Attachment 1: Estimation of BSE Prevalence in Canada

1. Introduction

The purpose of this document is to estimate the prevalence of bovine spongiform encephalopathy (BSE) in the adult cattle population of Canada. The detection of Canada's first native BSE case was confirmed on May 20, 2003. As of August 23, 2006, a total of nine BSE cases of Canadian origin had been confirmed in North America (CFIA 2006). This total includes a case of BSE that was confirmed in Washington State on December 25, 2003. By comparison, the United Kingdom (UK) had detected 184,453 cases of BSE as of September 1, 2006 (OIE 2006a).

The number of BSE cases detected through surveillance understates the disease prevalence because exposed animals may be incubating disease and carrying infectious material in their tissues without presenting clinical symptoms. Like many transmissible spongiform encephalopathies (TSEs), BSE has an incubation period of several years. Therefore, the disease is not detectable in its early stages with current technology. Moreover, surveillance will miss a proportion of detectable cases. Therefore, statistical methods are applied to the available epidemiologic and surveillance data to estimate, with attendant uncertainty, the prevalence of BSE in Canada.

Two related, but distinct methods were used to estimate BSE prevalence in Canada. Given its international prominence, we used the European Union (EU) BSurvE model (Wilesmith *et al*. 2004, 2005), recently developed for the purpose of estimating BSE prevalence in national herds. The BSurvE model is noteworthy for its sound epidemiologic structure, including stratifying cattle by age and cause of death (healthy slaughter, fallen stock, casualty slaughter, or clinical suspect) and accounting for the relative likelihood of detecting BSE in various strata (EFSA 2004). The primary prevalence estimation method used in this document, referred to as the Bayesian Birth Cohort (BBC) model, takes advantage of the BSurvE model structure to calculate BSE surveillance point values - random sample size equivalents - represented by targeted Canadian sampling of certain groups of cattle in which BSE cases are more likely to be detected. The Bayesian Birth Cohort model adopts a Bayesian statistical framework to incorporate prior information about the decreased incidence of BSE observed in animals born after a feed ban equivalent to the initial ruminant-to-ruminant feed ban introduced in the UK in 1988. For the purposes of comparison and sensitivity analysis, the prevalence of BSE in Canada also is estimated using BSurvE.

2. Data

2.1 BSurvE Model Structure for Input Data

Applying the BSurvE model structure to estimate a country's BSE prevalence requires knowledge of the cattle population size and age structure and involves important assumptions regarding the classification of tested animals by age and cause of death, called surveillance streams. These surveillance streams are described as: healthy

slaughter, fallen stock, casualty slaughter, or clinical suspect (Wilesmith *et al*. 2004, 2005). In consultation with U.S. animal health surveillance analysts, Canadian Food Inspection Agency (CFIA) officials organized the available Canadian BSE surveillance evidence as input data for the BSurvE model (Murray 2006).

2.2 Canadian Cattle Population Size and Age Structure

BSurvE relies on the female cattle population data because (1) the information is more demographically stable and more readily available than for males, and (2) females comprise the majority of the standing adult cattle population (Wilesmith *et al*. 2005). Murray (2006) derived the number of Canadian animals in the beef and dairy reproductive female populations from cattle inventory data reported by Statistics Canada (2004). Because age-specific mortality rates and slaughter rates are unavailable for the Canadian cattle population, the population estimates were stratified by age based on the cattle population demographics estimated for the U.S. by the "Harvard-Tuskegee Study" (Cohen *et al*. 2003). It is reasonable to assume that the same rates would be applicable to Canada as the cattle industries in both countries are virtually identical. For example, the relative proportion of beef and dairy cattle (80% and 20% respectively), management practices (such as breeding, feeding and rearing), and slaughtering practices are essentially the same in both countries (NASS 2006, Statistics Canada 2001). The age-specific population profiles for the beef and dairy population were combined to give an overall estimate of the age-specific profile of the Canadian cattle population. These data (Table 1) are entered in BSurvE as the "idealized count" for age distribution. This distribution results in an estimated adult (2+ years of age) Canadian cow population of 5,979,757 animals.

Murray (2006) provides the age distribution for animals up to 20 years of age. However, for the purpose of characterizing the age distribution, BSurvE only accepts count data for cattle up to 16 years of age. BSurvE uses the cattle age distribution to calculate exit constants. These constants represent age-specific rates of removal from the herd. The decision to exclude cattle 17 to 20 years of age results in no change in the estimated exit rates, while the alternative of redistributing animals estimated to be over 16 years of age into younger age groups would have artificially altered the exit rate assumptions used in deriving the distribution and affected the BSE surveillance point calculations.

