Annex II Non-Confidential Annex of CLH report of SAS

Summary tables from the study report of Fraunhofer 2019 with histopathological findings induced by SAS 1 and 2 in the lymph nodes.

Table 1: After 3 months inhalation (K0)

Group	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**	
Dose	**Air**		**SAS 1 0.5 mg/m³**		**SAS 1 1.0 mg/m³**		**SAS 1 2.5 mg/m³**		**SAS 1 5.0 mg/m³**		**SAS 2 0.5 mg/m³**		**SAS 2 1.0 mg/m³**		**SAS 2 2.5 mg/m³**		**SAS 2 5.0 mg/m³**	
After 3 months inhalation (K0)																		
No. of mediastinal lymph nodes/sex affected / mean severity	**(7) M**	**(2) F**	**(6) M**	**(7) F**	**(6) M**	**(4) F**	**(6) M**	**(8) F**	**(10) M**	**(8) F**	**(9) M**	**(9) F**	**(10) M**	**(10) F**	**(10) M**	**(10) F**	**(9) M**	**(8) F**
Granulomas	0	0	0	0	2/2.0	2/1.0	5/2.0	6/1.3	0	4/2.3	9/2.7	7/2.4	10/3.8	9/3.8	10/4.0	10/3.9	1/2.0	5/3.4
Granulomatous inflammation	0	0	0	0	0	0	0	0	0	0	2/1.5	4/2.5	8/1.1	9/2.2	9/1.9	10/2.0	1/2.0	5/2.0
Lymphoid hyperplasia	0	0	0	0	2/2.0	1/2.0	4/2.0	3/2.0	0	0	8/1.8	6/1.5	10/2.0	9/2.2	10/2.2	10/2.2	0	4/2.0
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	0	2/1.0	9/1.0	5/1.0	8/1.0	6/1.0	0	3/1.0
Masson T: Fibrosis	0	0	0	0	0	0	0	0	0	0	0	1/1.0	0	1/1.0	3/1.3	6/1.2	0	2/1.0
No. of tracheobronchial lymph nodes/sex affected / mean severity	**(10) M**	**(9) F**	**(10) M**	**(6) F**	**(8) M**	**(8) F**	**(7) M**	**(8) F**	**(10) M**	**(9) F**	**(10) M**	**(9) F**	**(9) M**	**(7) F**	**(10) M**	**(6) F**	**(10) M**	**(9) F**
Granulomas	0	0	0	0	2/1.5	3/1.7	4/2.0	6/1.8	10/2.5	9/2.7	4/3.0	6/2.5	2/2.0	5/2.2	3/3.0	4/2.8	10/3.8	9/3.6
Granulomatous inflammation	0	0	0	0	0	0	4/2.0	0	1/1.0	0	6/1.8	2/2.0	4/2.3	2/2.5	6/3.0	3/2.0	7/1.9	8/2.0
Lymphoid hyperplasia	0	0	1/2.0	1/1.0	0	1/2.0	2/1.5	2/1.5	1/2.0	3/1.0	5/2.0	0	2/2.0	1/1.0	5/2.0	0	10/1.8	6/2.2
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	1/1.0	2/1.0	0	3/1.0	2/1.0	2/1.0	2/1.0	1/1.0
Masson T.: Fibrosis	0	0	0	0	0	0	0	0	0	0	0	0	2/1.0	1/2.0	6/1.0	0	9/1.3	8/1.3

Table 2: After 3 months recovery (R1)

