Appendix 1: Check list of industries with industry specific questionnaire

Industry	
Mining	☐ Yes ☐ No
Oil and Gas	☐ Yes ☐ No
Construction	☐ Yes ☐ No
Pulp and paper industry	☐ Yes ☐ No
Chemical industry	☐ Yes ☐ No
Ceramics, stone, clay, glass or concrete	☐ Yes ☐ No
Metal industry	☐ Yes ☐ No
Manufacturing of heating equipment	☐ Yes ☐ No
Manufacturing of industrial machinery	☐ Yes ☐ No
Manufacturing of computer equipment	☐ Yes ☐ No
Manufacturing of semi-conductors and related devices	☐ Yes ☐ No
Manufacturing of electrical equipment	☐ Yes ☐ No
Repairing of electrical equipment	☐ Yes ☐ No
Manufacturing of automotive electrical equipment	☐ Yes ☐ No
Repairing/rebuilding of automotive electrical equipment	☐ Yes ☐ No
Manufacturing/rebuilding of non-electrical vehicle parts	☐ Yes ☐ No
Manufacturing/rebuilding of truck trailers	☐ Yes ☐ No
Ship building	☐ Yes ☐ No
Ship repair	☐ Yes ☐ No
Manufacturing of parts/components for guided missiles or space vehicles	☐ Yes ☐ No
Manufacturing of dental equipment/supplies	☐ Yes ☐ No
Manufacturing of jewelry/precious metal goods	☐ Yes ☐ No
Repairing of jewelry/precious metal goods	☐ Yes ☐ No
Metal working	☐ Yes ☐ No
Manufacturing of nuclear weapons	☐ Yes ☐ No
Recycling	☐ Yes ☐ No
Manufacturing fluorescent lamps	☐ Yes ☐ No
Armed forces	☐ Yes ☐ No
Lumber/wood products	☐ Yes ☐ No
Farming or other agricultural work	☐ Yes ☐ No
Firefighting	☐ Yes ☐ No
Slaughterhouse or meat-packing	☐ Yes ☐ No
Animal handler/veterinarian	☐ Yes ☐ No
Health care sector	☐ Yes ☐ No

Appendix 2: Sample size needed to detect a gene-environment interaction

The number of cases needed to detect a gene environment interaction is determined by the anticipated size of the associated odds ratio. Using all information available from published studies on the relation of Glu^{69} to sarcoidosis, and the risks of CBD in the presence of beryllium and the variant form, the estimate obtained for the odds ratio of interaction is 6.74. Given a real uncertainty about the weight that can be put on this estimate we calculated sample size using estimates for the gene environment interaction that span this value (3, 6 and 9). A study of 617 cases and 1234 referents would be able to detect a gene-environment interaction odds ratio of 3, given 5% of referents "exposed" to beryllium. In the 1:2 designs, the interaction odds ratio of 6 is detected with 660 cases even if only 1.5% of referents "exposed" to beryllium (not shown in the table).

Number of sets for gene-environment interaction for beryllium

Prevalence of beryllium exposure in general population	**Odds ratio of sarcoidosis among exposed population with susceptible genotype**	**Number of cases to achieve power 80%**	
		1 control/case	2 controls/case
0.01	3	**4235**	**2837**
0.03	3	**1460**	**986**
0.05	**3**	**906**	**617**
0.10	**3**	**495**	**343**
0.01	6	**1545**	**976**
0.03	6	**536**	**344**
0.05	6	**335**	**218**
0.10	6	**187**	**126**
0.01	9	**1032**	**633**
0.03	9	**360**	**225**
0.05	9	**226**	**144**
0.10	9	**128**	**86**

* Following assumption were made in the sample size calculations: level of significance = 5%; prevalence of sarcoidosis in Canada =30 per 100,000; frequency of *HLA-DPB1* Glu^{69} allele (susceptible genotype) in the general population = 30%; odds ratio of sarcoidosis among unexposed population with susceptible genotype =1.00; odds ratio sarcoidosis among exposed population with wild type genotype =1.10, implying marginal odds ratio of exposure of ~2.0 when the interaction odds ratio=3; unmatched analysis by logistic regression.