Table 1. Age Distribution for Canadian Cattle Population

Age (years)	Female Cattle
0	1,194,932
1	1,104,087
2	1,065,899
3	965,795
4	856,719
5	723,068
6	561,567
7	434,748
8	331,917
9	257,258
10	201,542
11	159,075
12	126,201
13	100,468
14	80,169
15	64,071
16	51,260

2.3 BSE Testing and Surveillance Data

2.3.1 December 2003 Washington State Case and Investigation Test Data

Because the animal was born in Canada, the BSE case detected in Washington State and confirmed in December 2003 was included as a Canadian case for the purpose of estimating the prevalence of BSE in Canada. None of the results of tests of Canadian cattle in the U.S. conducted during the epidemiologic investigation of the December 2003 case were included. That is, the BSE positive animal was included in the numerator, but none of the corresponding negative results were considered in the denominator of this analysis. Similarly, the analysis excludes the negative results of all of the BSE tests conducted in the course of epidemiologic investigations of the other eight BSE cases of Canadian origin confirmed to date in North America. Thus, only those samples collected as part of Canada's BSE surveillance program were included in the denominator of the analysis. Excluding the negative results from animals tested in follow-up investigations acts to overstate prevalence, but these negative results increase confidence that no unidentified cases are present in local association with the BSE positive animals.

2.3.2 BSE Surveillance Streams

BSurvE requires that the BSE test data be stratified by surveillance stream and age of animal. In accordance with World Organization for Animal Health (OIE) guidelines for BSE surveillance (OIE 2006), Canada's enhanced BSE surveillance program specifically targets certain risk groups amongst which BSE cases are much more likely to be found (CFIA 2006):

- cattle of all ages displaying clinical signs consistent with BSE (clinical suspects)

- cattle over 30 months of age from the 4-D categories:
    - animals found dead (dead stock)
    - animals that are non-ambulatory (downers)
    - animals presented for emergency slaughter (dying)
    - animals sent to slaughter that are found to deviate from normal behavior or appearance at ante mortem inspection (diseased)

BSurvE (Wilesmith *et al*. 2004, 2005) uses four surveillance streams which are related to the risk groups targeted in Canada as follows:

- healthy slaughter (not included in Canada's surveillance program)
- fallen stock (equivalent to Canada's dead stock category)
- casualty slaughter (equivalent to Canada's categories for downers, dying and diseased animals)
- clinical suspects

Animals are not specifically identified as BSE clinical suspects in the CFIA's laboratory database. However, Murray (2006) estimated the likely number of clinical suspects by determining which BSE related laboratory accessions could reasonably be classified as clinical suspects on the basis of the following selection criteria:

OIE (2006, Article 3.8.4.2) defines cattle displaying behavioral or clinical signs consistent with BSE as those that are affected by illnesses that are refractory to treatment AND display progressive behavioral changes (excitability, persistent kicking when milked, changes in herd hierarchical status, hesitation at doors, gates and barriers) OR display progressive neurological signs without signs of infectious illness.

To satisfy these conditions and classify an animal as a clinical suspect, Murray (2006) determined that the pathology history would need to indicate that an animal was suffering from a chronic condition (at least one week), loss of productivity, weight loss AND some sort of neurological symptom such as ataxia or behavioral changes such as nervousness or apprehensiveness. Animals suspected of rabies also were classified as clinical suspects. In classifying clinical suspects, Murray (2006) ruled out: short term conditions (duration of less than one week); injuries associated with recent calving (obturator paralysis etc.); signs of infectious illness such as Johne's disease; other explanations for locomotory disturbance such as sole ulceration; conditions that had been present for longer than six months; and unilateral lameness.

2.3.3 Tests from Animals of Unknown Age

Where birth records are unavailable, the age of animals may be estimated by dentition. Historically, the age of animals tested under Canada's BSE surveillance program has not been routinely captured. However, age associated data is available for approximately 50% of the BSE tests undertaken within CFIA's TSE network laboratories in 2004 and 2005. This subset represents over 20,000 animals. Considering the large number of animals with age data and the lack of appreciable differences in age related trends among

these years, a pooled estimate of age stratification for each BSurvE surveillance stream was determined. Murray (2006) used this estimate to stratify the surveillance results for tested animals where age was unavailable.

2.3.4 Stratified Canadian BSE Surveillance Data

Murray (2006) provides the available Canadian BSE surveillance data collected from 1992 through August 15, 2006, stratified by age and surveillance stream. However, under OIE (2006), BSE surveillance points only remain valid for 7 years. Therefore, the estimated prevalence of BSE in Canada is based on surveillance data accumulated over a 7-year period beginning August 16, 1999 and ending August 15, 2006. This surveillance period includes the 9th BSE case of Canadian origin confirmed on August 23, 2006. Since the surveillance data are reported on a calendar year basis, the number of samples for the 1999 strata was reduced proportionately to the extra months of data captured for 2006 (i.e., the 1999 data were reduced by 62.5%, or prorated to 4.5 months). Table 2 presents the surveillance testing data stratified in the BSurvE format used to estimate the prevalence of BSE in Canada.

