Molecular Weight: 30.02

Color: Clear Colorless.

pH (1% soln/water): 3 [Acidic.] pH of the solution as is.

Boiling Point: 98°C (208.4°F)

Melting Point: -15°C (5°F)

Critical Temperature: The lowest known value is 240°C (464°F) (Methyl alcohol).

Specific Gravity: 1.08 (Water = 1)

Vapor Pressure: 2.4 kPa (@ 20°C)

Vapor Density: 1.03 (Air = 1)

Volatility: 100% (w/w).

Odor Threshold: The highest known value is 100 ppm (Methyl alcohol)

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Non-ionic.

Dispersion Properties: See solubility in water, diethyl ether, acetone.

Solubility:
Easily soluble in cold water, hot water. Soluble in diethyl ether, acetone, alcohol

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Heat, ignition sources (flames, sparks), incompatible materials

Incompatibility with various substances:
Reactive with oxidizing agents, reducing agents, acids, alkalis. Slightly reactive to reactive with metals.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:
Also incompatible with urea, phenol, isocyanates, anhydrides, amines, AZO compounds, carbonyl compounds, oxides(e.g. nitrogen dioxide), performic acid, dithiocarbmates, or peroxides. Polymerization can be inhibited by the addition of methanol or stabilizers such as hydorxypropyl methyl cellulose, methyl ethyl celluloses, or isophthalobisguanamine.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Dermal contact. Eye contact. Inhalation.

Toxicity to Animals:
Acute oral toxicity (LD50): 42 mg/kg [Mouse]. (Formaldehyde) Acute dermal toxicity (LD50): 15800 mg/kg [Rabbit]. (Methyl alcohol). Acute toxicity of the mist(LC50): 454000 mg/m 4 hours [Mouse]. (Formaldehyde) 3

Chronic Effects on Humans:
CARCINOGENIC EFFECTS: Classified A2 (Suspected for human.) by ACGIH, 2A (Probable for human.) by IARC [Formaldehyde]. MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. [Formaldehyde]. Mutagenic for bacteria and/or yeast. [Formaldehyde]. Mutagenic for mammalian somatic cells. [Methyl alcohol]. Mutagenic for bacteria and/or yeast. [Methyl alcohol]. TERATOGENIC EFFECTS: Classified POSSIBLE for human [Methyl alcohol]. DEVELOPMENTAL TOXICITY: Not available May cause damage to the following organs: kidneys, liver, central nervous system (CNS).

Other Toxic Effects on Humans:
Very hazardous in case of ingestion, . Hazardous in case of skin contact (irritant, sensitizer, permeator), of eye contact (corrosive), of inhalation (lung corrosive). Slightly hazardous in case of skin contact (corrosive).

Special Remarks on Toxicity to Animals:
Formaldehyde: LD50 [Rabbit] - Route: Skin; Dose: 270 ul/kg

Special Remarks on Chronic Effects on Humans:
Exposure to Formaldehyde and Methanol may affect genetic material (mutagenic). Exposure to Formaldehyde and Methanol may cause adverse reproductive effects and birth defects(teratogenic). Adverse reproductive effects of Formaldehyde as well as Methanol are primarily based on animal studies. Very few human studies have been done on the adverse reproductive effects from exposure to Formaldehyde. Studies produced a weak association (limited evidence) between advese human female reproductive effects and occupational exposure. Furthermore, no human data could be found on adverse reproductive effects from occupational exposure to Methanol. Exposure to Formaldehyde may cause cancer.

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: Corrosive. Causes skin irritation which may range from mild to severe with possible burns depending on the extent of exposure and concentration of solution. Other symptoms may include brownish discoloration of the skin, urticaria, and pustulovesicffular eruptions. May be absorbed through skin with symptoms paralleling those of ingestion. Eyes: Corrosive. Contact with liquid causes severe eye irritation and burns. It may cause irreversible eye damage (severe corneal Solutions containing low formaldehyde concentrations may produce transient discomfort and irritation. Inhalation: Causes irritation of the respiratory tract (nose, throat, airways). Symptoms may include dry and sore mouth and throat, thirst, and sleep disturbances, difficulty breathing, shortness of breath, coughing, sneezing, wheezing rhinitis, chest tightness, pulmonary edema, bronchitis, tracheitis, laryngospasm, pneumonia, palpitations. It may also affect metabolism weight loss, metabolic acidosis), behavior/central nervous system (excitement, central nervous system depression, somnolence, convulsions, stupor, aggression, headache, weakness, dizziness, drowsiness, coma), peripheral nervous system, and blood. Ingestion: Harmful if swallowed. May be fatal. Causes gastrointestinal irritation with nausea, vomiting (possibly with blood), diarrhea, severe pain in mouth, throat and stomach, and possible corrosive injury to the gastrointestinal mucosa/ulceration or bleeding from stomach. May also affect the liver(jaundice), urinary system/kidneys (difficulty urinating, albuminuria, hematuria, anuria), blood, endocrine system, respiration (respiratory obstruction, pulmonary edema, bronchiolar obstruction), cardiovascular system (hypotension), metabolism (metabolic acidosis), eyes (retinal changes, visual field changes), and behavior/central nervous system (symptoms similar to those for inhalation). Contains Methanol which may cause blindness if swallowed. Chronic Potential Health Effects: Skin: Prolonged or repeated exposure may cause contact dermatits both irritant and allergic. It may also cause skin discoloration. Inhalation: Although there is no clear evidence, prolonged or repeated exposure may induce allergic asthma. Other effects are similar to that of acute exposure. Ingestion: Prolonged or repeated ingestion may cause gastrointestinal tract irritation and ulceration or bleeding from the stomach. Other effects may be similar to that of acute ingestion.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are less toxic than the product itself.

