



# Bay of Quinte

Remedial Action Plan

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## Bay of Quinte Remedial Action Plan Redesignation Report

Beneficial Use Impairment #4  
Fish tumours and other deformities



January 2016

**Bay of Quinte Area of Concern  
Beneficial Use: #4 Fish Tumours or Other Deformities  
Redesignation Report Recommending a Status of 'Not Impaired'**

**Bay of Quinte Remedial Action Plan Restoration Council  
January 6, 2016**

## Summary

This document is the official report from the Bay of Quinte Area of Concern Restoration Council recommending that the status of the Beneficial Use #4: Fish Tumours or Other Deformities is changed from 'requires further assessment' to 'not impaired'.

The criteria for assessment focused on whether there were a significant number of tumours in fish (Brown Bullhead) liver in the Bay of Quinte at Trenton compared to reference sites. Fish were collected between 2001 and 2008 from suitable reference sites. A database of information from 1150 fish was created and used to determine that this combined group had a 2% prevalence of tumours. This 2% value is called the 'Impairment Criteria'.

A review of recent sediment studies undertaken in the Bay of Quinte shows that aside from localized areas in the Belleville and Trenton waterfronts, sediment contaminants in the bay are low, and typically are due to metals and some organic compounds that are present at concentrations slightly above the MOECC PSQG LELs (Golder 2012). Thus this study focused on Trenton and Belleville, with Deseronto as the local reference site.

Brown Bullhead were collected from the Bay of Quinte in 2004 and 2005 from the Trenton, Belleville and Deseronto waterfronts, and analyzed for liver tumours. It was determined that the 4% liver tumour prevalence in Brown Bullhead collected in the Bay of Quinte at Trenton is not significantly different than the 2% Impairment Criteria derived from the reference sites located throughout the Lower Great Lakes. Thus this beneficial use should be considered to be 'not impaired' for the Bay of Quinte Area of Concern.

The assessment which provided the bases for this redesignation report was directed by Dr. Paul C. Baumann, from the U. S. Geological Survey and Ohio State University. Dr. Baumann has over 25 years of experience in working on beneficial use impairment (BUI) delisting criteria for tumour prevalence, selecting standardized tumour prevalence criteria and using historical data to determine background tumour prevalence. He is an international expert and is considered to be a leader in this field of research.

**Bay of Quinte AOC**  
**BUI #4: Fish Tumours or Other Deformities**

**Recommended BUI Status:** Not Impaired

**Delisting Criteria**

Demonstrate no environmental significant difference between the type, frequency and occurrence of tumours in Bay of Quinte Brown Bullheads and an unimpaired Great Lakes site with similar physical and chemical characteristics as the Bay of Quinte OR an unimpaired site outside the Great Lakes basin with similar population characteristics as the Bay of Quinte.

**Background**

In the Bay of Quinte Stage 1 Report (Bay of Quinte Remedial Action Plan Coordinating Committee 1990) it was stated that “On the basis of professional observations and public anecdotal reports, tumors or other deformities have not been identified as an impaired beneficial use in the Bay of Quinte.”

However, in the Bay of Quinte Stage 2 Report (Bay of Quinte Remedial Action Plan Coordinating Committee 1993) uncertainty had developed, and the beneficial use was identified as requiring further assessment. Delisting criteria was developed, against which this BUI would be assessed:

By virtually eliminating the inputs of persistent toxic contaminants, restore the Bay of Quinte ecosystem to conditions that pose no danger to the health or reproductive successes of its fish populations. This objective shall be achieved when no fish tumours or other deformities exist which are attributable to anthropogenic sources of contamination from within the Area of Concern.

This was amended in 2007 to scientifically defensible delisting criteria:

Demonstrate no environmental significant difference between the type, frequency and occurrence of tumours in Bay of Quinte Brown Bullheads and an unimpaired Great Lakes site with similar physical and chemical characteristics as the Bay of Quinte OR an unimpaired site outside the Great Lakes basin with similar population characteristics as the Bay of Quinte.

