NOTE: Data with an asterisk to the right has been updated in this MSDS version.
Updated: January 20, 2005

RESEARCH MATERIAL SAFETY DATA SHEET

IL-12

Wyeth
P.O. Box 8299
Philadelphia, PA 19101
(610) 688-4400
CHEMTREC USA, CAN, PR (800) 424-9300
CHEMTREC International (202) 483-7616

Section 1. Product Identification

Chemical or Common Name: Interleukin 12
Molecular Formula: No data
Molecular Weight: No data
CAS No.: No data
Chemical Family: No data
Synonyms: IL-12, rhIL-12, Interleukin 12, Recombinant Human Interleukin Twelve, WAY-144120

Section 2. Composition – Information on Ingredients

Component	CAS No.	Percentage	R Phrase as Pure	*
IL-12	No data	1-2 mg/ml	Not determined	

Section 3. Hazards Identification

Acute Eye Contact: No data

Acute Skin Contact: No data

Acute Inhalation: No data

Chronic Health Effect: No data

Other: IL-12 affects the immune system, specifically cell-mediated immunity (CMI). IL-12 might be useful in treating diseases for which enhanced CMI could facilitate a favorable outcome, including certain cancers, viral infections, and other intercellular pathogens. *

Dosing range studied in humans is: 3-2100 ng/kg, SC; 3-1000 ng/kg, IV; 0.25-4 ug, IM; 5-200 ug, intravesical; 1 ug, inhalation. Adverse events observed across all clinical studies are: fever, asthenia, chills, headache, nausea, and myalgia. Grade 3 or 4 laboratory toxicities reported most frequently are: elevations in liver function tests, neutropenia, anemia, leucopenia, hyperglycemia.

Section 4. First Aid Measures-by medical responders using “Universal Precautions”

Eye Contact:	Remove contact lenses if present. Flush with copious amounts of water for 15 minutes. Separate eyelids with fingers while flushing. Call physician and treat symptoms.
Skin Contact:	Wash with copious amounts of water. Remove contaminated clothing. See physician if redness or irritation develops.
Inhalation:	Remove to fresh air. Call physician and treat symptoms
Ingestion:	Flush out mouth with water. Call physician and treat symptoms

Section 5. Fire Fighting Measures

Flash Point:	No data
Flammable Limits:	**LEL** - No data **UEL** - No data
Auto-Ignition Temperature:	No data
Extinguishing Media:	All media are acceptable. Choose as appropriate for surrounding fire and materials.
Special Fire Procedures:	Wear protective clothing and self-contained breathing apparatus.
Unusual Fire/Explosion:	Dry material is assumed to be combustible. Avoid accumulations and keep away from ignition sources .

Section 6. Accidental Release Measures

Small Spill:	Clean up small spills with a damp towel. Avoid creating airborne material. Place in an appropriate container for waste disposal. Wash with water and ventilate area. Wear protective clothing.
Large Spill:	HEPA vacuum larger powder spills. Avoid creating airborne material. Place in an appropriate container for waste disposal. Wash with water and ventilate area. Wear protective clothing.

Section 7. Handling and Storage

Storage/Handling Precautions:	No special storage precautions are indicated. Store at 2-8 C for product integrity.
Other Precautions:	Avoid contact and inhalation. Use with adequate ventilation and avoid generating airborne particles. Wash thoroughly after handling. Do not eat, drink, or smoke near material.

Section 8. Exposure Controls and Personal Protection

Component	**Exposure Guideline**
IL-12	No data
Ventilation/ Exposure	Enclose operations to prevent dust generation into the work

Controls:	environment. Handle material in well ventilated area. Provide local exhaust ventilation for operations with potential to generate dust until an effective enclosure is implemented. Limit access to the operations, only personnel trained on the handling of the material should be permitted in the area.
Respiratory:	Based on limited toxicity and health hazard data available for the material, it is recommended that powered air purifying respirators with N100 or P3 cartridges be used as the minimum respiratory protection. A lower level of respiratory protection can be considered if a hazard evaluation of the operation indicates it is appropriate.
Eye Protection:	Wear safety glasses with side shields.
Protective Gloves:	Wear nitrile or latex gloves.
Protective Clothing:	Use as required to prevent skin contact.
Work/Hygienic Practices:	Investigational drug - handle with caution.

