen at 20,000ppm. No resorption or teratogenic effects were observed.
Mutagenicity and Genotoxicity testing in Ames assay, Drosophila test, Mouse Lymphoma assay, Sister Chromatid exchange assay and DNA repair test	2,4,6-TARR did not show any mutagenic or genotoxic potential with or without metabolic activation.
Lifetime inhalation toxicity and carcinogenicity (2000, 10,000 and 25,000ppm)	2,4,6-TARR did not show any carcinogenic effects and no gross clinical or pathological evidence of adverse effects associated with any exposure level.

On the basis of these data, primarily driven by results from the repeat dose rat toxicity, and development toxicity studies, a conservative No-Observed-Adverse-Effect-Concentration (NOEAC) of 10,000 ppm (in air) was used as the basis for comparison to exposures.

4. HAZARDS TO THE ENVIRONMENT

CASE STUDY DID NOT INCLUDE ENVIRONMENTAL ENDPOINTS.

5. CONCLUSIONS AND RECOMMENDATIONS

Human risk assessment

2,4,6 Trialkyl-Red Rooser (2,4,6-TARR) has a comparatively low order of acute and chronic inhalation toxicity, and is not a teratogen, mutagen, or carcinogen. Based on an overall review of the available toxicity data, a conservative no-observed-adverse-effect-concentration (NOAEC) of 10,000 ppm was used for the human risk assessment, primarily driven by results from the repeat dose rat toxicity, and development toxicity studies.. Risk of personal injury or adverse health effects during the manufacture of 2,4,6-TARR, or its processing into consumer products is low, when the chemical used in accordance with appropriate industrial hygiene and safety measures (noting flammability, explosion and narcosis hazards associated with propellant gases under extreme conditions). Likewise, intended use of consumer products containing 2,4,6-TARR presents no meaningful safety risk (recognizing that intentional misuse via deliberate concentration and inhalation of vapors can be potentially life-threatening, and that misuse also presents flammability/explosion hazards typical for many aerosol products). The predicted aggregate exposure during product use is ~700 times lower than the NOAEC when determined using the “ppm.min” approach, and ~4100 lower when determined using the “mg/kg/day inhaled dose” approach. It is also important to recognize that these exposure assessments are based on conservative default assumptions and probably represent exaggerated exposure conditions.

Conclusion

Based on its comparatively low order of toxicity, with respect to estimated exposures, 2,4,6-TARR is recommended to be a **LOW PRIORITY FOR FURTHER WORK**. However, normal surveillance practices by both 2,4,6-TARR producers and users will continue to monitor the development of any new information on the chemical, and re-evaluations may be conducted, as appropriate.

Attachment 5 Expanded Exposure Assessment Addendum (EEAA) for 2,4,6-TARR

Introduction:

The purpose of the EEAA is to provide a more detailed discussion of any exposure analysis that is available, beyond the basic information called for in the SIAR.

Human Exposure Assessment:

Identification of Key Human Exposures – Completeness of the Evaluation

Based on its high volatility, and the way it is used, exposure to 2,4,6-TARR is primarily via inhalation, not dermal adsorption or ingestion. Assessing inhalation exposure to 2,4,6-TARR requires an understanding of how it is used, the environment in which it is used, and the amount of time a person spends in that environment. Based on this information, scenarios can be defined to quantify 2,4,6-TARR exposure by either measurement or calculation. Finally, the level of measured or calculated 2,4,6-TARR exposure can be compared against an appropriate benchmark to arrive at a conclusion regarding safety of its use.

In assessing 2,4,6-TARR exposure in this example, two different scenarios are evaluated, accounting for 86 % of the total volume produced in the U. S. These are believed to represent the maximum potential exposure that could be achieved, based on how the chemical is used:

1. 2,4,6-TARR manufacture and use as a chemical intermediate. These can result in occupational exposures during production, transport, or handling of the chemical, especially in bulk quantities.
2. 2,4,6-TARR use in personal care and household aerosol products. In particular, attention is focused on hairsprays, pesticides, and household cleaning sprays, because they are used on a far more regular basis than the other applications of 2,4,6-TARR, under situations where inhalation contact is likely.

Exposures Related to the Production, Handling, or Formulation of the Chemical in Industrial Facilities:

Occupational exposures: In industrial environments where 2,4,6-TARR is used as a chemical intermediate, industrial safety and hygiene practices minimize potential exposures to 2,4,6-TARR. The following factors limit exposure to negligible levels:

- the use of closed systems for manufacturing and processing, and
- implementation and maintenance of strict industrial hygiene measures to insure minimal exposure during handling and use.