Group	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**	
Dose	**Air**		**SAS 1 0.5 mg/m³**		**SAS 1 1.0 mg/m³**		**SAS 1 2.5 mg/m³**		**SAS 1 5.0 mg/m³**		**SAS 2 0.5 mg/m³**		**SAS 2 1.0 mg/m³**		**SAS 2 2.5 mg/m³**		**SAS 2 5.0 mg/m³**	
After 3 months recovery (R1)																		
No. of mediastinal lymph nodes/sex affected / mean severity	**(2) M**	**(1) F**	**(3) M**	**(3) F**	**(1) M**	**(3) F**	**(4) M**	**(3) F**	**(4) M**	**(4) F**	**(2) M**	**(1) F**	**(3) M**	**(0) F**	**(0) M**	**(3) F**	**(3) M**	**(2) F**
Granulomas	0	0	0	0	0	0	2/2.0	1/2.0	2/2.5	0	1/3.0	1/2.0	1/3.0	-	-	2/3.0	1/4.0	2/3.0
Granulomatous inflammation	0	0	0	0	0	0	0	0	0	0	1/2.0	1/3.0	1/2.0	-	-	2/3.0	1/3.0	2/4.0
Lymphoid hyperplasia	0	0	0	0	0	0	0	1/1.0	1/1.0	0	1/2.0	1 /2.0	0	-	-	0	1/3.0	2/2.0
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	0	¨0	1/1.0	-	-	0	0	0
Masson T: Fibrosis	0	0	0	0	0	0	0	0	0	0	1/2.0	1 /2.0	0	-	-	2/1.5	1/1.0	2/1.5
No. of tracheobronchial lymph nodes/sex affected / mean severity	**(5) M**	**(4) F**	**(4) M**	**(3) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(4) F**	**(5) M**	**(5) F**
Granulomas	0	0	0	0	2/1.0	0	5/1.8	3/2.0	4/2.3	5/2.2	3/3.0	5/2.8	5/3.2	5/3.0	4/3.0	4/3.0	5/3.6	3/2.7
Granulomatous inflammation	0	0	0	0	0	0	0	0	1/1.0	2/2.0	3/2.3	5/3.0	5/3.0	5/3.2	5/3.2	4/3.8	5/3.2	5/3.8
Lymphoid hyperplasia	0	0	0	0	0	0	1/1.0	0	2/1.0	1/2.0	1/2.0	5/2.0	4/2.0	4/2.0	3/2.0	4/2.0	5/2.0	5/2.2
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	1/1.0	0	0	1/1.0	1/1.0	5/1.0	2/1.0	2/1.0	0	0	0
Masson T.: Fibrosis	0	0	0	0	0	0	0	0	0	0	2/1.0	5/1.4	2/1.0	3/2.0	2/1.0	4/2.0	3/1.7	5/1.6

Table 3: After 6 months recovery (R2)

Group	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**	
Dose	**Air**		**SAS 1 0.5 mg/m³**		**SAS 1 1.0 mg/m³**		**SAS 1 2.5 mg/m³**		**SAS 1 5.0 mg/m³**		**SAS 2 0.5 mg/m³**		**SAS 2 1.0 mg/m³**		**SAS 2 2.5 mg/m³**		**SAS 2 5.0 mg/m³**	
After 6 months recovery (R2)																		
No. of mediastinal lymph nodes/sex affected / mean severity	**(3) M**	**(3) F**	**(3) M**	**(3) F**	**(5) M**	**(5) F**	**(4) M**	**(3) F**	**(5) M**	**(3) F**	**(3) M**	**(3) F**	**(4) M**	**(4) F**	**(5) M**	**(3) F**	**(4) M**	**(3) F**
Granulomas	0	0	0	0	0	0	0	1/1.0	3/1.3	1/2.0	2/2.5	0	3/2.3	3/3.0	4/3.0	3/3.3	2/2.5	2/2.5
Granulomatous inflammation	0	0	0	0	0	0	0	0	0	0	2/2.5	1/1.0	3/3.0	3/3.0	4/2.5	3/3.3	2/3.0	2/3.5
Lymphoid hyperplasia	0	0	0	0	0	0	2/1.0	0	2/1.0	0	2/2.0	0	3/1.7	3/1.7	4/2.8	3/2.0	2/2.5	2/1.5
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	2/1.0	0	2/1.0	3/1.3	3/1.3	2/1.0	1/1.0	0
Masson T: Fibrosis	0	0	0	0	0	0	0	0	0	0	1/2.0	0	2/2.0	3/1.3	1/1.0	2/1.0	2/1.5	2/2.0
No. of tracheobronchial lymph nodes/sex affected / mean severity	**(5) M**	**(5) F**	**(5) M**	**(4) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(4) M**	**(5) F**	**(4) M**	**(5) F**	**(5) M**	**(4) F**
Granulomas	0	0	0	0	0	0	5/1.0	3/1.3	4/1.8	2/2.0	5/2.2	4/2.5	4/1.8	4/2.8	3/2.0	3/3.0	5/2.8	3/2.7
Granulomatous inflammation	0	0	0	0	0	0	0	0	1/1.0	2/1.0	5/2.0	4/2.5	4/2.5	5/3.0	3/3.0	4/3.5	5/2.8	4/3.3
Lymphoid hyperplasia	1/1.0	0	0	0	0	0	0	0	0	1/1.0	3/2.0	3/2.0	3/1.7	4/2.0	3/2.0	3/2.0	5/2.4	3/1.7
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	3/1.0	1/1.0	4/1.5	3/1.3	2/1.0	2/1.0	1/1.0	3/1.3
Masson T.: Fibrosis	0	0	0	0	0	0	0	0	0	0	3/1.0	2/1.5	4/1.5	3/1.3	3/1.0	4/1.5	4/1.8	3/2.0