Table 2. Canadian BSE surveillance stream test data for 16 Aug. 1999 – 15 Aug. 2006

Testing Year	Age	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2006 thru Aug 15	<2yo	0	0	6	0	10	0
	2	333	0	233	0	0	0
	3	1724	0	1020	0	12	0
	4	2072	0	1443	1	17	0
	5	2210	0	1546	0	35	0
	6	2425	1	1490	0	25	1
	7	1655	0	1079	0	8	0
	8	2247	0	1427	0	14	0
	9	981	0	700	0	4	0
	10	2255	0	1575	0	27	1
	11	560	0	480	0	6	0
	12	1716	0	1447	0	14	0
	13	568	0	423	0	10	0
	14	799	0	755	0	10	0
	15	811	0	818	0	6	1
	16	414	0	368	0	0	0
	17+	353	0	490	0	8	0

Table 2 (cont'd)

Testing Year	Age	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2005	<2yo	0	0	5	0	2	0
	2	486	0	484	0	17	0
	3	3007	0	1644	0	26	0
	4	3493	0	2019	0	31	0
	5	3896	0	2271	0	53	0
	6	4387	0	2330	0	36	0
	7	2795	0	1602	0	26	1
	8	3404	0	2175	0	42	0
	9	1699	0	1125	0	20	0
	10	3778	0	2692	0	54	0
	11	950	0	798	0	17	0
	12	2504	0	2160	0	25	0
	13	755	0	703	0	14	0
	14	1101	0	923	0	16	0
	15	1163	0	1232	0	25	0
	16	302	0	352	0	9	0
	17+	559	0	549	0	14	0
2004	<2yo	0	0	2	0	1	0
	2	185	0	217	0	7	0
	3	1143	0	737	0	11	0
	4	1328	0	905	0	13	0
	5	1480	0	1018	0	23	0
	6	1667	0	1044	0	15	0
	7	1062	0	718	0	11	0
	8	1294	0	975	0	18	1
	9	646	0	504	0	9	0
	10	1436	0	1207	0	24	0
	11	361	0	358	0	7	0
	12	952	0	968	0	11	0
	13	287	0	315	0	6	0
	14	418	0	414	0	7	0
	15	442	0	552	0	11	0
	16	115	0	158	0	4	0
	17+	212	0	246	0	6	0

Table 2 (cont'd)

Testing Year	Age	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2003	<2yo	0	0	0	0	1	0
	2	19	0	39	0	11	0
	3	117	0	131	0	18	0
	4	136	0	161	0	21	0
	5	152	0	181	0	35	0
	6	171	0	185	2	24	0
	7	109	0	128	0	18	0
	8	133	0	173	0	28	0
	9	66	0	90	0	14	0
	10	147	0	214	0	36	0
	11	37	0	64	0	11	0
	12	98	0	172	0	17	0
	13	29	0	56	0	9	0
	14	43	0	73	0	10	0
	15	45	0	98	0	17	0
	16	12	0	28	0	6	0
	17+	22	0	44	0	9	0
2002	<2yo	0	0	1	0	2	0
	2	6	0	52	0	18	0
	3	38	0	178	0	28	0
	4	45	0	219	0	33	0
	5	50	0	246	0	56	0
	6	56	0	253	0	38	0
	7	36	0	174	0	28	0
	8	43	0	236	0	44	0
	9	22	0	122	0	21	0
	10	48	0	292	0	57	0
	11	12	0	86	0	18	0
	12	32	0	234	0	26	0
	13	10	0	76	0	15	0
	14	14	0	100	0	16	0
	15	15	0	134	0	26	0
	16	4	0	38	0	10	0
	17+	7	0	60	0	15	0

Table 2 (cont'd)

Testing Year	Age	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
2001	<2yo	0	0	0	0	2	0
	2	0	0	20	0	25	0
	3	0	0	68	0	39	0
	4	0	0	84	0	45	0
	5	0	0	94	0	77	0
	6	0	0	97	0	52	0
	7	0	0	67	0	39	0
	8	0	0	90	0	61	0
	9	0	0	47	0	29	0
	10	0	0	112	0	79	0
	11	0	0	33	0	25	0
	12	0	0	90	0	36	0
	13	0	0	29	0	20	0
	14	0	0	38	0	23	0
	15	0	0	51	0	36	0
	16	0	0	15	0	14	0
	17+	0	0	23	0	20	0
2000	<2yo	0	0	0	0	2	0
	2	0	0	12	0	18	0
	3	0	0	40	0	28	0
	4	0	0	50	0	33	0
	5	0	0	56	0	56	0
	6	0	0	57	0	38	0
	7	0	0	39	0	28	0
	8	0	0	54	0	44	0
	9	0	0	28	0	21	0
	10	0	0	66	0	58	0
	11	0	0	20	0	18	0
	12	0	0	53	0	26	0
	13	0	0	17	0	15	0
	14	0	0	23	0	16	0
	15	0	0	30	0	26	0
	16	0	0	9	0	10	0
	17+	0	0	14	0	15	0

Table 2 (cont'd)

Testing Year	Age	Fallen stock tested	Fallen stock positive	Casualty slaughter tested	Casualty slaughter positive	Clinical suspects tested	Clinical suspects positive
1999* (37.5% of total in strata)	<2yo	0	0	0	0	1.125	0
	2	0	0	1.5	0	10.5	0
	3	0	0	5.25	0	16.125	0
	4	0	0	6.75	0	18.75	0
	5	0	0	7.5	0	32.25	0
	6	0	0	7.875	0	21.75	0
	7	0	0	5.25	0	16.125	0
	8	0	0	7.125	0	25.5	0
	9	0	0	3.75	0	12.375	0
	10	0	0	9	0	33	0
	11	0	0	2.625	0	10.5	0
	12	0	0	7.125	0	15	0
	13	0	0	2.25	0	8.625	0
	14	0	0	3	0	9.375	0
	15	0	0	4.125	0	15	0
	16	0	0	1.125	0	5.625	0
	17+	0	0	1.875	0	8.625	0

*Data prorated for 1999. See accompanying text.

