# PHARMACIA & UPJOHN COMPANY

Thomas W. Avery
Kalamazoo Site Compliance

Pharmacia Corporation
7000 Portage Road
Kalamazoo, Michigan 49001
tel 269.833.3815
fax 269.833.2000
www.pharmacia.com

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## SOLU-MEDROL® TSE DECLARATION

Pharmacia & Upjohn Company declares that SOLU-MEDROL® contains the ingredients mentioned below:

| Component | Origin of Material | Country of Origin and Tissue used | CEP# |
|---|---|---|---|
| Monobasic Sodium Phosphate Anhydrous USP | Synthetic | Not Applicable | Not Applicable |
| Dibasic Sodium Phosphate Anhydrous USP | Synthetic | Not Applicable | Not Applicable |
| Methylprednisolone Hemisuccinate | Animal | See Discussion Below | R0-CEP 2000-365-Rev 00 |
| 10% Solution Sodium Hydroxide | Synthetic | Not Applicable | Not Applicable |
| Benzyl Alcohol NF | Synthetic | Not Applicable | Not Applicable |
| Lactose NF Monohydrate | Animal | See Discussion Below | Not Applicable (Not TSE Relevant) |
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All raw materials used in Solu-Medrol® manufactured at Pharmacia & Upjohn Company, 7000 Portage Road, Kalamazoo, MI 49001, USA have been investigated regarding the origin and use of animal material.

**LARD OIL**

The Pfizer suppliers of lard oil have certified that the porcine used in the manufacture of lard oil are sourced from the United States. In addition to non-ruminant source material, the suppliers have described additional measures that are being undertaken to prevent, minimize or eliminate microbial contamination.

**NUTRIENT BROTH**

Pfizer supplier of nutrient broth received a TSE Certificate of Suitability for nutrient broth from the European Directorate for the Quality of Medicines (EDQM) on 1 October 2001. The certificate number is RO-CEP-2000-248-Rev 01.

Nutrient broth contains animal sourced components of bovine and porcine origin. The bovine sourced components are obtained from the United States, Canada and Australia, and the porcine sourced components are obtained from the United States.

Detail of the animal based nutrient broth components is as follows:

**Beef Extract**

Skeletal Muscle and Hearts from bovine.

**Peptone** (Gelatin hydrolyzate with porcine Pancreas and bovine bile)

Gelatin (alkaline treated): Sourced from bovine bone which is free from skulls, and spinal cords, connective tissues , and skin.

Pancreas: Porcine pancreas tissue

Bile: bovine bile

The supplier of nutrient broth has described additional measures that are being taken to minimize the risk for transmission of TSE. They are as follows: 1) When tissues are removed, material of a low risk group does not come in contact with material from a high risk group. 2)Body fluids are collected with minimal damage to tissues. 3) Tissues are removed at USDA, AG Canada, or AQUIS regulated slaughter houses. 4) The animals are declared fit for human consumption. 5) Specific processing steps are undertaken to prevent, minimize or eliminate microbial contamination.

**EDAMIN®**

The Pfizer supplier of Edamin® (lactalbumin hydrolyzate) has certified that the animal sourced components are of porcine and bovine origin. The porcine enzyme used in the manufacture of Edamin® is sourced from the United States and Canada. The milk extract lactalbumin for the manufacture of Edamin® are sourced from healthy bovine animals in Australia and New Zealand. Additionally, a milk derived lactose carrier for the production of the dried enzymes is obtained from the United States. In addition to non-ruminant source material and low risk bovine milk, The supplier has indicated that specific processing steps are undertaken to prevent, minimize or eliminate microbial contamination.

## CATALASE

The Pfizer supplier of catalase received a Certificate of Suitability for Catalase from the European Directorate for the Quality of Medicines (EDQM) on 11 June 2001. The Certificate number is R1-CEP 2001-168-Rev 00.

Catalase contains an animal based component of bovine origin. The component is bovine liver and it is sourced from the United States. When tissues are removed, material of a low risk group does not come in contact with material from a high risk group. The animals are declared fit for human consumption.

## SOY FLOUR HYDROLYZATE

Soy flour Hydrolyzate contains animal based components of porcine origin. The supplier of soy flour hydrolyzate has certified that the porcine raw material used in the manufactured of soy flour hydrolyzate are sourced from Canada and the United States. The supplier has described additional measures that are being taken to minimize the risk for transmission of TSE, as follows: Specific high temperature processing steps are undertaken to prevent, minimize or eliminate microbial contamination. All processes are traceable and take place in an FDA regulated food plant.

## POLYSORBATE 80

Polysorbate 80 was changed to vegetable source in April 2002. The previous Pfizer supplier of animal sourced Polysorbate 80 has obtained a TSE Certificate of Suitability from EDQM for the Oleic Acid animal component. The certificate number is RO-CEP 2001-079-Rev 01.

The bovine and porcine based tallow used in the manufacture of Polysorbate 80 was sourced from animals that were raised in the United States and Canada. However, the manufacture has indicated that the tallow is processed with temperatures in excess of 240 deg. At corresponding pressure for at least 30 minutes. According to current European guidelines, this is considered to be a rigorous process that renders the tallow as a no risk material.

In addition to the use of only low to minimal risk animal-derived materials in the synthesis of Methylprednisolone Acetate, Pfizer also uses only non-animal source cleaning agents for manufacturing equipment. Pfizer also has procedures and systems in place for the potential event of undesired material entering the plant, for the assurance of traceability for raw materials, intermediates, and final API's, for the auditing of raw material suppliers, and for internal auditing with regard to TSE risk.

Hence, the materials used in the production of Methylprednisolone Acetate have demonstrated compliance with the note for guidance on minimizing the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (EMEA/410/01 Rev. 2) in line with the legal requirement as inscribed in Annex I to Directives 2001/82/EC (veterinary medicines) or Directive 2001/83/EC as amended by Directive 2003/63/EC (medicines for human use).

**LACTOSE NF MONOHYDRATE**

The animal component of Lactose NF Monohydrate is bovine milk. The bovine milk used in the production of Lactose NF Monohydrate is sourced from healthy animals under the same conditions as milk collected for human consumption. Bovine used in the production of lactose originate in the United States of America. No other ruminant materials are used during this process. Enzyme products used are microbially produced and are not derived from animal sources (i.e. calf rennet is not used).

According to information obtained from the suppliers, the remaining materials used in the production of Solu-Medrol® are not of animal origin.

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Thomas W. Avery, Senior Specialist
Regulatory CMC, Kalamazoo Michigan, USA