The subsequent fish tumour assessment was undertaken in 2009-2010, and the results below have been taken from the report *Data Analysis and Fish Tumour BUI Assessment For the Lower Great Lakes and Interconnecting Waterways* by Paul C. Baumann, PhD (March, 2010). The Baumann (2010) report assessed tumour prevalence in Brown Bullhead (*Ameiurus nebulosus*) in all the AOCs in the lower Great Lakes and their associated far field and reference sites (Table 1). Sampling for the current monitoring

project took place between 2001 and 2008, with many locations being sampled in several different years.

### Research

Tumour epizootics in fish were first linked to environmental contaminants in the sixties (Dawe et al., 1964). In the seventies the first study was published implicating environmental carcinogens as part of the etiology of papillomas in White Suckers in the Great Lakes (Sonstegard, 1977). In the 1980s the first liver cancer epizootic in Brown Bullhead from the Great Lakes drainage basin was reported in the Black River, Ohio (Baumann, et al., 1982). Research since that time has demonstrated elevated tumour prevalence in a variety of species across North America (Baumann 1998). Concern over these discoveries resulted in fish tumours being designated as a Beneficial Use Impairment (BUI) used to determine Areas of Concern (AOC) in Annex 2 of the 1987 Protocol Amending the Great Lakes Water Quality Agreement. The IJC delisting guidelines from 1991 state that this Beneficial Use may be deemed to be ‘not impaired’ “when the incidence rates of fish tumours or other deformities do not exceed rates at unimpacted control sites or when survey data confirm the absence of neoplastic or preneoplastic liver lesions in bullheads or suckers” (International Joint Commission, 1991). Details about the actual methodology used to establish this criterion were not provided, and as time has passed the understanding of what comprises accurate methodology in fish tumour surveys has changed (Blazer et al. 2006).

**Table 1. AOC locations and their associated far field and reference locations with the years sampled for Brown Bullhead tumour studies (from west to east).**

<b>AOC Location</b>	<b>Far Field Site</b>	<b>Reference Site</b>	<b>Years Sampled</b>
<b>Detroit River</b>	<b>Grosse Isle</b>	<b>Peche Isle</b>	<b>2002</b>
<b>Wheatley Harbour</b>	<b>NA</b>	<b>Hillman Marsh, Port Rowan</b>	<b>2002, 2006</b>
<b>Niagara River</b>	<b>Queenston</b>	<b>Point Abino</b>	<b>2004, 2008</b>
<b>Hamilton Harbour</b>	<b>NA</b>	<b>Jordan Harbour</b>	<b>2001, 2005, 2007</b>
<b>Toronto and Region</b>	<b>NA</b>	<b>Frenchman’s Bay</b>	<b>2003, 2006</b>
<b>Bay of Quinte</b>	<b>Belleville</b>	<b>Prince Edward Bay, Deseronto</b>	<b>2004, 2005</b>
<b>St. Lawrence River (Cornwall)</b>	<b>Gray’s Creek</b>	<b>Morrisburg</b>	<b>2004, 2005</b>

A sample size of one hundred Brown Bullhead (*Ameiurus nebulosus*) was set for collection in each of the AOCs, far field sites and reference locations. In the Bay of Quinte, the bullheads were captured using a Smith Root electrofishing boat.