Appendix 3: Referent diagnoses (ICD code) and final group

ICD 9 codes	N	Group
Acute bronchitis and bronchiolitis, 466	8	Other
Bronchitis, not specified as acute or chronic, 490	44	COPD
Chronic bronchitis, 491	95	COPD
Emphysema, 492	123	COPD
Asthma, 493	838	Asthma
Bronchiectasis, 494	32	Other
Chronic airway obstruction, not elsewhere classified, 496	97	COPD
Asbestosis, 501	4	Other
Pneumoconiosis due to other silica or silicates, 502	1	Other
Pneumonitis due to solids and liquids, 507	1	Other
Empyema, 510	10	Other
Pleurisy, 511	62	Other
Pneumothorax, 512	8	Other
Abscess of lung and mediastinum, 513	2	Other
Pulmonary congestion and hypostasis, 514	1	Other
Post-inflammatory pulmonary fibrosis, 515	30	Other
Other alveolar and parietoalveolar pneumonopathy, 516	34	Other
Lung involvement in conditions classified elsewhere, 517	7	Other
Other disease of lung, 518	57	Other
Total	1454	

Appendix 4:

Diagnoses by years employed by Glu 69: industry with 50+ employed (Men)

	Years Exposed	Glu 69	Sarcoidosis		Asthma		COPD		Other		Total		$p(x^2)$
			N	%	N	%	N	%	N	%	N	%	
Oil and Gas													
	None	-	165	35.3	154	32.9	81	17.3	68	14.5	468	100.0	0.37
		+	112	35.3	118	37.2	53	16.7	34	10.7	3.7	100.0	
		Total	**277**	**35.3**	**272**	**34.6**	**134**	**17.1**	**102**	**13.0**	**785**	**100.0**	
	<10	-	40	38.5	41	39.4	15	14.4	8	7.7	104	100.0	0.45
		+	22	29.7	29	39.2	13	17.6	10	13.5	74	100.0	
		Total	**62**	**34.8**	**70**	**39.3**	**28**	**15.7**	**18**	**10.1**	**178**	**100.0**	
	≥10	-	24	35.3	19	27.9	10	14.7	15	22.1	68	100.0	0.37
		+	15	38.5	13	33.3	6	15.4	5	12.8	39	100.0	
		Total	**39**	**36.4**	**32**	**29.9**	**16**	**15.0**	**20**	**18.7**	**107**	**100.0**	
Construction													
	None	-	150	36.3	147	35.6	59	14.3	57	13.8	413	100.0	0.80
		+	100	36.0	108	38.8	36	12.9	34	12.2	278	100.0	
		Total	**250**	**36.2**	**255**	**36.9**	**95**	**13.7**	**91**	**13.2**	**691**	**100.0**	
	<10	-	59	36.0	50	30.5	31	18.9	24	14.6	164	100.0	0.20
		+	33	31.4	40	38.1	24	22.9	8	7.6	105	100.0	
		Total	**92**	**34.2**	**90**	**33.5**	**55**	**20.4**	**32**	**11.9**	**269**	**100.0**	
	≥10	-	20	31.7	17	27.0	16	25.4	10	15.9	63	100.0	0.99
		+	16	34.0	12	25.5	12	25.5	7	14.9	47	100.0	
		Total	**36**	**32.7**	**29**	**26.4**	**28**	**25.5**	**17**	**15.5**	**110**	**100.0**	
Chemical Industry													
	None	-	216	35.9	206	34.2	97	16.1	83	13.8	602	100.0	0.59
		+	138	35.0	145	36.8	67	17.0	44	11.2	394	100.0	
		Total	**354**	**35.5**	**351**	**35.2**	**164**	**16.5**	**127**	**12.8**	**996**	**100.0**	
	<10	-	11	36.7	8	26.7	5	16.7	6	20.0	30	100.0	0.45
		+	8	26.7	14	46.7	4	13.3	4	13.3	30	100.0	
		Total	**19**	**31.7**	**22**	**36.7**	**9**	**15.0**	**10**	**16.7**	**60**	**100.0**	
	≥10	-	2	25.0	0	0.0	4	50.0	2	25.0	8	100.0	0.38
		+	3	50.0	1	16.7	1	16.7	1	16.7	6	100.0	
		Total	**5**	**35.7**	**1**	**7.1**	**5**	**35.7**	**3**	**21.4**	**14**	**100.0**	