Special Remarks on the Products of Biodegradation:
Methanol in water is rapidly biodegraded and volatilized. Aquatic hydrolysis, oxidation, photolysis, adsorption to sediment, and bioconcentration are not significant fate processes. The half-life of methanol in surfact water ranges from 24 hrs. to 168 hrs. Based on its vapor pressure, methanol exists almost entirely in the vapor phase in the ambient atmosphere. It is degraded by reaction with photochemically produced hydroxyl radicals and has an estimated half-life of 17.8 days. Methanol is physically removed from air by rain due to its solubility. Methanol can react with NO2 in pollulted to form methyl nitrate. The half-life of methanol in air ranges from 71 hrs. (3 days) to 713 hrs. (29.7 days) based on photooxidation half-life in air. (Methyl alcohol)

Section 13: Disposal Considerations

Waste Disposal:
Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification:
CLASS 3: Flammable liquid. Class 8: Corrosive material

Identification: : Formaldehyde Solution, flammable (Methyl alcohol) UNNA: 1198 PG: III

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:
California prop. 65: This product contains the following ingredients for which the State of California has found to cause cancer, birth defects or other reproductive harm, which would require a warning under the statute: Formaldehyde California prop. 65 (no significant risk level): Formaldehyde: 0.04 mg/day (inhalation) California prop. 65: This product contains the following ingredients for which the State of California has found to cause cancer which would require a warning under the statute: Formaldehyde Solution Connecticut hazardous material survey.: Formaldehyde; Methyl alcohol Illinois toxic substances disclosure to employee act: Formaldehyde; Methyl alcohol Illinois chemical safety act: Formaldehyde; Methyl alcohol New York release reporting list: Formaldehyde; Methyl alcohol Rhode Island RTK hazardous substances: Formaldehyde; Methyl alcohol Pennsylvania RTK: Formaldehyde; Methyl alcohol Minnesota: Formaldehyde gas; Methyl alcohol Massachusetts RTK: Formaldehyde; Methyl alcohol Massachusetts spill list: Formaldehyde; Methyl alcohol New Jersey: Formaldehyde; Methyl alcohol New Jersey spill list: Formaldehyde; Methyl alcohol Louisiana RTK reporting list: Formaldehyde Louisiana spill reporting: Formaldehyde; Methyl alcohol California Director's List of Hazardous Substances: Formaldehyde; Methyl alcohol TSCA 8(b) inventory: Formaldehyde gas; Methyl alcohol; Water TSCA 4(f) priority risk review: Formaldehyde, Reagnt, ACS SARA 302/304/311/312 extremely hazardous substances: Formaldehyde SARA 313 toxic chemical notification and release reporting: Formaldehyde; Methyl alcohol CERCLA: Hazardous substances.: Formaldehyde: 100 lbs. (45.36 kg); Methyl alcohol: 5000 lbs. (2268 kg);

Other Regulations:
OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200). EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada):
CLASS B-3: Combustible liquid with a flash point between 37.8°C (100°F) and 93.3°C (200°F). CLASS D-1A: Material causing immediate and serious toxic effects (VERY TOXIC). CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

DSCL (EEC):

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 2

Reactivity: 0

Personal Protection: G

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 2

Reactivity: 0

Specific hazard:

Protective Equipment:
Gloves (impervious). Lab coat. Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate. Safety glasses.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

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EXHIBIT F

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Health	2
Fire	1
Reactivity	0
Personal Protection	E

Material Safety Data Sheet
Thimerosal MSDS

Section 1: Chemical Product and Company Identification

Product Name: Thimerosal

Catalog Codes: SLT1411

CAS#: 54-64-8

RTECS: OV8400000

TSCA: TSCA 8(b) inventory: Thimerosal

CI#: Not available.

Synonym: Ethylmercurithiosalicylic acid sodium salt; Merthiolate

Chemical Name: Thimerosal

Chemical Formula: C9H9HgNaO2S

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call: 1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Thimerosal	54-64-8	100

Toxicological Data on Ingredients: Thimerosal: ORAL (LD50): Acute: 75 mg/kg [Rat]. 91 mg/kg [Mouse].

Section 3: Hazards Identification

Potential Acute Health Effects:
Hazardous in case of skin contact (irritant), of ingestion, of inhalation. Slightly hazardous in case of eye contact (irritant). Severe over-exposure can result in death.

Potential Chronic Health Effects:
CARCINOGENIC EFFECTS: Not available. MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. The substance may be toxic to kidneys, liver, spleen, bone marrow, central nervous system (CNS). Repeated or prolonged exposure to the substance can produce target organs damage. Repeated exposure to a highly toxic material may produce general deterioration of health by an accumulation in one or many human organs.

Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention if irritation occurs.

Skin Contact:
In case of contact, immediately flush skin with plenty of water. Cover the irritated skin with an emollient. Remove contaminated clothing and shoes. Cold water may be used.Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention.

Serious Skin Contact:
Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation:
If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Serious Inhalation:
Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. Seek medical attention.

Ingestion:
If swallowed, do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. Loosen tight clothing such as a collar, tie, belt or waistband. Get medical attention immediately.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: May be combustible at high temperature.

Auto-Ignition Temperature: Not available.

Flash Points: CLOSED CUP: >250°C (482°F).

Flammable Limits: Not available.

Products of Combustion: These products are carbon oxides (CO, CO2). Some metallic oxides.

Fire Hazards in Presence of Various Substances:
Slightly flammable to flammable in presence of heat. Non-flammable in presence of shocks.

Explosion Hazards in Presence of Various Substances:
Slightly explosive in presence of open flames and sparks. Non-explosive in presence of shocks.

Fire Fighting Media and Instructions:
SMALL FIRE: Use DRY chemical powder. LARGE FIRE: Use water spray, fog or foam. Do not use water jet.

Special Remarks on Fire Hazards: As with most organic solids, fire is possible at elevated temperatures

Special Remarks on Explosion Hazards:
Fine dust dispersed in air in sufficient concentrations, and in the presences of an ignition source is a potential dust explosion hazard.

Section 6: Accidental Release Measures

Small Spill: Use appropriate tools to put the spilled solid in a convenient waste disposal container.

Large Spill:
Poisonous solid. Stop leak if without risk. Do not get water inside container. Do not touch spilled material. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Eliminate all ignition sources. Call for assistance on disposal. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:
Keep away from heat. Keep away from sources of ignition. Do not ingest. Do not breathe dust. Avoid contact with skin. Wear suitable protective clothing. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label.

Storage:
Keep container tightly closed. Keep container in a cool, well-ventilated area. Sensitive to light. Store in light-resistant containers.

Section 8: Exposure Controls/Personal Protection

Engineering Controls:
Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection: Safety glasses. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:
Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:
TWA: 0.1 from ACGIH (TLV) [United States] [1995] Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (crystalline powder.)