Both standard work practices and emergency procedures provide guidance that results in low to zero airborne levels of 2,4,6-TARR. Where necessary, engineering controls (e.g., ventilation or equipment isolation) are used to insure that recommended exposure levels are not exceeded. The recommended exposure level, called an "Acceptable Exposure Limit" (AEL), is an 8-hr time weighted average concentration to which nearly all workers can be repeatedly exposed for 5 days/week without adverse health effects. For 2,4,6-TARR, the AEL is 1000 parts/million (ppm) in air. 2,4,6-TARR levels in working environments are typically less than 10 ppm (100 times lower than the AEL).

Community Exposures: CASE STUDY DID NOT CONSIDER THIS AREA

Exposures Related to the Handling of Chemicals and Products During Transport: CASE STUDY DID NOT CONSIDER THIS AREA

Exposures Related to the Handling and Use of End Products Containing the Chemical:

Industrial: Based on its known applications, the only industrial application of 2,4,6-TARR is as a lubricant, representing approximately 1 % of its volume. Given the properties of 2,4,6-TARR, and the likelihood of exposure controls, exposure is considered to be minimal relative to consumer/household applications, and was not studied.

Institutional/Commercial: The primary use of 2,4,6-TARR in commercial products is as a propellant/solvent in commercial spray paints (6 % of production). THE CASE STUDY DID NOT INCLUDE AN ANALYSIS OF THIS USE.

Consumer exposure: As noted above, consumer exposure to 2,4,6-TARR is the primary area of interest for this report, since it may occur directly following use of aerosol products containing this material as a propellant. The analysis focuses hairspray, household pesticides, and household cleaner sprays, as used by the general public. The case study did not address the use of these products in institutional settings. Other listed consumer product applications for the chemical are omitted, because they are either intermittent in nature or do not result in direct consumer exposure. Such exposures are assessed here in 3 different ways (calculations summarized in Attachment 6):

1. Estimating exposure based on measurements of airborne 2,4,6-TARR concentrations from use of representative aerosol products in an experimental environment, and published habits and practices data for the length of time that they are typically used. This number provides one estimate for "aggregate consumer exposure" and is expressed in "ppm•minute" units. It defines a maximum amount of 2,4,6-TARR to which a consumer would be exposed, but does not estimate what may actually be inhaled.
2. Calculating an inhaled dose of 2,4,6-TARR based on measured airborne levels and time of product use for an average body weight and breathing rate, assuming that 100 % of that which is inhaled is also absorbed by the body.
3. Calculating an inhaled dose of 2,4,6-TARR based on estimated airborne levels and time of product use for an average body weight and breathing rate. In the absence of measured data, airborne levels can be estimated knowing amounts of 2,4,6-TARR discharged during aerosol use and the size of the room in which use occurs. This "theoretical" calculation can be used to validate calculations made in #2 above.

Method #1: Consumer Aggregate Exposure Estimate - Concentration.Time

This estimate of exposure (Attachment 6, Part A) presents an indication of the length of time consumers may spend in an atmosphere containing 2,4,6-TARR following use of consumer products. It is estimated by multiplying the length of time spent conducting a product use "task" by the airborne concentration of 2,4,6-TARR during that task. This information is then used to quantify weekly exposure in "ppm.minutes." The result of this analysis is:

Consumer aggregate exposure estimate: 24,850 ppm.min

As noted above, a no-observable-adverse-effect-concentration (NOAEC) of 10,000 ppm in air has been chosen as a conservative toxicity threshold, based on available hazards data. This level, converted in the same fashion as the aggregate exposure, is:

18,000,000 ppm.min

Method #2: Consumer Aggregate Exposure Estimate - Inhaled Dose

This estimate of exposure (Attachment 6, Part B) presents an indication of the quantity of 2,4,6-TARR that consumers may actually inhale and have available for systemic absorption following use of consumer products. In reality, it is unlikely that all inhaled 2,4,6-TARR is truly retained and delivered to potential target organs; much will be expired with exhaled air before it has the chance to be absorbed. As a result, these calculations are conservative.

Consumer aggregate exposure estimate of inhaled dose: 1.59 mg/kg/day

For reference, the dose delivered in a representative animal study at the NOAEC, calculated in the same fashion, is:

6,500 mg/kg/day

Method #3: Theoretical Estimate for Use of a Hairspray Product

In this example (Attachment 6, Part C), exposure to 2,4,6-TARR following use of a hairspray product is calculated in a way that relates 2,4,6-TARR concentration in the finished product with habits and practices information pertaining to the product use task. This figure is then compared to the estimate for hairspray use derived in the second example, to help calibrate and verify the integrity of the second aggregate assessment. With complete habits and practices data for all product types formulated with 2,4,6-TARR (not available for preparation of this case example), a total aggregate assessment could be made in this fashion. This calibration exercise serves to demonstrate another way of calculating exposure, in addition to supporting integrity of the method used above.