	Years Exposed	Glu 69	Sarcoidosis		Asthma		COPD		Other		Total		$p(x^2)$
			N	%	N	%	N	%	N	%	N	%	
Metal Industry													
	None	-	224	36.5	206	33.6	99	16.1	85	13.8	614	100.0	0.64
		+	140	34.7	148	36.6	68	16.8	48	11.9	404	100.0	
		Total	**364**	**35.8**	**354**	**34.8**	**167**	**16.4**	**133**	**13.1**	**1018**	**100.0**	
	<10	-	3	17.6	7	41.2	4	23.5	3	17.6	17	100.0	0.20
		+	5	29.4	10	58.8	2	11.8	0	0.0	17	100.0	
		Total	**8**	**23.5**	**17**	**50.0**	**6**	**17.6**	**3**	**8.8**	**34**	**100.0**	
	≥10	-	2	22.2	1	11.1	3	33.3	3	33.3	8	100.0	0.53
		+	4	44.4	2	22.2	2	22.2	1	11.1	8	100.0	
		Total	**6**	**33.3**	**3**	**16.7**	**5**	**27.8**	**4**	**22.2**	**18**	**100.0**	
Armed Forces													
	None	-	219	36.0	206	33.8	97	15.9	87	14.3	609	100.0	0.36
		+	142	35.0	156	38.4	62	15.3	46	11.3	406	100.0	
		Total	**361**	**35.6**	**362**	**35.7**	**159**	**15.7**	**133**	**13.1**	**1015**	**100.0**	
	<10	-	6	28.6	5	23.8	6	28.6	4	19.0	21	100.0	0.77
		+	7	29.2	4	16.7	10	41.7	3	12.5	24	100.0	
		Total	**13**	**28.9**	**9**	**20.0**	**16**	**35.6**	**7**	**15.6**	**45**	**100.0**	
	≥10	-	4	40.0	3	30.0	3	30.0	0	0.0	10	100.0	-
		+	0	0.0	0	0.0	0	0.0	0	0.0	0	100.0	
		Total	**4**	**40.0**	**3**	**30.0**	**3**	**30.0**	**0**	**0.0**	**10**	**100.0**	
Lumber and Wood													
	None	-	197	34.7	193	34.0	93	16.4	85	15.0	568	100.0	0.19
		+	138	35.7	146	37.7	63	16.3	40	10.3	387	100.0	
		Total	**335**	**35.1**	**339**	**35.5**	**156**	**16.3**	**125**	**13.1**	**955**	**100.0**	
	<10	-	22	39.3	16	28.6	12	21.4	6	10.7	56	100.0	0.32
		+	9	26.5	11	32.4	6	17.6	8	23.5	34	100.0	
		Total	**31**	**34.4**	**27**	**30.0**	**18**	**20.0**	**14**	**15.6**	**90**	**100.0**	
	≥10	-	10	62.5	5	31.2	1	6.2	0	0.0	16	100.0	0.10
		+	2	22.2	3	33.3	3	33.3	1	11.1	9	100.0	
		Total	**12**	**48.0**	**8**	**32.0**	**4**	**16.0**	**1**	**4.0**	**25**	**100.0**	

	Years Exposed	Glu 69	Sarcoidosis		Asthma		COPD		Other		Total		p(x^2)
			N	%	N	%	N	%	N	%	N	%	
Agriculture													
	None	-	189	36.0	176	33.5	85	16.2	75	14.3	525	100.0	0.47
		+	123	34.6	135	37.9	57	16.0	41	11.5	356	100.0	
		Total	**312**	**35.4**	**311**	**35.3**	**142**	**16.1**	**116**	**13.2**	**881**	**100.0**	
	<10	-	20	31.2	22	34.4	14	21.9	8	12.5	64	100.0	0.77
		+	18	40.0	12	26.7	10	22.2	5	11.1	45	100.0	
		Total	**38**	**34.9**	**34**	**31.2**	**24**	**22.0**	**13**	**11.9**	**109**	**100.0**	
	≥10	-	20	39.2	16	31.4	7	13.7	8	15.7	51	100.0	0.54
		+	8	27.6	13	44.8	5	17.2	3	10.3	29	100.0	
		Total	**28**	**35.0**	**29**	**36.2**	**12**	**15.0**	**11**	**13.8**	**80**	**100.0**	
Health Care													
	None	-	216	35.5	201	33.0	102	16.7	90	14.8	609	100.0	0.31
		+	135	33.8	150	37.5	69	17.2	46	11.5	400	100.0	
		Total	**351**	**34.8**	**351**	**34.8**	**171**	**16.9**	**136**	**13.5**	**1009**	**100.0**	
	<10	-	9	39.1	12	52.2	1	4.3	1	4.3	23	100.0	0.27
		+	7	36.8	6	31.6	3	15.8	3	15.8	19	100.0	
		Total	**16**	**38.1**	**18**	**42.9**	**4**	**9.5**	**4**	**9.5**	**42**	**100.0**	
	≥10	-	4	50.0	1	12.5	3	37.5	0	0.0	8	100.0	0.07
		+	7	63.6	4	36.4	0	0.0	0	0.0	11	100.0	
		Total	**11**	**57.9**	**5**	**26.3**	**3**	**15.8**	**0**	**0.0**	**19**	**100.0**	