Odor: Not available.

Taste: Not available.

Molecular Weight: 404.82 g/mole

Color: Off-white. White.

pH (1% soln/water): 6.7 [Neutral.]

Boiling Point: Not available

Melting Point: Decomposition temperature: 232°C (449.6°F)

Critical Temperature: Not available.

Specific Gravity: Not available.

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:
Easily soluble in cold water, hot water. Insoluble in diethyl ether. 1 gram dissolves in about 1 ml of water. 1 gram dissolves in about 8 ml of alcohol. Practically insoluble in benzene

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Excess heat, light, dust generation, incompatible materials

Incompatibility with various substances: Reactive with oxidizing agents, acids, alkalis.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Light sensitive.

Special Remarks on Corrosivity: Not available.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Inhalation. Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 75 mg/kg [Rat].

Chronic Effects on Humans:
MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. May cause damage to the following organs: kidneys, liver, spleen, bone marrow, central nervous system (CNS).

Other Toxic Effects on Humans: Hazardous in case of skin contact (irritant), of ingestion, of inhalation.

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans:
May cause cancer based on animal data. No human data found. May cause adverse reproductive effects(female fertility - post implanation mortality, fetotoxicity)and birth defects. May affect genetic material

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: Causes skin irritation. Eyes: Causes eye irritation. May cause chemical conjunctivitis. Inhalation: Causes respiratory tract irritation. May cause allergic respiratory tract irritation. Exposures to high concentrations may produce unconsciousness with cyanosis(a bluish discoloration of the skin due to deficient oxygenation of the blood) and cold extremities and may also affect the cardiovascular system (rapid pulse). Acute exposure to high concentrations of mercury vapors may also cause kidney damage and affect behavior/central nervous system, peripheral nervous system and autonomic nervous system, and liver and cause gastrointestinal effects (nausea, abdominal pain, vomiting). Ingestion: Harmful if swallowed. May cause gastrointestinal tract irritation with nausea, vomiting and diarrhea, headache. Exposure to high concentrations may affect respiration and cardiovascular system which may produce unconciousness with cyanosis, cold extremities and rapid pulse. May also cause central nervous system effects and/or neurological effects, and may affect the urinary system (kidneys),and liver. Chronic Potential Health Effects: Skin: Prolonged or repeated skin contact may cause skin sensitization, an allergic reaction. Inhalation and Ingestion: Repeated or prolonged exposure may cause cause kidney damage, and may affect the liver, and bone marrow. Chronic exposure to mercury vaporsbehavior/central nervous system and peripheral nervous system (depression, irritability, nervousness, weakness, ataxia, fatigue, tremor, jerky gait, limb spasms, personality changes), metabolism (anorexia, weight loss) and cause gastrointestinal disturbances which is collectively referred to as "aesthenic-vegetative syndrome." Chronic ingestion may cause accumulation of mercury in body tissues and may result in salicylism which is characterized by nausea, vomiting, gastric ulcers, and hemorrhagic strokes.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are less toxic than the product itself.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:
Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: CLASS 6.1: Poisonous material.

Identification: : Mercury compound, solid, n.o.s. (Thimerosal) UNNA: 2025 PG: III

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:
California prop. 65: This product contains the following ingredients for which the State of California has found to cause cancer, birth defects or other reproductive harm, which would require a warning under the statute: Thimerosal California prop. 65: This product contains the following ingredients for which the State of California has found to cause birth defects which would require a warning under the statute: Thimerosal TSCA 8(b) inventory: Thimerosal SARA 313 toxic chemical notification and release reporting: Thimerosal CERCLA: Hazardous substances.: Thimerosal

Other Regulations:
OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200). EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada):
CLASS D-1B: Material causing immediate and serious toxic effects (TOXIC). CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

DSCL (EEC):

HMIS (U.S.A.):

Health Hazard: 2

Fire Hazard: 1

Reactivity: 0

Personal Protection: E

National Fire Protection Association (U.S.A.):

Health: 2

Flammability: 1

Reactivity: 0

Specific hazard:

Protective Equipment:
Gloves. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Safety glasses.

Section 16: Other Information

References: Not available.

Other Special Considerations:
Thimerosal is a Mercury compound. It is on the Prop. 65 list as a Mercury compound. Under Prop. 65, Mercury and Mercury compounds are listed as "Chemicals known to the State of California to Cause Reproductive Toxicity."

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Last Updated: 05/21/2013 12:00 PM

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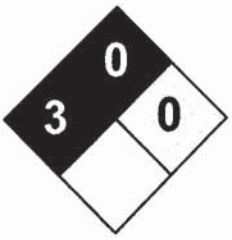

Health	3
Fire	0
Reactivity	0
Personal Protection	

Material Safety Data Sheet
Mercury MSDS

Section 1: Chemical Product and Company Identification

Product Name: Mercury

Catalog Codes: SLM3505, SLM1363

CAS#: 7439-97-6

RTECS: OV4550000

TSCA: TSCA 8(b) inventory: Mercury

CI#: Not applicable.

Synonym: Quick Silver; Colloidal Mercury; Metallic Mercury; Liquid Silver; Hydragyrum

Chemical Name: Mercury

Chemical Formula: Hg

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: **1-800-901-7247**
International Sales: **1-281-441-4400**

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call: 1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Mercury	7439-97-6	100

Toxicological Data on Ingredients: Mercury LD50: Not available. LC50: Not available.

Section 3: Hazards Identification

Potential Acute Health Effects:
Very hazardous in case of skin contact (irritant), of eye contact (irritant), of ingestion, of inhalation. Hazardous in case of skin contact (corrosive, permeator). Liquid or spray mist may produce tissue damage particularly on mucous membranes of eyes, mouth and respiratory tract. Skin contact may produce burns. Inhalation of the spray mist may produce severe irritation of respiratory tract, characterized by coughing, choking, or shortness of breath. Severe over-exposure can result in death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:
Hazardous in case of skin contact (permeator). CARCINOGENIC EFFECTS: Classified A5 (Not suspected for human.) by ACGIH. 3 (Not classifiable for human.) by IARC. MUTAGENIC EFFECTS: Not available. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. The substance may be toxic to blood, kidneys, liver, brain, peripheral nervous system, central nervous system (CNS). Repeated or prolonged exposure to the substance can produce target organs damage. Repeated or prolonged contact with spray mist may produce chronic eye irritation and severe skin irritation.