2.4 Feed Ban Evidence

Canada introduced a feed ban in 1997. The Canadian BSE surveillance program has been intensified since the first native case was detected in 2003, and the surveillance data available to date indicate that the country's feed ban has kept the level of disease in subsequent birth year cohorts at a low level. Due to BSE's long incubation period and the low prevalence of BSE in Canada, however, the available surveillance data provides limited information about the trajectory of disease incidence over time. However, implementation of feed mitigations has been demonstrated to dramatically decrease the risk of new BSE cases, and this knowledge provides information about the status of disease before consideration of the animal health surveillance data. For the purpose of this analysis, empirical evidence following the 1988 UK feed ban provides prior information about the effect of a reasonably effective feed ban on the incidence of BSE. These data are used as surrogate data to predict the decline in prevalence in Canadian cattle cohorts born after the 1997 Canadian ban.

Retrospective analysis of the incidence of BSE by birth year cohort demonstrated that the UK's BSE epidemic was on the upswing before a ruminant-to-ruminant feed ban was introduced in July 1988, but the incidence of disease declined rapidly for each cohort of cattle born after the ban (Schreuder *et al*. 1997). As clearly shown in the epidemic curve (Figure 1), the UK ruminant-to-ruminant feed ban introduced in 1988 substantially decreased the number of new cases in subsequent birth year cohorts, although it was insufficient to eradicate the disease immediately.

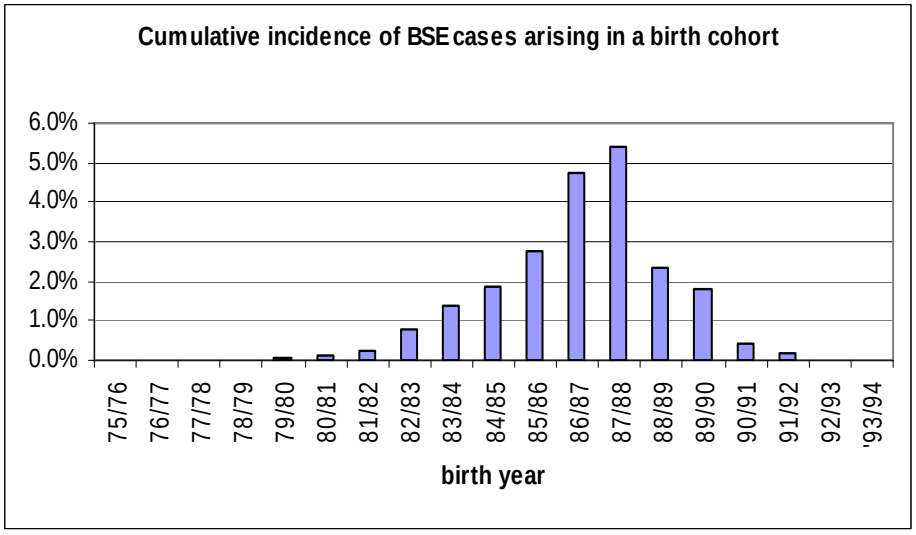

Figure 1. Cumulative incidence of BSE in the UK by birth year cohort.
Source: Schreuder *et al*. (1997)

Applying the method described by Schreuder *et al*. (1997) to the cumulative UK BSE surveillance data available as of November 2005 (DEFRA 2005), Animal and Plant Health Inspection Service (APHIS) Centers for Epidemiology and Animal Health (CEAH) staff updated the cumulative incidence for each UK birth year cohort (Table 3). In comparison to the initial ruminant-to-ruminant feed ban introduced in the UK in 1988, the Canadian feed ban introduced in 1997 is considered equivalent or more restrictive, prohibiting feeding of most mammalian proteins to ruminants. In 1994, the UK feed ban was amended to become a more restrictive mammalian-to-ruminant feed ban. Therefore, the UK-based evidence about the effect of a feed ban on BSE prevalence was incorporated into the analysis for Canadian cohorts born in the first five years following Canada's 1997 rule. Thus, the Canadian feed ban was assumed to be at least as effective as the first five years of the initial UK feed ban (Table 3).