Exposure - ppm.min method

0.61 mg/kg/day

Exposure - habits/practices method

0.21 mg/kg/day

As can be seen, these values compare favorably, despite the fact that the approaches used to make the estimates differed significantly.

Other Exposures

Based on the ways it is used, and its high volatility, indirect exposure human via contact with 2,4,6-TARR from indoor air, ambient levels, and other sources is expected to be negligible in comparison to exposures occurring during execution of the actual “tasks” associated with use of these consumer products, and are therefore not considered in these calculations.

Ecological Exposure Assessment:

CASE STUDY DID NOT INCLUDE ECOLOGICAL EXPOSURES

Hazard/Exposure-Based Human Safety Assessment:

2,4,6-TARR has a low order of acute and chronic inhalation toxicity, and it is not a teratogen, mutagen, or carcinogen. Risk of personal injury or adverse health effects during the manufacture of 2,4,6-TARR or its processing into consumer products is acceptably low, when used in accordance with appropriate industrial hygiene and safety measures (noting flammability, explosion and narcosis hazards associated with propellant gases under extreme conditions). Likewise, intended use of consumer products containing 2,4,6-TARR presents no safety risk (recognizing that intentional misuse via deliberate concentration and inhalation of vapors can be potentially life-threatening, and that misuse also presents flammability/explosion hazards typical for aerosol products). The predicted aggregate exposure is ~700 times lower than the no-observed-adverse-effect-concentration (NOAEC) in the repeat dose rat study when determined using the “ppm.min” approach, and ~4100 lower when determined using the “mg/kg/day inhaled dose” approach. It is also important to recognize that these exposure assessments are highly conservative and most likely represent an exaggerated exposure. As a consequence of this screening level analysis, 2,4,6-TARR is recommended to be a low priority for future work.

Attachment 6

Summarizing Individual Exposure Evaluations for Consumer Products Use of 2,4,6-TARR

METHOD 1 Consumer Aggregate Exposure Estimate (ppm•minute method)

Aggregate exposure can be estimated by multiplying the length of time spent conducting a product use “task” by the airborne concentration of 2,4,6-TARR during that task. This information has been used to quantify weekly exposure in “ppm.minutes” based on actual measurement of 2,4,6-TARR airborne concentrations during simulated use of consumer aerosol products, as follows:

Weekly exposure	ppm.minutes*
Hairspray	= 9,450
Insecticide	= 7,700
Household cleaner spray	= <u>7,700</u>
Total	= 24,850 ppm.min

[Note that selected product categories have been omitted from this aggregate example either because exposure is very intermittent (e.g., adhesives; paints) or contained (e.g., tire inflators). Furthermore, selected product categories studied in the original reference for these measurements are not included in this example because 2,4,6-TARR is no longer used as a propellant for these product types (i.e., body deodorant spray; air fresheners)].

Similarly, the 10,000 ppm NOAEC determined from toxicity testing (Attachment 4) is converted from a ppm exposure concentration to a weekly “ppm.minutes” value as follows:

NOAEC X	5 days/week	X	6hrs/day	X	60 min/hr	
10,000 X	5	X	6	X	60	= 18,000,000 ppm.min

*Values are derived from L. J. M. Bohnenn (Aerofako), presented at the annual meeting of the Western Aerosol Information Bureau, Las Vegas, Nevada, October 16 and 17, 1980.

METHOD 2
Consumer Aggregate Exposure Estimate for Inhaled Dose

A more detailed assessment of estimated exposure can be obtained by converting the weekly ppm.min 2,4,6-TARR vapor exposure values to relative inhaled doses, considering ventilation rate and expressing per unit body weight. Exposure assumptions made in this calculation include:

weekly ppm.min as shown in Part A
1 ppm = 1.88 mg/m³
58 kg = average (female) adult body weight
0.83 m³/hr = human ventilation rate

Exposure Equation:

$$\begin{array}{cccccccccccc} \text{Wk. Exp. Rate} & \times & \text{weeks/day} & \times & \text{ppm convert} & \times & \text{vent. rate} & \times & \text{hr/min} & \times & \text{1/body wt.} & = & \text{exposure} \\ \hline \text{---- ppm.min} & \times & \text{1 wk} & \times & \text{1.88 mg/m}^3 & \times & \text{0.83 m}^3 & \times & \text{1 hr} & \times & \text{1} & = & \text{mg/kg/day} \\ \text{wk} & & \text{7 days} & & \text{1ppm} & & \text{hr} & & \text{60 min} & & \text{58 kg} & & \end{array}$$

Estimates:

Hairspray

$$\begin{array}{cccccccccccc} \text{9,450 ppm.min} & \times & \text{1 wk} & \times & \text{1.88 mg/m}^3 & \times & \text{0.83 m}^3 & \times & \text{1 hr} & \times & \text{1} & = & \text{0.61 mg/kg/day} \\ \text{wk} & & \text{7 days} & & \text{1ppm} & & \text{hr} & & \text{60 min} & & \text{58 kg} & & \end{array}$$

