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RESEARCH DEPARTMENT

Chemical Hygiene Fellowship
MELLON INSTITUTE
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Calidria Asbestos-Resin Grade RG 244

Tracheal Insufflation of Rat Lungs with Interpretation of Pathology after 30, 60, 90 and 180 Days

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For: UNION CARBIDE CORPORATION, Chemicals and Plastics Operations Division

Sample

A 500-gram sample of Resin Grade RG 244 UCC Calidria Asbestos was received 11-30-70, from King City, California, pursuant to arrangements made by Paul McDaniel of the New York Office. The sample was identified by the Chemical Hygiene Fellowship #33-251.

Tracheal Insufflation

A 1% (W/V) suspension of the RG 244 sample was prepared in 0.85% saline. All needles, syringes and suspensions were sterilized prior to use. Either 1 ml or 0.5 ml amounts of the sterile 1% suspension were injected into the rat lung through the trachea, exposed by blunt dissection, after a midline cervical incision. Following injection of these 200 to 300 gram, male albino, Harlan Wistar rats the incisions were closed with Michael wound clamps until healing ensued.

A total of 13 rats were dosed with 1 ml and 15 with 0.5 ml of the 1% suspension while 11 control rats received 1 ml of sterile 0.85% NaCl. Three rats from each asbestos dosed group and 2 controls were killed for histopathologic examination of the lung after intervals of 30, 60 and 90 days which left groups of 4, 6 and 5 rats on the 1 ml, 0.5 ml asbestos and control for the 180 day sacrifice.

Summary of Microscopic Pathology Found 30, 60, 90 and 180 Days Following Tracheal Insufflation of Rats

The 30-day pathology was marked by the presence of granulation tissue with thickening of the structural elements of the lung (stroma) and the accumulation of giant cells often associated with foreign bodies.

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After 60 days one rat on the 0.5 ml dosage level had inflammation and ingrowth of connective tissue which blocked a terminal bronchus. Two of 3 rats on both the 1.0 and 0.5 ml dosage level had atelectasis (collapse) of one or more lobes of the lung. Fibrotic foreign body nodules were present in all cases.

After 90 days there was chronic foreign body pneumonia in 2 of 3 rats at both dosage levels, fibrotic foreign nodules in 3 of 3 and emphysema in 2 of 3. Chronic inflammatory cell foci and atelectasis were present. Bronchioles were dilated in 2 of 3 rats on both dosage levels and all but one on both dosage levels had some lung hemorrhage.

The final 180 day sacrifice revealed interstitial pneumonia in 4 rats on the 0.5 ml dose. This is a chronic form of pneumonia of interstitial tissue with decrease of the normal lung tissue. Atelectasis was present in the 4 rats on 1 ml and on 1 rat on the 0.5 ml dose of asbestos with the 5 controls normal. Fibrotic foreign body tissue was present in all dosed lungs with none in the controls. Pink hyalin material was found in 2 of 4 lungs from rats on the 1 ml dose while in 3 of 4 there was a bluish homogeneous material evident.

In essence, a total of 10 of 13 rats on the 1 ml dose and 12 of 15 on the 0.5 ml dose had fibrotic foreign body nodules or tissue. There were 3 cases of emphysema on the high dose and 4 on the low dose and 1 in the control. Atelectasis (essentially collapse of lung alveoli) was present in 9 rats on 1 ml and 6 on 0.5 ml of asbestos with none reported in the controls. In general, because of the overwhelming preponderance of effect in the asbestos dosed lungs versus the controls, we have sufficient evidence of damage to warn us to do our best to prevent inhalation of concentrations of asbestos in excess of the Threshold Limit Value proposed for 1970, (Threshold Limit Values of Airborne Contaminants and Intended Changes. Adopted by ACGIH for 1970. American Conference of Governmental Hygienists, 1014 Broadway, Cincinnati, Ohio 45202).

Summary Tables for each of the four sacrifices are included. Detailed pathology reports on each animal are available and copies can be furnished if the need for them arises. A literature review prepared in connection with another request for information is attached although not requested.

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Acknowledgments:

Inhalation Studies

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Table 34-19

Tracheal Insufflation to Rats Sacrificed 30 Days After Dosing

		Ml of 1% Solution		
		1	0.5	0.0
TOTAL NUMBER EXAMINED GROSSLY:		3	3	2
LUNG: Number Examined	(M)	3	3	2
Pneumonia	(G)	3	3	0
Hemorrhage	(G)	1	0	0
Pleural adhesions	(G)	1	2	0
Stromal thickening	(M)	3	2	0
Foam cell accumulations	(M)	3	2	0
Granulation tissue foci	(M)	3	3	0
Multinucleated giant cells	(M)	3	2	0
Abscess bronchopneumonia	(M)	0	1	0
Round cell accumulations	(M)	0	0	1
TRACHEA: Number Examined	(M)	3	3	2
Chronic tracheitis	(M)	0	0	1

The following tissues were examined microscopically on all animals: Lung, Liver, Kidney, Heart, Spleen, Adrenal, Thyroid, Parathyroid, Trachea and Esophagus. G = Gross M = Microscopic