Repeated or prolonged exposure to spray mist may produce respiratory tract irritation leading to frequent attacks of bronchial infection. Repeated exposure to a highly toxic material may produce general deterioration of health by an accumulation in one or many human organs.

Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. WARM water MUST be used. Get medical attention immediately.

Skin Contact:
In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:
Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation:
If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation:
Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. WARNING: It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:
Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: Not applicable.

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of mechanical impact: Not available. Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards:
When thrown into mercury vapor, boron phosphodiiodide ignites at once. Flame forms with chlorine jet over mercury surface at 200 deg to 300 deg C. Mercury undergoes hazardous reactions in the presence of heat and sparks or ignition.

Special Remarks on Explosion Hazards:
A violent exothermic reaction or possible explosion occurs when mercury comes in contact with lithium and rubidium. CHLORINE DIOXIDE & LIQUID HG, WHEN MIXED, EXPLODE VIOLENTLY. Mercury and Ammonia can produce an

explosive compound. A mixture of the dry carbonyl and oxygen will explode on vigorous shaking with mercury. Methyl azide in the presence of mercury was shown to be potentially explosive.

Section 6: Accidental Release Measures

Small Spill: Absorb with an inert material and put the spilled material in an appropriate waste disposal.

Large Spill:
Corrosive liquid. Poisonous liquid. Stop leak if without risk. Absorb with DRY earth, sand or other non-combustible material. Do not get water inside container. Do not touch spilled material. Use water spray curtain to divert vapor drift. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:
Keep locked up.. Keep container dry. Do not ingest. Do not breathe gas/fumes/ vapor/spray. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as oxidizing agents, metals.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area. Do not store above 25°C (77°F).

Section 8: Exposure Controls/Personal Protection

Engineering Controls:
Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapors below their respective threshold limit value. Ensure that eyewash stations and safety showers are proximal to the work-station location.

Personal Protection:
Face shield. Full suit. Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Gloves. Boots.

Personal Protection in Case of a Large Spill:
Splash goggles. Full suit. Vapor respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:
TWA: 0.025 from ACGIH (TLV) [United States] SKIN TWA: 0.05 CEIL: 0.1 (mg/m3) from OSHA (PEL) [United States] Inhalation TWA: 0.025 (mg/m3) [United Kingdom (UK)] Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid. (Heavy liquid)

Odor: Odorless.

Taste: Not available.

Molecular Weight: 200.59 g/mole

Color: Silver-white

pH (1% soln/water): Not available.

Boiling Point: 356.73°C (674.1°F)

Melting Point: -38.87°C (-38°F)

Critical Temperature: 1462°C (2663.6°F)

Specific Gravity: 13.55 (Water = 1)

Vapor Pressure: Not available.

Vapor Density: 6.93 (Air = 1)

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: Not available.

Solubility: Very slightly soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials

Incompatibility with various substances: Reactive with oxidizing agents, metals.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity:
Ground mixtures of sodium carbide and mercury, aluminum, lead, or iron can react vigorously. A violent exothermic reaction or possible explosion occurs when mercury comes in contact with lithium and rubidium. Incompatible with boron diiodophosphide; ethylene oxide; metal oxides, metals(aluminum, potassium, lithium, sodium, rubidium); methyl azide; methylsilane, oxygen; oxidants(bromine, peroxyformic acid, chlorine dioxide, nitric acid, tetracarbonynickel, nitromethane, silver perchlorate, chlorates, sulfuric acid, nitrates,); tetracarbonylnickel, oxygen, acetylinic compounds, ammonia, ethylene oxide, methylsiliane, calcium,

Special Remarks on Corrosivity:
The high mobility and tendency to dispersion exhibited by mercury, and the ease with which it forms alloys (amalga) with many laboratory and electrical contact metals, can cause severe corrosion problems in laboratories. Special precautions: Mercury can attack copper and copper alloy materials.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Dermal contact. Eye contact. Inhalation. Ingestion.

Toxicity to Animals:
LD50: Not available. LC50: Not available.

Chronic Effects on Humans:
CARCINOGENIC EFFECTS: Classified A5 (Not suspected for human.) by ACGIH. 3 (Not classifiable for human.) by IARC. May cause damage to the following organs: blood, kidneys, liver, brain, peripheral nervous system, central nervous system (CNS).

Other Toxic Effects on Humans:
Very hazardous in case of skin contact (irritant), of ingestion, of inhalation. Hazardous in case of skin contact (corrosive, permeator).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans:

May affect genetic material. May cause cancer based on animal data. Passes through the placental barrier in animal. May cause adverse reproductive effects(paternal effects- spermatogenesis; effects on fertility - fetotoxicity, post-implantation mortality), and birth defects.

Special Remarks on other Toxic Effects on Humans:

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are less toxic than the product itself.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:
Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Class 8: Corrosive material

Identification: : Mercury UNNA: 2809 PG: III

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:
California prop. 65: This product contains the following ingredients for which the State of California has found to cause cancer, birth defects or other reproductive harm, which would require a warning under the statute: Mercury California prop. 65: This product contains the following ingredients for which the State of California has found to cause birth defects which would require a warning under the statute: Mercury Connecticut hazardous material survey.: Mercury Illinois toxic substances disclosure to employee act: Mercury Illinois chemical safety act: Mercury New York acutely hazardous substances: Mercury Rhode Island RTK hazardous substances: Mercury Pennsylvania RTK: Mercury Minnesota: Mercury Massachusetts RTK: Mercury New Jersey: Mercury New Jersey spill list: Mercury Louisiana spill reporting: Mercury California Director's List of Hazardous Substances.: Mercury TSCA 8(b) inventory: Mercury SARA 313 toxic chemical notification and release reporting: Mercury CERCLA: Hazardous substances.: Mercury: 1 lbs. (0.4536 kg)

Other Regulations:
OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200). EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada):
CLASS D-1A: Material causing immediate and serious toxic effects (VERY TOXIC). CLASS D-2A: Material causing other toxic effects (VERY TOXIC). CLASS E: Corrosive liquid.