Table 4: After 12 months recovery (R3)

Group	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**	
Dose	**Air**		**SAS 1 0.5 mg/m³**		**SAS 1 1.0 mg/m³**		**SAS 1 2.5 mg/m³**		**SAS 1 5.0 mg/m³**		**SAS 2 0.5 mg/m³**		**SAS 2 1.0 mg/m³**		**SAS 2 2.5 mg/m³**		**SAS 2 5.0 mg/m³**	
After 12 months recovery (R3)																		
No. of mediastinal lymph nodes/sex affected / mean severity	**(5) M**	**(2) F**	**(4) M**	**(5) F**	**(3) M**	**(4) F**	**(1) M**	**(4) F**	**(4) M**	**(3) F**	**(4) M**	**(2) F**	**(3) M**	**(3) F**	**(5) M**	**(5) F**	**(4) M**	**(2) F**
Granulomas	0	0	0	0	0	0	0	0	0	0	1/2.0	1/4.0	1/3.0	2/2.5	3/2.0	3/2.3	3/2.7	1/3.0
Granulomatous inflammation	0	0	0	0	0	0	0	0	0	0	2/2.0	1/2.0	1/3.0	1/3.0	0	1/3.0	1/2.0	2/2.5
Lymphoid hyperplasia	0	0	0	0	1/1.0	0	0	0	0	0	0	0	0	0	1/1.0	2/2.0	3/2.0	1/2.0
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2/1.5	0	0
Masson T: Fibrosis	0	0	0	0	0	0	0	0	0	0	1/1.0	1/2.0	0	2/2.0	0	1/2.0	2/1.5	2/2.0
No. of tracheobronchial lymph nodes/sex affected / mean severity	**(5) M**	**(5) F**	**(4) M**	**(5) F**	**(4) M**	**(4) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**	**(5) M**	**(4) F**	**(5) M**	**(5) F**	**(5) M**	**(5) F**
Granulomas	0	0	0	0	0	0	1/1.0	1/1.0	1/1.0	0	3/2.0	2/2.0	2/3.0	1/3.0	4/2.3	3/2.3	4/2.5	4/3.0
Granulomatous inflammation	0	0	0	0	0	0	0	0	0	0	1/2.0	1/1.0	2/2.0	2/2.0	1/2.0	1/2.0	0	3/2.3
Lymphoid hyperplasia	2/1.5	0	0	0	1/1.0	0	1/2.0	0	1/2.0	0	1/1.0	2/1.5	1/2.0	0	4/2.0	0	3/1.7	0
Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	0	1/1.0	0	1/2.0	0	1/1.0	0	0
Masson T.: Fibrosis	0	0	0	0	0	0	0	0	0	0	1/1.0	2/1.5	2/1.0	1/1.0	1/1.0	2/2.0	4/1.3	4/2.0