Diagnoses by years employed by Glu 69: industry with 50+ employed (Women)

	Years Exposed	Glu 69	Sarcoidosis		Asthma		COPD		Other		Total		p(x^2)
			N	%	N	%	N	%	N	%	N	%	
Oil and Gas													
	None	-	142	27.1	230	43.9	93	17.7	59	11.3	524	100.0	0.59
		+	115	30.2	170	44.6	59	15.5	37	9.7	381	100.0	
		Total	**257**	**28.4**	**440**	**44.2**	**152**	**16.8**	**96**	**10.6**	**905**	**100.0**	
	<10	-	13	38.2	14	41.2	3	8.8	4	11.8	34	100.0	0.90
		+	4	28.6	6	42.9	2	14.3	2	14.3	14	100.0	
		Total	**17**	**35.4**	**20**	**41.7**	**5**	**10.4**	**6**	**12.5**	**48**	**100.0**	
	≥10	-	1	12.5	4	50.0	2	25.0	1	12.5	8	100.0	0.53
		+	2	33.3	3	50.0	0	0.0	1	16.7	6	100.0	
		Total	**3**	**21.4**	**7**	**50.0**	**2**	**14.3**	**2**	**14.3**	**14**	**100.0**	
Agriculture													
	None	-	148	28.1	229	43.5	91	17.3	59	11.2	527	100.0	0.87
		+	111	29.8	165	44.2	59	15.8	38	10.2	373	100.0	
		Total	**259**	**28.8**	**394**	**43.8**	**150**	**16.7**	**97**	**10.8**	**900**	**100.0**	
	<10	-	3	13.6	12	54.5	5	22.7	2	9.1	22	100.0	0.17
		+	7	38.9	9	50.0	2	11.1	0	0.0	18	100.0	
		Total	**10**	**25.0**	**21**	**52.5**	**7**	**17.5**	**2**	**5.0**	**40**	**100.0**	
	≥10	-	5	29.4	7	41.2	2	11.8	3	17.6	17	100.0	0.73
		+	3	30.0	5	50.0	0	0.0	2	20.0	10	100.0	
		Total	**8**	**29.6**	**12**	**44.4**	**2**	**7.4**	**5**	**18.5**	**27**	**100.0**	
Health Care													
	None	-	125	30.4	175	42.6	69	16.8	42	10.2	411	100.0	0.97
		+	90	30.9	125	43.0	45	15.5	31	10.7	291	100.0	
		Total	**215**	**30.6**	**300**	**42.7**	**114**	**16.2**	**73**	**10.4**	**702**	**100.0**	
	<10	-	18	21.2	36	42.4	17	20.0	14	16.5	85	100.0	0.09
		+	17	34.0	23	46.0	8	16.0	2	4.0	50	100.0	
		Total	**35**	**25.9**	**59**	**43.7**	**25**	**18.5**	**16**	**11.9**	**135**	**100.0**	
	≥10	-	13	18.6	37	52.9	12	17.1	8	11.4	70	100.0	0.88
		+	14	23.3	31	51.7	8	13.3	7	11.7	60	100.0	
		Total	**27**	**20.8**	**68**	**52.3**	**20**	**15.4**	**15**	**11.5**	**130**	**100.0**	

Appendix 5: Genotype (Glu69 marker) by diagnosis and sex

Diagnosis	Men			Women		
	N	Glu 69 positive	%	N	Glu 69 positive	%
Sarcoidosis	378	149	39.4	277	121	43.7
Asthma	374	160	42.8	427	179	41.9
COPD	178	72	40.4	159	61	38.4
Other	140	49	35.0	104	40	38.5
Total	1070	430	40.2	967	401	41.5