DSCL (EEC):
R23- Toxic by inhalation. R33- Danger of cumulative effects. R38- Irritating to skin. R41- Risk of serious damage to eyes. R50/53- Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. S2- Keep out of the

reach of children. S7- Keep container tightly closed. S26- In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S39- Wear eye/face protection. S45- In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). S46- If swallowed, seek medical advice immediately and show this container or label. S60- This material and its container must be disposed of as hazardous waste. S61- Avoid release to the environment. Refer to special instructions/Safety data sheets.

HMIS (U.S.A.):

Health Hazard: 3

Fire Hazard: 0

Reactivity: 0

Personal Protection:

National Fire Protection Association (U.S.A.):

Health: 3

Flammability: 0

Reactivity: 0

Specific hazard:

Protective Equipment:
Gloves. Full suit. Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate. Face shield.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

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EXHIBIT G

Events Surrounding the DeStefano et al (2004) MMR-Autism Study

Prepared by Dr. William E. Thompson

September 9, 2014

Background

My primary job duties while working in the Immunization Safety Branch from 2000 to 2006 were to lead or co-lead three major vaccine safety studies.

1. VSD Thimerosal Neurodevelopment Study (Thompson et al, NEJM, 2007)
2. VSD Thimerosal Autism Study (Price, Thompson et al, Pediatrics, 2010)
3. MADDSP MMR-Autism Case-Control Study (DeStefano et al, Pediatrics, 2004)

The MADDSP MMR-Autism Cases Control Study was being carried out in response to the Wakefield (1998) Lancet study that suggested an association between the MMR vaccine and an autism-like health outcome. There were several major concerns among scientists and consumer advocates outside the CDC in the fall of 2000 regarding in the execution of the Verstraeten et al (2003) study[1]. The Verstraeten Study was the first study the CDC carried out to examine the association between thimerosal and neurodevelopmental outcomes including autism. Some of the major concerns included 1) many of the statistical analyses were carried out post-hoc after an initial set of analyses were run, 2) the study protocol evolved over time, and 3) the CDC did not share many of the internal study findings with individuals and constituents outside the CDC.

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One of the important goals that was determined up front in the spring of 2001 before any of these studies started was to have all three study protocols vetted outside the CDC prior to the start of analyses so that consumer advocates could not claim that we were presenting analyses that suited our own goals and biases.

My primary responsibilities for the MADDSP MMR-Autism Study were:

1. Lead the large majority of the study-related meetings with all coauthors.
2. Write all the SAS programs for all the statistical analyses associated with the paper.
3. Summarize and present the statistical results to the coauthors on a regular basis.

In addition, all SAS programs and statistical analyses were reviewed by both Dr. Margarette Kolzcak and Dr. Andrew Autry. All data management work was led by Tanya Karapukar and she also reviewed the data management-related activities and decisions included in the SAS programs. All of my statistical analyses were run off of data sets cleaned and provided to me by Tanya Karapukar.

On September 5, 2001, we finalized the vetted study analysis plan for MADDSP MMR-Autism Study. (See Final Analysis Plan dated September 5, 2001). The study protocol included a timeline and the goal

[1] Thomas Verstraeten, et al., Safety of Thimerosal-Containing Vaccines: A Two-Phased Study of Computerized Health Maintenance Organization Databases (Verstraeten, et al., Pediatrics 112:5, 2003)

112

was to finish the analyses and submit the manuscript for publication to the New England Journal of Medicine by December 1, 2000. **The final analysis plan described analyses for the TOTAL sample and the BIRTH CERTIFICATE sample which included assessment of the RACE variable. (See pages 7 and 8 of the Final Analysis Plan). There were two primary endpoints for the study. One was using a threshold of 36 months (see Table 3a of Final Analysis Plan), and the second was a threshold of 18 months. (See Table 3b of Final Analysis Plan).** We hypothesized that if we found statistically significant effects at either the 18-month or 36-month threshold, we would conclude that vaccinating children early with the MMR vaccine could lead to autism-like characteristics or features. We never claimed or intended that if we found statistically significant effects in the TOTAL SAMPLE, we would ignore the results if they could not be confirmed in the BIRTH CERTIFICATE SAMPLE.

Timeline of Events:

1. In general, all coauthors attended the meetings I scheduled to discuss analyses with the exception of other conflicting meetings when one of us could not attend. The meetings began at least as early as March 2001.

2. On August 29, 2001, I outlined the method that would be used to code RACE for the TOTAL Sample and the Birth Certificate Sample. (See scanned notes from 2001-2002).

3. On September 5, 2001, we all met and finalized the study protocol and analysis plan. The goal was to not deviate from the analysis plan to avoid the debacle that accord with the Verstraeten Thimerosal Study published in Pediatrics in 2003. At the September 5th meeting we discussed in detail how to code RACE for both the TOTAL SAMPLE and the BIRTH CERTIFICATE SAMPLE. (See Page 7 of Agendas Attachment).

4. On October 15, 2001, I ran matched and unmatched analyses for whites and blacks. I would only do this if I had found statistically significant effects by RACE. (See 2001-2002 notes dated October 15, 2001).

5. On October 24th, I wrote in my notes that we have selected the New England Journal of Medicine as the target journal for the manuscript. (See 2001-2002 notes dated October 24th, 2001).

6. On October 31, 2001, all coauthors discussed the study initial results. (See page 8 of Agendas Attachment).

7. On November 2nd, I wrote in my notebook to run analyses for whites and blacks for the early-vaccinated and late-vaccinated subjects. These analyses were run for the TOTAL sample. I would have only run those types of analyses if we had been attempting to explore why we had found significant RACE effects. (See 2001-2002 notes dated November 2, 2001)

8. On November 6, 2001, I have written notes instructing myself to run 4 group analyses and BLACK analyses. Again, I would have only been doing this if we had found concerning results for blacks. (See 2001-2002 notes dated November 6, 2001).

9. On November 8, 2001, I continued to write that the Black/White comparisons need to be continued. (See 2001-2002 notes dated November 8, 2001).

10. On February 20, 2002, all coauthors met and discussed statistical analyses for the Total Sample and the Birth Certificate Sample. (See page 14 of agendas attachment).