Table 3. Observed (UK) and Expected (Canada) Decline in BSE Incidence by Birth Year Cohort Following Feed Ban Introduction

Years since feed ban	UK Birth cohort	BSE cases in the UK cohort	Proportion of the 1987/88 UK cohort's incidence	Canadian Birth cohort	Years since feed ban	Expected proportion of the 1997 Canadian cohort's incidence *
0	1987/88	39201	1.0000	1997	0	1.0000
1	1988/89	16556	0.4223	1998	1	0.4223
2	1989/90	11044	0.2817	1999	2	0.2817
3	1990/91	5036	0.1285	2000	3	0.1285
4	1991/92	4348	0.1109	2001	4	0.1109
5	1992/93	3231	0.0824	2002	5	0.0824
6	1993/94	2517	0.0642	2003	6	n/a
7	1994/95	1675	0.0427	2004	7	n/a
8	1995/96	444	0.0113	2005	8	n/a

*Assuming Canadian feed ban was as effective as the initial UK feed ban in its first five years.

Additional information provided by Cohen *et al*. (2003) indicates that the prevalence of BSE is expected to decline in the U.S. in response to the domestic feed ban. U.S. epidemiologists reviewed records and conducted site visits to Canadian facilities to evaluate the Canadian feed ban, its implementation and compliance. USDA (2005) concluded that the Canadian feed ban is not substantially different from the U.S. feed ban. Because the Canadian ban is similar to the U.S. ban and deemed to be effectively enforced, the decline predicted by Cohen *et al*. (2003) would likely apply to the Canadian population as well. In sum, knowledge of the effect of a feed ban provides substantial information about BSE prevalence before consideration of the surveillance data.

3. Methods

3.1 BSurvE Model

The BSurvE model was developed to provide a method for evaluation of national surveillance data and optimization of national surveillance strategies for BSE (Wilesmith *et al*. 2004). BSurvE uses epidemiologic information about the disease that was accumulated during the UK and European outbreaks to predict parameters such as incubation period of BSE, probable length of an infected animal's life, and the dynamics of disease expression in infected animals. BSurvE combines this information with country-specific demographic information about a national herd (size and age distribution) and national BSE surveillance data to achieve a set of point values for samples taken from cattle of different age and surveillance streams—healthy slaughter, fallen stock, casualty slaughter, or clinical suspect. The points represented by an animal tested for BSE are based on the relative likelihood that the disease would be detected in an animal leaving the herd at a particular age and by a particular surveillance stream. Under this scheme, one point is equivalent to an animal randomly selected for testing from the national herd (Wilesmith *et al*. 2004).

The BSurvE model is implemented as a Microsoft© Excel™ spreadsheet application. The analysis herein based on the BSurvE model was performed using BSurvE Version 06.03 (downloaded March 22, 2006 from http://www.bsurve.com). The BSurvE spreadsheet model and documentation are available on the BSurvE website (http://www.bsurve.com/forum/forum.asp?$sid=&id=10). The BSurvE website includes updates made to the BSurvE model when a new version is released and documentation that provides detailed description of the underlying functions of the model as well as step by step user instructions.

For the purpose of estimating the prevalence of BSE in Canada, BSurvE was used in two ways. First, for the purposes of estimating the prevalence of BSE in Canada using the Bayesian Birth Cohort (BBC) model including the UK feed ban evidence, BSE surveillance point values allocated to the 1991-2005 birth year cohorts were calculated by entering individual surveillance year data (Table 2) into the BSurvE model and then summing the BSE surveillance points calculated by the model for each birth cohort over the 7-year surveillance period ending August 15, 2006. Note that Murray (2006, Table 26) presents BSE surveillance points allocated to each birth cohort accumulated over more than 14 years, dating back to the 1992 surveillance year.

Second, for the purposes of comparison, the prevalence of BSE in Canada also is estimated using the unembellished BSurvE model application intended for application to countries where BSE is non-endemic, or where the infection rate is independent of birth year cohort, with animals from different birth year cohorts having the same underlying probability of infection. The BSurvE model developers refer to this prevalence estimation method as BSurvE Prevalence B (Wilesmith *et al*. 2004, 2005). The latter BSE prevalence estimation method makes no assumptions about feed ban efficacy and relies on the surveillance data alone. In contrast to OIE (2006), which permits accumulation of BSE surveillance points over 7 years, BSurvE (Version 06.03, downloaded 3/22/06 from http://www.bsurve.com) allows entry of no more than 5 years of surveillance data at a time. Therefore, for the purposes of estimating the prevalence of BSE in Canada using BSurvE Prevalence B, testing data (Table 2) were combined for 1999-2002 for entry into the model. Recall that the surveillance points calculated by BSurvE depend on the age and health strata of animals when they are tested and that BSurvE Prevalence B assumes a constant probability of infection over time. In contrast to BSurvE Prevalence B, the BSurvE application intended for application to countries where BSE is endemic (BSurvE Prevalence A) is designed to permit an assessment of changes in BSE prevalence across birth year cohorts. As discussed below, however, the Canadian BSE surveillance data provide no statistical basis for distinguishing BSE prevalence among birth year cohorts. Therefore, BSurvE Prevalence B is used here to provide a sensitivity analysis of the effect of incorporating the UK feed ban data on the estimated BSE prevalence in Canada, and more importantly, the overall results of the risk assessment.