As stated above, the IJC delisting guidelines from 1991 state that this Beneficial Use may be deemed to be 'not impaired' "when the incidence rates of fish tumours or other deformities do not exceed rates at unimpacted control sites or when survey data confirm the absence of neoplastic or preneoplastic liver lesions in bullheads or suckers" (International Joint Commission, 1991). The use of other, external lesions including lip papillomas as criteria related to carcinogen exposure is no longer recommended. Certain types of papilloma have been demonstrated conclusively to be caused by a retrovirus (Baumann and Okihiro 2000), including one type of papilloma occurring on White Sucker (Premdas and Metcalfe, 1996). Papilloma prevalence in Brown Bullhead does not correlate well with liver tumour prevalence either across locations or on individual fish within locations (Baumann et al. 1987). It is our current inability to tease apart the interaction of contaminants (both carcinogens and promoters) and virus infection that prevents us from confidently using external lesions as a criterion for BUI evaluation. On the other hand, liver lesions in wild fish including Brown Bullhead from the Great Lakes are caused by chemical contaminants (Baumann et al. 1996, Baumann and Okihiro 2000). In particular, polynuclear aromatic hydrocarbons (PAHs) have been proven by an extensive array of laboratory experiments to induce liver cancer in fish (Baumann and Okihiro 2000). Also no liver cancer in any species of fish has ever been diagnosed with a viral etiology (Dr. John Harshbarger, Director of the Tumour Registry in Lower Animals, Smithsonian Institution, Washington, DC). Furthermore, field studies have correlated a decline in tumour incidence with a decline in PAH contamination in sediment (Baumann and Harshbarger, 1995) and have shown that fish exposed to elevated PAH concentrations in the wild had significantly higher liver neoplasm prevalence than those that were not (Vogelbein et al. 1990; Baumann and Okihiro 2000). Thus liver neoplasms are the most consistent markers of carcinogen exposure.

The original wording of the "Fish Tumours or Other Deformities" BUI as described by the IJC included the occurrence of "neoplastic or preneoplastic liver tumours in Brown Bullhead or Suckers". However, no specifics were given for the definition of preneoplastic lesions. Foci of cellular alteration, depending upon morphological and staining characteristics, can be classified as basophilic, eosinophilic, vacuolated, and clear cell. Basophilic foci have been reported to advance to hepatocellular carcinoma in several species of fish (Blazer et al. 2006). However not all basophilic foci advance (Hinton et al. 1988, Baumann and Okihiro 2000). There is no definitive evidence that other types of altered foci progress to neoplasia (Bunton, 1996). No studies on progression of any foci of cellular alteration have been performed on suckers or bullheads.

Liver tumours in fish are, with rare stem cell exceptions, derived from either liver cells (hepatocellular) or bile duct cells (cholangiocellular). A proliferation of bile duct cells has been demonstrated following laboratory carcinogen exposure in a number of species (Blazer et al. 2009). Similarly such lesions (bile duct hyperplasia and cholangiocellular

fibrosis) have been reported along with tumours in wild populations from contaminated locations (Blazer et al. 2009). However none of these non-neoplastic cholangiocellular changes have been experimentally demonstrated as progressing to tumours. Also, at least in bullhead, a myxozoan parasite has been implicated in bile duct proliferation and fibrosis (Baumann et al. 2008). Because of the uncertainties concerning progression of both foci of cellular alteration (hepatic) and cholangiocellular proliferation and fibrosis (biliary), it is best that none of these preneoplastic lesions be used as an actual impairment criterion.