11. On May 22, 2002, all coauthors met and discussed analysis of the 24 month threshold for the Total Sample. We did this because there were many statistically significant effects at the 24 month threshold. (See page 16 of Agendas Attachment).

12. On June 28, 2002, all coauthors met and examined subgroup analyses by RACE for Whites and Blacks. (See page 17 in the Agendas Attachment and handout that includes Table 5).

13. In the Excel File named "describe_results_2002_0702.xls", Table 7 shows the RACE analyses that I had run using ONLY the BIRTH CERTIFICATE Sample --- the unadjusted RACE effect was statistically significant. (OR=1.51, [95%CI 1.02 - 2.24]). At the bottom of Table 7, it also shows that for the NON-BIRTH Certificate Sample, the adjusted RACE effect statistically significance was HUGE. (OR=2.94 [95%CI 1.48 - 5.81). That is the main reason why we decided to report the RACE effects for ONLY the BIRTH Certificate Sample.

004

14. In the Excel File named "describe_results_2002_0801.xls", I split Table 7 into three different Tables (Table 7a, Table 7b, and Table 7c) to further investigate the RACE subgroup analyses.

15. All the coauthors met and decided sometime between August 2002 and September 2002 not to report any RACE effects for the paper.

16. Sometime soon after the meeting where we decided to exclude reporting any RACE effects, also between August 2002 and September 2002, the coauthors scheduled a meeting to destroy documents related to the study. Dr. Coleen Boyle was not present at the meeting even though she was involved in scheduling that meeting. The remaining 4 coauthors all met and brought a big garbage can into the meeting room and reviewed and went through all our hard copy documents that we thought we should discard and put them in the large garbage can. However, because I assumed this was illegal and would violate both FOIA laws and DOJ requests, I kept hard copies of all my documents in my office and I retained all the associated computer files. This included all the Word files (agendas and manuscript drafts), Excel files with analysis and results, and SAS files that I used to generate the statistical findings. I also kept all my written notes from meetings. All the associated MMR-Autism Study computer files have

been retained on the Immunization Safety Office computer servers since the inception of the study and they continue to reside there today.

17. On or about September 3, 2002, I informed Dr. Melinda Wharton, the Division Chief for the Branch I worked in, that we had concerning results from the MMR-Autism Study that we would like to discuss with her.

18. Dr. Melinda Wharton formally reprimanded Dr. Bob Chen, my Branch Chief, on September 18, 2002. As I stated in my e-mails to both Dr. Melinda Wharton and to Dr. Walt Orenstein, I believe this was an intimidating personnel action and threatened the credibility of the entire branch. It also put a big black cloud over our branch and demoralized many of the staff.

19. On October 9, 2002, Dr. Margarette Kolczak, an extremely reputable biostatistician, reviewed my SAS programs and made a suggestion for testing the RACE Interaction. This was a post-hoc decision and an attempt to absolve us from reporting the RACE effects.

20. On October 16, 2002, I asked Dr. Walt Orenstein to remove the formal reprimand of Dr. Chen because I said there was false information included in it. (See e-mail RE Dr. Robert Chen's Reprimand).

21. On October 20, 2002, I described to Dr. Orenstein the dilemma I was in regarding the concerning MMR-Autism Study results and the reprimand of Dr. Chen. I told him I felt intimidated by the move and I linked it to them knowing the results would be problematic if they were shared outside the CDC.

22. On October 22, 2002, Dr. Boyle was assigned to brief Dr. Orenstein and Dr. Jose Cordero (the new Center Director for the National Center of Birth Defects and Developmental Disabilities).

23. Between October 22, 2002 and January 2004, there were significantly fewer hand written notes for the MMR-Autism Study because we had finalized the results and were writing the manuscript up for publication. I have many draft manuscripts that were written and are dated.

24. On January 8, 2004, I began to present draft PowerPoint presentations of the MMR-Autism Study for the Institute of Medicine meeting that I was scheduled to present on February 9, 2004 in Washington DC. I have copies of each of those PowerPoint presentations. During the next 30 days, I presented the results to the Division Director of ESD in the National Immunization Program, and the Director of the National Immunization Program. I would also present the results in the offices of Dr. Julie Gerberding.

25. On January 27, 2004, I had lunch with Dr. Marshalyn Yeargin-Allsopp. She told me that Dr. Frank DeStefano still currently reported to her.

115

26. On February 2, 2004, I met with Dr. Steve Cochi (the new Director of the National Immunization Program) and Dr. Melinda Wharton. During that meeting I provided Dr. Cochi with a draft of my letter to Dr. Julie Gerberding and sought his input. He requests that I remove any criticism of NIP in the letter.

27. During the February 2 meeting with Dr. Cochi and Dr. Wharton, I also requested that Dr. Walter Orenstein be brought into the meeting because he had arrived in the building that morning. Dr. Cochi suggested that Dr. Orenstein was "heading off into the sunset" and that we shouldn't bother him with these issues. Although Dr. Orenstien had announced his retirement in January 2004, he was still coming for meetings on a regular basis.

28. On this same day, Brooke Barry, a CDC public health analysis and someone I trusted very much, informed me that the "autism caucus" was meeting on February 3rd and that they were initiating or requesting a formal investigation of the National Immunization Program.

29. On February 2, 2004, after meeting with Dr. Cochi and Dr. Wharton, I delivered my letter for Dr. Julie Gerberding regarding my concerns regarding results from the MMR-Autism Study just before I had to present them to the Institute of Medicine on February 9, 2004. (See scanned letter to Dr. Gerberding dated February 2, 2004).

30. On March 9th, I was put on administrative leave. In the Annex to the memorandum, they provided a list of my "inappropriate and unacceptable behavior in the work place" which included "you criticized the NIP/OD for doing very poor job of representing vaccine safety issues, claimed that NIP/OD had failed to be proactive in their handling of vaccine safety issues, and you requested that Dr. Gerberding reply to your letter from a congressional representative before you made your presentation to the IOM." (See scanned Memorandum dated January 9, 2004.). I stand by that statement and I do not think it was unacceptable to convey that to Dr. Gerberding.