Insecticide

$$\begin{array}{cccccccccccc} \text{7,700 ppm.min} & \times & \text{1 wk} & \times & \text{1.88 mg/m}^3 & \times & \text{0.83 m}^3 & \times & \text{1 hr} & \times & \text{1} & = & \text{0.49 mg/kg/day} \\ \text{wk} & & \text{7 days} & & \text{1ppm} & & \text{hr} & & \text{60 min} & & \text{58 kg} & & \end{array}$$

Household spray

$$\begin{array}{cccccccccccc} \text{7,700 ppm.min} & \times & \text{1 wk} & \times & \text{1.88 mg/m}^3 & \times & \text{0.83 m}^3 & \times & \text{1 hr} & \times & \text{1} & = & \text{0.49 mg/kg/day} \\ \text{wk} & & \text{7 days} & & \text{1ppm} & & \text{hr} & & \text{60 min} & & \text{58 kg} & & \end{array}$$

Total= 1.59mg/kg/day

Similarly, the NOAEC determined from toxicity testing (Attachment 4) can be converted from a ppm in air exposure concentration to an inhaled dose expressed per unit body weight. Exposure assumptions made in this calculation include:

10,000 ppm = NOAEC
1 ppm = 1.88 mg/m³
0.25 kg = average rat weight
240 ml/min = rat ventilation rate
6 hour daily exposure

Exposure Equation

$$\begin{array}{cccccccccccc} \text{NOAEC} & \times & \text{ppm convert} & \times & \text{m}^3/\text{l convert} & \times & \text{l/ml convert} & \times & \text{vent rate} & \times & \text{min/hr convert} & \times & \text{hr/day exp.} & \times & \text{1/body wt.} & = & \text{exposure} \\ \hline \text{10,000 ppm} & \times & \text{1.88 mg/m}^3 & \times & \text{m}^3 & \times & \text{0.001 l} & \times & \text{240 ml} & \times & \text{60 min} & \times & \text{6 hr} & \times & \text{1} & = & \text{6,500 mg/kg/day} \\ & & \text{1 ppm} & & \text{1000 l} & & \text{1 ml} & & \text{min} & & \text{hr} & & \text{day} & & \text{0.25 kg} & & \end{array}$$

METHOD 3
Theoretical Estimate Based on Use of a Hairspray Product

As a calibration exercise, estimated human exposure to 2,4,6-TARR during use of a hairspray product was calculated in a different way. In the previous example, published values for “ppm.minutes” of exposure to various products formulated with 2,4,6-TARR were used to derive an aggregate estimate of daily inhaled 2,4,6-TARR following use of consumer products. In this hairspray example, the airborne 2,4,6-TARR concentration is first calculated (estimated) based upon a representative use scenario (incorporating concentration of 2,4,6-TARR in the finished product as well as habits and practices information pertaining to product use). Then, estimated 2,4,6-TARR inhalation is calculated as in the previous example. Exposure assumptions made in this calculation include:

- 35% = maximum concentration of 2,4,6-TARR used as a hairspray propellant
- 1.5 g_s = amount of product dispenses/use; product used 2x/day
- 18 m³ = representative room size (bathroom) for task
- 15 min = duration of exposure (2,4,6-TARR release in bathroom following use of hairspray)
- 58 kg = nominal (female) adult body weight
- 0.83 m³/hr = human ventilation rate

Exposure Equation

$$\begin{array}{cccccccccccc}
 \text{Prod. Level} & \times & \text{g product/use} & \times & \text{uses/day} & \times & \text{1/Room vol.} & \times & \text{vent. rate} & \times & \text{Task duration} & \times & \text{hr/min} & \times & \text{1/body wt.} & = & \text{exposure} \\
 \frac{0.35 \text{ g 2,4,6-TARR}}{\text{g product}} & \times & \frac{1.5 \text{ g product}}{\text{use}} & \times & \frac{2 \text{ uses}}{\text{day}} & \times & \frac{1}{18 \text{ m}^3} & \times & \frac{0.83 \text{ m}^3}{\text{hr}} & \times & \frac{15 \text{ min}}{60 \text{ min}} & \times & \frac{1 \text{ hr}}{60 \text{ min}} & \times & \frac{1}{58 \text{ kg}} & = & \text{exposure}
 \end{array}$$

$$\text{Exposure} = 2.1 \times 10^{-4} \text{ g/kg/day} = 0.21 \text{ mg/kg/day}$$

As is demonstrated in this example, this estimate of 2,4,6-TARR exposure following use of a hairspray compares favorably with the estimate derived using the published ppm.min values for exposure. Calibration of exposure estimates using various approaches like this can help lend confidence to the method chosen for conduct of the aggregate assessment.