#### *Age and Gender:*

Two variables which might influence tumour prevalence are the age of the fish and fish gender. Age has long been recognized as being positively correlated with tumour prevalence (Baumann, 1992). This is not only because older fish have usually been exposed to environmental contaminants longer, but also because there is a latent period between induction and tumour development. For instance the prevalence of spontaneous neoplasms in medaka (*Oryzias latipes*) of ages 1 through 5 was greatest in females of age 4 and 5 and males of age 5 (Masahito et al. 1989). This same positive correlation between age and tumour prevalence has also been noted in wild populations of several species exposed to contaminants. English sole from contaminated locations in Puget Sound had a nearly 40% increased probability for having a hepatic neoplasm with each additional year lived (Rhodes et al. 1987). Similarly bullhead from the Potomac River also had an increased risk of hepatic carcinomas with age (3.5 times greater per year) (Pinkney et al. 2001). Brown Bullhead from the Black River, Ohio were found to have a significantly ( $p < 0.05$ ) higher prevalence of biliary liver cancers at ages 4 and 5 (35.5%) than at ages 2 and 3 (18.4%) (Baumann et al. 1990). Blazer (2009) also reported an increasing prevalence of liver tumours with age in Bullhead from Presque Isle Bay, particularly at ages 8 and older. Furthermore Slooff (1983) found that of 7,209 Bream necropsied in Europe, all fish with grossly visible tumours were age 7 or older. White Sucker have also shown this age and neoplasm link. In samples from five locations in the St. Lawrence Basin lip neoplasms occurred almost exclusively in fish  $> 350$ mm (length being an age surrogate) (Mikaelian et al. 2000). Thus it is important to consider age when comparing neoplasm prevalence among populations. Gender related differences in tumour prevalence have been less consistently reported than age related differences, particularly in wild exposed populations. Several species of laboratory fish have been reported to have a higher prevalence of spontaneous tumours in females (Baumann 1992). However gender was not a significant factor in the prevalence of hepatic lesions in English Sole from Puget Sound (Rhodes et al. 1987). Female Brown Bullhead from the Black River, Ohio had a significantly higher ( $P < 0.05$ ) incidence of hepatocellular carcinoma only, but not of any other neoplasms. A review of Great Lakes Brown Bullhead data taken at United States locations since 1991 reinforces the view that gender differences are not discernable. However, an analysis of the Brown Bullhead data base for Chesapeake Bay found that being female as a significant ( $P < 0.001$ ) positive co-variant for liver neoplasms (Pinkney et al. 2009). Gender equivalency among samples should be considered for comparative purposes.

### *Variability and Statistics:*

Determining whether a fish has a tumour provides a “yes” or “no” answer (binary response) rather than a number. Thus contingency table analysis is required for statistical differentiation of population values. Such statistics will test if tumour incidence is similar or different at two locations at some level of confidence. The level of confidence is determined by selecting a level of probability (P value) to indicate significance. The typical P value for biological studies is 0.05 (a 5% or one in twenty random chance of being wrong). Thus P values less than or equal to 0.05 would indicate a real difference between the tumour prevalence at the sites being compared. There are two methods which are commonly used to compute a P value from a contingency table: Chi-square and Fisher’s exact test. Fisher’s exact test gives the exact P value, while the Chi-square test calculates an approximate P value (Graphpad Software 2009). Chi-square often works better with multiple rows and columns, but the data here only has two of each.

Additionally, Fisher’s exact test is supposed to perform better when the expected values are small, which is the case here. Thus Fisher’s exact test was used to determine the P values when comparing tumour prevalence at AOC locations and reference sites. Statistical calculations were done using a QuickCalcs online calculator by GraphPad Software (Graphpad Software 2009).

This software includes a statement acknowledging that the Fisher’s test actually has three methods that can be used to compute the two-sided (two-tailed) P value. The software used here incorporated the method of summing small P values.

### *Determining Background Tumour Prevalence: Reference and Urban Non-Point Sites:*

Theoretically one reference location should have the same tumour prevalence as any other reference location (given a certain variation around the true mean, and if age and gender are not badly skewed). In fact reference site liver neoplasm prevalence by location seems to be very consistent (Table 2). The only reference location not included was Hillman Marsh at Wheatley Harbour, since that location had 9% neoplasm prevalence which would exclude its use as a reference site. The eight remaining locations only varied from 0% to 2%. Median ages ranged from 5 to 7 except for Jordan Harbour (age 4), with an overall median age of 6. Females comprised 46% of the fish sampled across locations. Nothing prevented combining the reference locations into a single data set. Thus Brown Bullhead in the combined reference data base have a liver neoplasm prevalence of 1% (n=701). This is a considerably lower prevalence than the 5% figure from Baumann et al. (1996). However this change was not unexpected, given the much expanded data base of cancer surveys in Great Lakes fish in the last fifteen years.