Conclusion

I believe we intentionally withheld controversial findings from the final draft of the DeStefano et al (2004) Pediatrics paper. We failed to follow the final approved study protocol and we ran detailed in depth RACE analyses from October 2001 through August 2002 attempting to understand why we were finding large vaccine effects for blacks. The fact that we found a strong statistically significant finding among black males does not mean that there was a true association between the MMR vaccine and autism-like features in this subpopulation. This result would have probably have led to designing additional better studies if we had been willing to report the findings in the study and manuscript at the time that we found them. The significant effect of early vaccination with the MMR vaccine might have also been a proxy for the receipt of thimerosal vaccines early in life but we didn't have the appropriate data to be able to code the level of thimerosal exposure from the MADDSP school records.

In addition to significant effects for black males, we also found significant effects for "isolated autism cases" and for the threshold of 24 months of age. If we had reported the 24 month effects, our justification for ignoring the 36 month significant effects would not have been supported. In the discussion section of the final published manuscript, we took the position that service seeking was the reason we found a statistically significant effect at 36 months. This was a post-hoc hypothesis regarding the findings after we confirmed one of our primary hypotheses. Because we knew that the threshold for 24 months was also statistically significant, reporting it would have undermined the hypothesis that service seeking was the reason we found an effect at 36 months. (See published paper).

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Frank

Age at First MMR Vaccination and Autism

Thompson William, Karapurkar Tanya, DeStefano Frank, Bolye Coleen, Doernberg Nancy, Murphy Catherine, Catherine Rice, Robert Chen, Yeargin-Allsopp Marshalyn

DRAFT

Not For Circulation

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May 22, 2002

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118

Abstract

Introduction

We conducted a matched case-control study utilizing the Centers for Disease Control and Prevention (CDC) Metropolitan Atlanta Developmental Disabilities Surveillance Program. The main objective of the study was to evaluate the association between autism and age of receipt of the MMR vaccine after controlling for background characteristics. We also examined several autism subgroups to determine if the more homogenous subgroups were more likely to be associated with the age of MMR vaccine.

Methods

The CDC's Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP) was used to identify children with autism (N=647) who met the MADDSP surveillance case definition for autism and had school records available in one of 9 school systems in the 5 county Atlanta surveillance region. Control children (N=1,891) were selected from regular education programs and were matched to case-children based on age, sex, and school of attendance at the time of abstraction. Trained abstractors collected vaccination histories for both cases and controls from the standardized State of Georgia immunization forms that all children are required to provide to attend public schools in Georgia. The primary exposure of interest was age of receipt of the first dose of the MMR vaccine. We used conditional logistic regression models stratified by matched sets to estimate the odds ratios for the association between age at MMR vaccination and autism. Potential confounding variables were evaluated individually for their impact on the MMR-autism association.

Introduction

Autism is a serious life-long developmental disorder characterized by marked impairments in social interactions, and communication skills; and repetitive, restrictive, or stereotyped behaviors. Recent studies have suggested that the prevalence of autism is higher (30–60 per 10,000 persons) (Baird et al., 2000; Bertrand et al., 2001; Yeargin-Allsopp et al., 2002) than in studies conducted 15-20 years ago (4-5 per 10,000; Fombonne, 1999). The increase in prevalence, coupled with reports of increasing numbers of children with autism being served by schools and service agencies (California Department of Developmental Services,1999) have prompted concerns about the role of environmental factors. One of the environmental factors implicated is vaccines particularly the MMR vaccine. The recommended Advisory Committee on Immunization Practices (ACIP) schedule for the MMR vaccine coincides temporally with the age of onset of autism.

Seems out of place here

The main support for the supposed association between MMR and autism comes from a report by

Wakefield and colleagues ~~have proposed that MMR vaccine may cause autism. They published a study~~ describing 12 patients with inflammatory bowel conditions and regressive developmental disorders, mostly autism (Wakefield et al, 1998). In 8 of the 12 cases, the child's parents or pediatrician suggested that MMR vaccine contributed to onset of behavioral problems. The authors hypothesized that MMR vaccine was responsible for bowel dysfunction (enterocolitis) and subsequent neurodevelopmental disorders. They ~~have~~ subsequently proposed a new syndrome consisting of certain gastrointestinal conditions, predominantly ileocolonic lymphonodular hyperplasia and mild intestinal inflammation, associated with behavioral regression (Wakefield, Anthony, et al, 2000) and reported identifying laboratory evidence of measles virus genome in the peripheral white blood cells and bowel biopsy specimens of a few such patients (Kawashimi et al, 2000; Torrente et al. 2002; Uhlmann et al., 2002). ~~Since the~~

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~~initial publication of the Wakefield report, several~~ epidemiologic studies have failed to find an association between MMR vaccination and autism (Dales et al, 2001; Farrington et al 2001; Gillberg et al, 1998; Kaye et al, 2001; Taylor et al., 1999). These studies, however, have been limited to varying degrees by incomplete case ascertainment, small sample sizes, and reliance on clinical diagnoses without standard case definitions. No studies have been published that included a concurrent comparison or control group with individual-specific vaccination histories.

We conducted a matched case-control study utilizing the Centers for Disease Control and Prevention (CDC) Metropolitan Atlanta Developmental Disabilities Surveillance Program. The main objective of the study was to compare the MMR vaccination histories of a nearly complete population-based sample of children with autism and school-matched controls who did not have autism. We also evaluated associations with MMR vaccination in subgroups of children according to different presentations within the broader category of autism spectrum disorders (ASD).

004

Methods

Study population

Children with autism were derived from the CDC's Metropolitan Atlanta Developmental Disabilities Surveillance Program (MADDSP), ~~a multiple-source~~ population based surveillance program that monitors the occurrence of selected developmental disabilities among children in the five-county metropolitan Atlanta area (Yeargin-Allsopp, M. et al., 2002). ~~MADDSP was established to ascertain all children with one or more of five developmental disabilities -- mental retardation, cerebral palsy, autism, hearing impairment, and vision impairment -- who were 3 to 10 years of age and whose parents resided in the five-county metropolitan Atlanta area.~~

121

Need to give more detail on:
1) source of cases (schools, providers, etc.)
2) Std. chart review of all available records by trained abstractors
3) Review by autism experts; 4) case defn.