Table 34-20

Tracheal Insufflation to Rats Sacrificed 60 Days After Dosing

		Ml of 1% Solution		
		1	0.5	0.0
TOTAL NUMBER EXAMINED GROSSLY:		3	3	2
LUNG: Number Examined	(M)	3	3	2
Hemorrhage	(G)	0	0	1
Pneumonia	(G)	3	3	0
Atelectasis	(G)	0	2	0
Edema	(G)	1	2	0
Hemorrhage	(M)	1	0	0
Atelectasis	(M)	2	2	0
Fibrotic foreign body nodules	(M)	3	3	0
Bronchiolitis fibrosa obliterans	(M)	0	1	0
KIDNEY: Number Examined	(M)	3	3	2
Round cell accumulations	(M)	1	0	0
HEART: Number Examined	(M)	3	3	2
Focal myocarditis	(M)	0	1	0
MUSCLE: Number Examined	(M)	1	0	0
Purulent mass	(G)	1	0	0
Large suppurative process, striated muscle	(M)	1	-	-

The following tissues were examined microscopically on all animals: Lung, Liver, Kidney, Heart, Spleen, Adrenal, Thyroid, Parathyroid, Trachea and Esophagus. G = Gross M = Microscopic

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Table 34-21

Tracheal Insufflation to Rats Sacrificed 90 Days After Dosing

		Ml of 1% Solution		
		1	0.5	0.0
TOTAL NUMBER EXAMINED GROSSLY:		3	3	2
LUNG: Number Examined	(M)	3	3	2
Pleural adhesions	(G)	0	2	0
Hemorrhage	(G)	0	2	0
Edema	(G)	3	3	0
Pneumonia	(G)	3	3	0
Chronic foreign body pneumonia	(M)	2	2	0
Fibrotic foreign body nodules	(M)	3	3	0
Emphysema	(M)	2	2	0
Chronic inflammatory cell foci	(M)	3	3	0
Round cell foci	(M)	0	1	1
Atelectasis	(M)	3	3	0
Bronchiectasis	(M)	2	2	0
Stromal thickening	(M)	1	0	0
Hemorrhage	(M)	3	2	0
Inhaled blood	(M)	0	1	0
KIDNEY: Number Examined	(M)	3	3	3
Hydronephrosis	(G)	0	0	1
Hydronephrosis	(M)	0	0	1
Round cell focus	(M)	0	1	0
TRACHEA: Number Examined	(M)	3	3	3
Chronic tracheitis	(M)	2	1	2
HEART: Number Examined	(M)	3	3	3
Myxoid change, interstitium	(M)	0	1	0

The following tissues were examined microscopically on all animals: Lung, Liver, Kidney, Heart, Spleen, Adrenal, Thyroid, Parathyroid, Trachea and Esophagus. G = Gross M = Microscopic

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Table 34-22

Tracheal Insufflation to Rats Sacrificed 180 Days After Dosing

		Ml of 1% Solution		
		1	0.5	0.0
TOTAL NUMBER EXAMINED GROSSLY:		4	6	5
LUNG: Number Examined	(M)	4	6	5
Edema	(G)	2	0	1
Pneumonia	(G)	4	5	1
Atelectasis	(G)	2	0	1
Emphysema	(G)	0	0	1
Emphysema	(M)	1	2	1
Atelectasis	(M)	4	1	0
Inhalation pneumonia	(M)	1	0	0
Interstitial pneumonia	(M)	0	4	0
Abscess bronchopneumonia	(M)	0	0	1
Suppurative bronchiectasis	(M)	1	0	0
Acute bronchitis	(M)	0	0	1
Lymphoid cell accumulations	(M)	3	0	0
Foam cell accumulations	(M)	2	1	3
Fibrotic foreign body tissue	(M)	4	6	0
Granulation tissue foci	(M)	0	1	0
Pink hyalin material	(M)	2	0	0
Bluish homogeneous material	(M)	3	1	0
Numerous mononuclear cells	(M)	1	0	0
Mucoid infiltration	(M)	2	0	0
Proliferation bronchiole epithelium	(M)	0	0	1
LIVER: Number Examined	(M)	4	6	5
Bile duct proliferation	(M)	0	2	1
Round cell foci	(M)	1	0	0
KIDNEY: Number Examined	(M)	4	6	5
Hydronephrosis	(G)	0	1	0
Sand calculi	(G)	0	1	0
Hydronephrosis	(M)	0	1	0
Sand calculi	(M)	0	1	0
Dilated tubules	(M)	0	2	2
Pink casts	(M)	0	2	1
Interstitial nephritis	(M)	0	1	0
Cellular infiltration	(M)	0	1	0
Slight tubular regeneration	(M)	0	1	3
Moderate tubular regeneration	(M)	0	0	1
TRACHEA: Number Examined	(M)	4	6	5
Acute tracheitis	(M)	1	0	0
Chronic tracheitis	(M)	0	4	0

The following tissues were examined microscopically on all animals: Lung, Liver, Kidneys, Heart, Spleen, Adrenal, Thyroid, Parathyroid, Trachea and Esophagus. G = Gross M = Microscopic

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