**Table 2. List of reference locations including number of fish sampled and number of fish with neoplasms.**

<b>Location</b>	<b>Sample Size</b>	<b>Median Age</b>	<b>% Female</b>	<b>Neoplasm (# /% )</b>
<b>Peche Island</b>	<b>34</b>	<b>5</b>	<b>56</b>	<b>0 / 0%</b>
<b>Port Rowan</b>	<b>99</b>	<b>6.5</b>	<b>35</b>	<b>1 / 1%</b>
<b>Point Abino</b>	<b>40</b>	<b>5</b>	<b>50</b>	<b>0 / 0%</b>
<b>Jordan Harbour</b>	<b>193</b>	<b>4</b>	<b>53</b>	<b>3 / 1.6%</b>
<b>Frenchman's Bay</b>	<b>101</b>	<b>7</b>	<b>50</b>	<b>1 / 1%</b>
<b>Prince Edward Bay</b>	<b>38</b>	<b>No age data</b>	<b>38</b>	<b>0 / 0%</b>
<b>Deseronto</b>	<b>96</b>	<b>5</b>	<b>41</b>	<b>2 / 2.1%</b>
<b>Morrisburg</b>	<b>100</b>	<b>5</b>	<b>49</b>	<b>0 / 0%</b>
<b>Total /average</b>	<b>701</b>	<b>6</b>	<b>46</b>	<b>7 / 1%</b>

The same sort of calculation was made using the Far Field locations sampled (Table 3). The number of bullhead with neoplasms in the four locations varied between 0% and 4% (Gross Isle with a very small sample size). The average median age was slightly younger (age 4) than at the reference locations, but the fish sampled for the group as a whole were evenly split between males and females. Again nothing prevented numbers from being combined, giving a combined prevalence of 2% (n=267). A data set of United States locations which correspond in some ways to the Canadian Far Field sites have a similar tumour prevalence (Table 4). The locations in this set include a “reference” location with modest PAH spikes near a railway bridge and a highway bridge (Old Woman Creek); two urbanized locations without a major point source (the Huron and Conneaut Rivers); and an AOC location that had undergone extensive remediation (the United States side of the Niagara River). The bullhead in this data set also have a liver neoplasm prevalence of 2% (n=204). This group from the United States combined with the Canadian Far Field locations would be best characterized as urban or having a low/moderate pollution level without a major point source. This combined group would have a liver tumour prevalence of 2% (n=471).

**Table 3. List of far field locations including number of fish sampled and number of fish with neoplasms.**

Location	Sample Size	Median Age	% Female	Neoplasms (# / %)
Gross Isle	25	5.5 (n=4)	56	1 / 4%
Queenston	43	4	48	0 / 0%
Belleville	99	4	51	2 / 2%
Gray's Creek	100	4	48	2 / 2%
Total/average	267	4	50	5 / 2%

**Table 4. Urbanized, reference (Old Woman Creek) and reclaimed AOC (Niagara) locations in the United States, including number of fish sampled and number of fish with neoplasms.**

Location	Sample Size	Neoplasms (# / %)
Huron River	62	1
Old Woman Creek	59	1
Conneaut River	43	1
Niagara River (US side)	40	1
Total	204	4 / 2%