3.2 Bayesian Birth Cohort Model

The Bayesian Birth Cohort (BBC) model combines prior evidence about the effect of a ruminant-to-ruminant feed ban on BSE dynamics with the surveillance points calculated by the BSurvE model, resulting in a more precise estimate of BSE prevalence. Like the BSurvE model, the BBC model prevalence estimate refers to all BSE-infected animals, regardless of whether they would be detectable or showing clinical signs. As a starting point, this method assumes that prevalence may be anything from 0 to 100% (i.e., the prior assumption was that prevalence is uniformly distributed between 0 and 100%). The model then updates the Canadian prevalence estimate based on the detected BSE cases, the expected decline in BSE incidence by birth year cohort following the first five years of the Canadian feed ban (Table 3), and the BSurvE point total for each birth year cohort assumed to contribute adult animals to the current standing population (birth years 1991-2005). The analysis considers animals tested over the 7 year surveillance period ending August 15, 2006; however, the surveillance points associated with animals born prior to 1991 do not enter the analysis under the BBC model because BSurvE only accepts data for cattle up to 16 years of age. To date, no BSE cases of Canadian origin have been detected in animals born prior to 1991.

The BBC model assumes that prevalence is constant for birth year cohorts 1991-97, with 1998 being the first cohort influenced by the 1997 feed ban. The prevalence of BSE in the adult cattle alive in 2006 was estimated as the weighted sum of the individual birth cohorts' prevalence levels, where the weights are the proportion of infected animals in each birth cohort that remain alive in 2006. The BBC model was implemented using two Bayesian analytical methods: Gibbs sampling and Sampling-Importance-Resampling (SIR).

3.2.1 Gibbs Sampling

Gibbs Sampling is a Monte Carlo Markov Chain (MCMC) statistical method (Vose 2000). MCMC methods are based on an iterative updating scheme that is repeated until the sequence of parameter vectors converges. In general, Bayesian Monte Carlo procedures update uncertainty with forward and backward propagation of the model (Brand and Small 1995). Vose (2006) recommended this method for implementing the BBC model and provided exemplar computer code using WinBUGS (Bayesian Inference Using Gibbs Sampling), a freeware statistical application. WinBUGS (Version 1.4.1, downloaded January 2006 from http://www.mrc-bsu.cam.ac.uk/bugs/winbugs/contents.shtml) was used to implement the BBC model using the code presented in Appendix 1. Two chains were initiated in WinBUGS to monitor convergence with starting values for prevalence (p) equal to 0.1 and 0.0001. A total of 100,000 iterations were performed, and data from the last 20,000 iterations were used for prevalence estimation.

3.2.2 Sampling-Importance-Resampling (SIR)

Using the same model inputs described above, an alternative Bayesian method was used to verify the BBC model results obtained using WinBUGS. In contrast to the iterative Gibbs sampling method, Sampling-Importance-Resampling (SIR) is a noniterative

algorithm used to simulate Bayesian posterior distributions (Rubin 1988). This procedure is also referred to as a weighted bootstrap (Smith and Gelfand 1992). In SIR, *m* samples are drawn from an initial approximation to the desired distribution, and then $l < m$ samples are randomly drawn from the first finite sample (*m*) with probability proportional to their importance (i.e., sampling weight). The rationale of the SIR algorithm is based on the fact that as $m/l \rightarrow \infty$, the *l* sample values represent independent draws from the desired posterior distribution (Rubin 1988).

In essence, the iterative MCMC procedures like Gibbs sampling converge on the desired posterior as the number of iterations approaches infinity, whereas the non-iterative SIR procedure converges to the desired posterior as the initial sample (*m*) gets infinitely larger than the resample (*l*). The SIR algorithm provides a useful check on the Gibbs procedure because the former is not prone to "getting stuck in a rut" (i.e., converging to local rather than global maxima). A disadvantage of the SIR algorithm is that its computational efficiency depends on having a good first approximation (prior), whereas the iterative procedures can be monitored for convergence and stopped once the convergence criteria are met.

The SIR algorithm proceeds by using Monte Carlo simulation methods to generate a first approximation to the pre-feed ban prevalence (*p*) uncertainty distribution that captures the entire range of feasible parameter values, evaluating the likelihood of discrete *p* values given the surveillance evidence, and then resampling from the uncertainty distribution proportional to importance weights (normalized likelihoods) of the discrete *p* values. The likelihood of *p*, given the surveillance evidence, is calculated assuming a binomial likelihood function:

$$\mathrm{Lik}(\mathrm{p} \mid \mathrm{s}) = \prod_{1991}^{2005} \mathrm{Binomial}(\mathrm{s}, \mathrm{n}, \mathrm{p})$$

where: s_i = number of BSE cases detected in the i^{th} birth year cohort
n_i = number of BSurvE points for the i^{th} birth year cohort
$p_{1991} = p_{1992} = \ldots = p_{1997} = p$
$p_{1998} = 0.4223 * p$
$p_{1999} = 0.2817 * p$
$p_{2000} = 0.1285 * p$
$p_{2001} = 0.1109 * p$
$p_{2002} = 0.0824 * p$
$p_{2003} = 0.0824 * p$
$p_{2004} = 0.0824 * p$
$p_{2005} = 0.0824 * p$