Section 9. Physical and Chemical Properties

Boiling Point:	No data	
Melting Point:	No data	
Specific Gravity (H20=1):	No data	
Vapor Pressure (mm Hg):	No data	
Percent Volatile by Volume:	No data	
Vapor Density (Air=1):	No data	
Evaporation Rate:	No data	
Solubility in Water:	Soluble	
Appearance and Odor:	Lyophilized product	*
pH:	No data	
Octanol/Water Partition:	No data	

Section 10. Stability and Reactivity

Stability:	Stable in regard to safety concerns
Hazardous Polymerization:	Not expected
Conditions to Avoid:	No data
Decomposition Product:	No data

Section 11. Toxicology Information

Acute Oral, Rat:	No data	
Acute Oral, Mouse:	No data	
Acute IV, Rat:	No data	
Acute IV, Mouse:	No data	
Acute Dermal Irritation:	No data	
Primary Eye Irritation:	No data	
Ames Test:	Negative	*
Listed as Carcinogen:	**OSHA:** No	
	NTP: No	
	IARC: No	
Other Carcinogenicity/	No data	

Mutagenicity Data:

Multiple Dose Toxicity Data: (No Toxicologic Effect Dose/ Species/Study Length)

No data

Other:

A series of single- and repeat-dose nonclinical studies were conducted with rmIL-12 and rhIL-12 in nonhuman primates with IV or SC administration. Single doses of rhIL-12 were well tolerated with only minor and transient clinical laboratory changes at doses of up to 10 ug/kg in cynomolgus monkeys and 500 ng/kg in chimpanzees. Repeat-dose studies demonstrated the primary adverse effects to be mortality, adverse clinical signs, decreased food consumption, weight loss, changes in peripheral hematology, acute phase responses, elevations of liver enzymes, diffuse activation of the mononuclear phagocyte system, scattered areas of perivascular mononuclear cell proliferation in numerous anatomical sites, and sciatic nerve and/or spinal cord degeneration. All repeat-dose adverse effects, other than mortality, slight degenerative changes in the sciatic nerve and spinal cord, and mild injection site inflammation, were transient and fully reversible after 28 days of recovery. The above adverse effects in repeat-dose, nonhuman primate studies occurred at dosages of 1 ug/kg/day and higher, and 0.1 ug/kg/day resulted in minimal adverse effects.

Special toxicity studies were conducted with rmIL-12 in mice and with rhIL-12 in cynomolgus monkeys. IL-12 demonstrated unique schedule dependency, whereby a single dose of IL-12 administered 1 week prior to repeat daily doses protected against much of the rmIL-12 associated toxicity in mice, rhIL-12-associated toxicity in monkeys, and immunophenotypic changes in mice. The low-dose delayed toxicity of rmIL-12 in mice was influenced to a greater extent by frequency of dosing than by cumulative dosage. In monkeys, there were no compound-related systemic or local effects of intravesically administered rhIL-12 and toxicities after liquid aerosol nebulization rhIL-12 delivery were of a similar nature as parenterally administered rhIL-12. In mice, rmIL-12 and X-irradiation combination treatment resulted in additive hematologic toxicity and liver toxicity of rmIL-12 may be increased when bound to the vaccine adjuvant Rehydragel HPA. Preliminary results of a neurotoxicity study in monkeys administered 10 ug/kg/day rhIL12 for 28 days indicated peripheral neuropathy and degenerative central nervous system changes; peripheral nervous system changes subsided after 13 weeks of recovery, and both peripheral and central nervous system changes were reversible after 52 weeks of recovery.

The reproductive toxicity was studied in mice and monkeys. In mice, rmIL-12 resulted in maternal toxicity at $\geq$ 2 ug/kg/day and reduced fertility at 100 ug/kg/day. Embryo-fetal toxicity consisting of embryo-fetal death or delayed development occurred at 10 ug/kg/day. In a dose-ranging

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reproductive toxicity study in monkeys, rhIL-12 resulted in embryo/fetal loss and maternal toxicity at 10 ug/kg/day.

Section 12. Ecological Information

Fate Data: No data

Effects Data: No data

Section 13. Disposal Considerations

Waste Disposal: Incinerate in an approved incinerator or take to an approved disposal site. Follow all Regional and National regulations.

Section 14. Transportation Information

Transportation Information: Follow all Regional and National regulations.

Section 15. Regulatory Information and Warning Labels

Regulatory Requirements: Not determined

Section 16. Other Key Information

Other Considerations: No data

Other

Issued By: Corporate Environment, Health & Safety
Date: January 20, 2005

Reference: -Il12MsdsV1 (Formerly GI022)
-IB, Recombinant Human Interleukin-12, May 2003