Cases

In the first MADDSP autism prevalence study, they identified 987 confirmed autism cases from 1,077 children who had information available for review from the multiple-source records (Yeargin-Allsopp, M. et al., 2002). For the purpose of this study, we identified 647 confirmed autism cases that also had records available from one of the nine participating school systems used as part of the MADDSP surveillance system. The remaining case children had either moved out of state, transferred to a school in a county that is not under MADDSP's jurisdiction, transferred to a private school that is not accessible by MADDSP, or are being home schooled. We searched for school records of case children across all school systems in order to identify their school of enrollment at the time of abstraction.

Controls

We attempted to obtain a 3:1 control to case ratio for this study. For 97% of the cases, we identified 3 controls while the remaining 3 percent of cases had fewer than 3 controls. Control children (N=1,891) were selected from regular education programs and were matched to case-children based on age, sex, and school of attendance at the time of abstraction. However, if a case-child was attending a school that was structured for special education students (e.g., psycho-educational school), controls were selected from the case-child's home school. A child's home school is the school in the child's neighborhood or residential area that the child would attend if the child did not have a disability. In addition, if a case-child was older than other children in their class and was in the last elementary grade level prior to middle school due to their disability, control children were selected from the middle school they would normally attend and would be matched to the case based on the established matching criteria. The names of control

children were verified in the MADDSP and special education files to assure that they were not receiving special education services **(in 1996 or ever???)**.

Vaccination history

Trained abstractors collected vaccination histories for both cases and controls from the standardized State of Georgia immunization forms that are required for all children who attend schools in Georgia. The forms are filed in each student's permanent school record ~~file that is kept at the school where the child is enrolled~~. During the period of this study, Georgia law required at least one dose of measles, mumps, and rubella vaccine in the form of either the MMR, MR, or single antigen vaccines at entry into elementary school. ~~Effective with the 1994-95 school year, for entrance into the sixth grade of school, a child needed to have received at least one additional dose of the MMR vaccine, for a total of two MMR vaccines administered on or after the child's first birthday and at least one month apart. Data regarding vaccination exemptions~~ (medical and religious) ~~were also recorded.~~

004

Family Background Characteristics and Other Data Collection

Demographic information including child's date of birth, gender, birth state, and race/ethnicity was obtained from the birth certificate that is kept in the child's permanent record. Like the vaccination form, all children must provide the school of enrollment with the birth certificate for entry into elementary school; the presence of a birth certificate is not mandatory for those entering middle school. For the records that were abstracted at middle schools, a school registration form was used to obtain the necessary demographic information.

Subsequently, cases and controls born in Georgia were matched to state birth certificate records in order to derive more information on child and maternal characteristics. The matching criteria used were birth certificate number and child's first and last name. Of the children

identified as being born in Georgia, 57% of cases (N=359) and 56% of controls (N=1,049) were successfully matched. Variables obtained from the birth certificate included child factors of birth weight and gestational age and maternal factors of parity, age, race/ethnicity, and education.

For children with autism, additional disability related information was obtained from the MADDSP data files. This included information on the presence of other developmental disabilities, epilepsy, a major associated medical condition of autism, other co-existing medical conditions, level of cognitive functioning, as well as prenatal and perinatal conditions. In addition, we identified major congenital malformations among the case children by matching with CDC's Metropolitan Atlanta Congenital Defects Program (MACDP), a population-based surveillance program of major structural malformations that covers the same geographic area (Edmonds et al, 1981).

MMR Exposure Variable

The primary exposure of interest in the study was age of receipt of the first dose of the MMR vaccine. We examined two alternative exposure periods for age of MMR vaccination: receipt of the MMR vaccine < 18 months of age and < 24 months of age. These exposure periods were chosen because regression occurs at approximately 18 months of age and the 24-month time period is well beyond the median age of first parental concern for autistic features as well as median date for the MMR vaccine (APA, 1994; Giacomo, A. & Fombonne, E., 1998;Taylor, B., 1999). Therefore the period after 24 months would be considered an unexposed period for the causal association between the timing of receipt of the vaccine and autism.

Classification of Autism Subgroups

The IOM (2001) specifically recommended additional research regarding the potential susceptibility of certain subgroups of autism. In an effort to examine differing effects of the

MMR vaccine in various subsets of children with autism, we reviewed the records of case children to identify additional information that would help classify cases into more homogenous subgroups, particularly children with indication of delay less than one year and children with pre-existing conditions. The information that was collected included age of first parental concern, the presence of a pre-existing condition, date of concern, and verbatim description of the behaviors that led to the concern. A family history of autism and related autism spectrum conditions, and other developmental disabilities was also recorded.

Did we use this?

Indication of developmental delay at less than one year was ~~described~~ determined by whether or not the child had developed *any* speech at appropriate ages, including cooing and babbling and whether or not the child was socially responsive in the first year of life, e.g., cuddling, appropriate eye contact, responding to parents voices. ~~Furthermore, type~~ Type of developmental concern was categorized as delay, regression, or plateau.

Need to define

Statistical Analyses

Add analysis comparing the overall distributions of age at vaccination.

We used conditional logistic regression models stratified by matched sets to estimate the odds ratios for the association between age at MMR vaccination and autism. Potential confounding variables were evaluated individually for their association with the autism case definition. Those with an odds ratio p-value < 0.20 were included as covariates in a conditional logistic regression model to estimate adjusted odds ratios for the association between age at vaccination and autism. **(should we describe referent groups and confounders ???)**

We examined two subgroups of autism cases: 1) case children with any pre-existing condition that was identified before the age of 1 year by either a medical provider or the parent and 2) case children with a regression or plateau of developmental milestones described in their records (????). Pre-existing conditions included an established cause for autism, a co-occurring

? add co-existing conditions

group of interest is actually those without pre-existing conditions

125

condition suggesting an early prenatal etiology (e.g., tuberous sclerosis, fragile X, or other congenital/chromosomal anomalies), parental concern before the age of one, and developmental disability ascertained by MADDSP that were diagnosed before age 1 years.

In the results, I think we should have separate tables for the ASD cases and the sub-categories

Table X: Associations c ASD

Total sample
B.C. sample (unadjusted)
B.C. sample (adjusted)

Table Y: Associations [redacted] selected ASD categories

No delay before 1 yr.

Total sample
B.C. (adj./unadj.)

No Co-occurring conditions

Total sample
B.C. (adj./unadj.)

Regression/ plateau

Total sample
B.C. sample (adj./unadj.)