The resampling weights (w) are equal to normalized likelihood values for discrete uncertainty realizations of *p*:

$$w_m = \frac{\mathrm{Lik}(p_m)}{\sum \mathrm{Lik}(p)}$$

Monte Carlo methods are used to resample from the uncertainty distribution for *p*, which is assumed to follow a beta distribution, the conjugate prior to the binomial (Vose 2000):

$$p \sim Beta(\alpha, \beta)$$

Based on the mean and variance obtained from the Monte Carlo simulation of *p*, the parameters of the beta distribution are estimated by the method of matching moments (Evans *et al*. 1993):

$$\hat{\alpha} = \bar{x}\{[\bar{x}(1-\bar{x})/s^2] - 1\}$$
$$\hat{\beta} = (1-\bar{x})\{[\bar{x}(1-\bar{x})/s^2] - 1\}$$

Based on the posterior for *p* obtained from these parameter estimates, the prevalence in the current adult standing cattle population in Canada is estimated as the weighted sum of the individual birth cohorts' prevalence levels, where the weights are the proportion of infected animals in each birth cohort that remain alive in 2006. The SIR method was implemented using Palisades© @Risk™ (Ver. 4.5), an add-on to Microsoft© Excel™ (Ver. 9.0). Monte Carlo simulation was performed with Latin Hypercube sampling (10,000 iterations).

4. Results

4.1 BSurvE Points by Birth Year Cohort

Table 4 presents the BSE surveillance points calculated by BSurvE from the Canadian BSE surveillance data and the Canadian BSE cases by birth year cohort. The increase in surveillance points between the 2004 to 2005 birth year cohorts is due to the larger number of animals tested in the clinical and casualty surveillance streams for the 2005 cohort. This can be seen by comparing the one-year age class in Murray (2006, Tables 23 and 24).

Table 4. BSurvE Points and BSE Cases by Birth Year Cohort

Birth year	BSurvE Points	BSE Cases
1991	24,737	1
1992	35,814	0
1993	61,914	0
1994	115,950	0
1995	183,528	0
1996	225,473	2
1997	217,155	2
1998	173,111	1

1999	142,290	0
2000	150,111	2
2001	128,565	0
2002	59,090	1
2003	13,894	0
2004	558	0
2005	2,170	0

4.2 No Statistically Significant Differences between Birth Year Cohorts

To determine whether there is any empirical basis for distinguishing BSE prevalence among Canadian birth year cohorts, we consider the BSurvE points calculated for the Canadian 1991-2005 birth year cohorts. Recalling that one BSurvE point is equivalent to one randomly sampled animal, multiple comparison tests were performed using BSE surveillance points accumulated for birth year cohorts as inputs to statistical methods designed to detect differences among random samples. The results indicate that the available surveillance data provide no empirical basis for distinguishing BSE prevalence among Canadian birth year cohorts. (To maintain an overall type I (false positive) error rate when conducting multiple comparisons tests, the comparison-wise error rate must be adjusted. To maintain an overall type I error rate of 5 percent, with 105 pairwise comparisons, the comparison-wise type I error rate (CER) is set to 0.05 percent (Sidak 1967). The multiple comparison test was repeated, removing the 1991 through 2002 cohorts in sequence and modifying the CER accordingly to maintain the overall type I error rate of 5 percent. In each application of the test, there were no statistically significant differences in BSE prevalence among birth year cohorts. Similarly, no statistically significant differences were found in a simple pairwise comparison of birth cohorts born before (1991-1997) or after (1998-2005) feed ban introduction. In summary, analysis of the Canadian BSE surveillance data provides no statistical basis for distinguishing BSE prevalence among birth year cohorts. Therefore, a single prevalence was estimated for the standing adult cattle population.

In addition to the lack of statistical evidence to distinguish among cohort prevalence estimates, there are biological reasons why birth cohorts should not be considered independent. Animals born within one or two years of a positive case have a similar likelihood of being exposed to the feed sources responsible for infecting the case (given no information about feed mitigations). Knowledge of BSE incidence in animals born in each of the 3 to 7 years prior to the birth date of a BSE case would also influence the prediction of the current prevalence, because infected tissues from these animals could have been recycled into the feed of the case's birth cohort (again assuming no knowledge of feed mitigations).

4.3 Prevalence Estimates

The WinBUGS implementation of the BBC model resulted in an expected prevalence value of 0.68 per million. In comparison, the SIR implementation of the BBC model resulted in an expected prevalence value of 0.65 per million. The 95% confidence levels also were virtually the same, 1.1 and 1.0 per million, respectively. Due to the negligible

difference in the two results, the expected value of the Bayesian Birth Cohort model was taken as 0.68 per million.

Table 5 summarizes the results of the estimation of BSE prevalence in the standing Canadian adult cattle population as of August 15, 2006. Based on the expected prevalence value under the BBC model and the estimated adult herd size (Table 1), the expected number of BSE-infected animals in the standing Canadian adult cattle population is 4.1. By comparison, the expected value obtained under BSurvE Prevalence B is 3.9 per million, which corresponds to an estimated 23.2 BSE-infected animals in the standing Canadian adult cattle population.

Table 5. Estimated Prevalence of BSE in Canada

Prevalence in adult cattle population	**Bayesian birth cohort method (BBC) with UK feed ban data**	**BSurvE Prevalence B estimate without including feed ban data**
Expected value	$0.68 * 10^{-6}$	$3.9 * 10^{-6}$
95% confidence level	$1.1 * 10^{-6}$	$6.8 * 10^{-6}$

It is important to note that the estimated prevalence distribution presented here represents uncertainty and not variability. At a given point in time, the proportion (i.e., probability) of infected animals in the population is a fixed value, but the exact magnitude of the value is uncertain. Further, assuming the probability of infection remains constant, the actual number of infected cattle in the population would still vary randomly about the mean of the probability distribution over time. Similarly, if we repeatedly draw a sample of animals from a population with a fixed prevalence (i.e., fixed probability of infection), the proportion of infected animals would vary randomly between samples. Assuming a constant probability of infection, the random variability in the number of BSE infected animals in the adult cattle population would follow a binomial distribution that is described by the prevalence and size of the population (Vose 2000). For a large sample size and low prevalence values, the Poisson distribution approximates the binomial variability distribution and is incorporated in the model supporting the exposure assessment for live bovines ([Section IV.A. and Attachment 2]) to represent variability around the prevalence estimates generated here.

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Appendix 1. WinBUGS Code Used to Implement BBC Model

Calculate probabilities of infection in each year. Probability of infection is assumed constant until the implementation of the feed ban in 1997. The level of reduction in each of the 5 years after the implementation of the ban is based on BSE incidence data from DEFRA (2005) based on methods described in Schreuder et al. (1997). The reductions only apply to first 5 years following the ban. After 5 years, there is assumed no further reduction associated with the ban.

```
model{
# Set prior
        P ~ dbeta(1,1) #prevalence in Population in year of Canadian ban

        P1991 <- P
        P1992 <- P
        P1993 <- P
        P1994 <- P
        P1995 <- P
        P1996 <- P
        P1997 <- P
        P1998 <- P*0.4223
        P1999 <- P*0.2817
        P2000 <- P*0.1285
        P2001 <- P*0.1109
        P2002 <- P*0.0824
        P2003 <- P*0.0824     # Set as conservatively high
        P2004 <- P*0.0824
        P2005 <- P*0.0824

# Calculate expected infections for the number of points accumulated for each year

                L1991 <- P1991*24737
                L1992 <- P1992*35814
                L1993 <- P1993*61914
                L1994 <- P1994*115950
                L1995 <- P1995*183528
                L1996 <- P1996*225473
                L1997 <- P1997*217155
                L1998 <- P1998*173111
                L1999 <- P1999*142290
                L2000 <- P2000*150111
                L2001 <- P2001*128565
                L2002 <- P2002*59090
                L2003 <- P2003*13894
                L2004 <- P2004*558
                L2005 <- P2005*2170
```

```
# Match Poisson(expected infections for points accumulated in year) to observed
infections

                S1991 ~ dpois(L1991)
                S1992 ~ dpois(L1992)
                S1993 ~ dpois(L1993)
                S1994 ~ dpois(L1994)
                S1995 ~ dpois(L1995)
                S1996 ~ dpois(L1996)
                S1997 ~ dpois(L1997)
                S1998 ~ dpois(L1998)
                S1999 ~ dpois(L1999)
                S2000 ~ dpois(L2000)
                S2001 ~ dpois(L2001)
                S2002 ~ dpois(L2002)
                S2003 ~ dpois(L2003)
                S2004 ~ dpois(L2004)
                S2005 ~ dpois(L2005)

# Sum [Prevalence in each year * number from each cohort expected to remain standing
in the 2005 Canadian population]
InfectedNow <- (0.0002 * P1991 + 0.0005 * P1992 + 0.001 * P1993 + 0.0017 * P1994 +
0.0042 * P1995 + 0.0093 * P1996 + 0.0186 * P1997 + 0.0344 * P1998 + 0.0667 * P1999
+ 0.131 * P2000 + 0.2538 * P2001 + 0.4659 * P2002 + 0.6811 * P2003 + 0.8002 *
P2004 + 0.8902 * P2005) * 1194932
PrevNow <- InfectedNow / 5979757
}

Data
# A list of the observed BSE cases in each year
list(S1991 = 1, S1992 = 0, S1993 = 0, S1994 = 0, S1995 = 0, S1996 = 2, S1997 = 2,
S1998 = 1, S1999 = 0, S2000 = 2, S2001 = 0, S2002 = 1, S2003 = 0, S2004 = 0, S2005
=0)

Initial values
# Two chains with different values for P to monitor convergence of the estimates
list(P=0.1)
list(P=0.0001)

# The output (node) is PrevNow
```