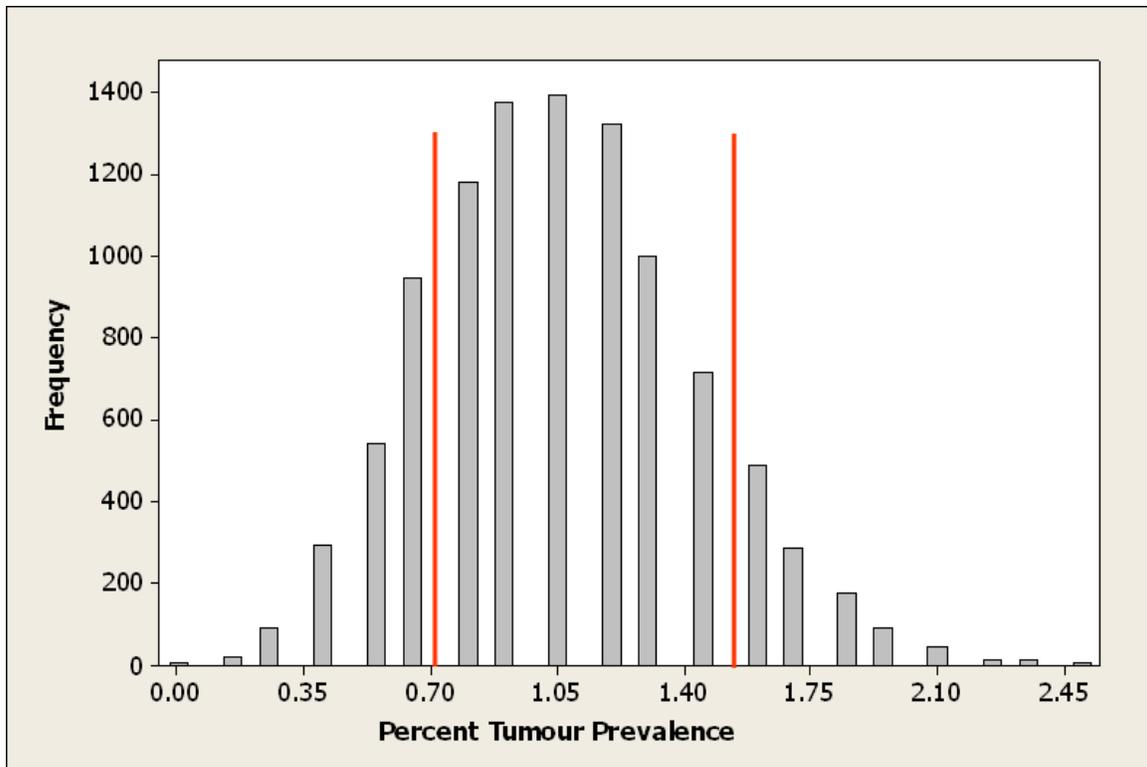
*Criterion Selection:*

The crux of criterion selection decision rests on being able to combine the reference location neoplasm data. With a data base of 700 reference fish, comparisons made with AOC locations are much more likely to be significant. The same is true of combining the Far Field and United States locations to achieve an n value of 471. The 1991 IJC guidelines state that locations determined to be impaired might be designated as restored when “tumours...do not exceed rates at unimpacted control sites”. However in decades since then there has been much discussion of how bullhead from more urbanized areas might have an increased probability of tumours even if point sources had been eliminated and exposed contaminated sediments eliminated. In other words, holding urban areas to pristine standards might not be achievable.

The list of mixed far field and other lower level polluted locations suggests that even in urbanized areas without a major point source we could reasonably expect to have a liver neoplasm prevalence of 2% or less. This leads to the question of whether the 1% prevalence seen in true reference sites can really be distinguished from the 2% prevalence in the urbanized areas with realistic manpower (budget) restraints. To answer this question we need to choose a P value to indicate significance. The typical P value for biological studies is 0.05. Using this value, even if we combine the reference data sets and then combine the far field data and United States data sets, the difference between the 1% and 2% tumour frequencies of these two groups is not significant according to Fisher's exact test.

Based on these data, the best choice for a criterion would be the 2% prevalence level, which should be achievable even in more urbanized locations. Furthermore if we apply a

bootstrapping technique to the reference site data base, the 95% confidence interval within which the true mean prevalence should exist, ranges from 0.73% to 1.5% (Figure 1). The 1.5% upper bound for the 95% confidence interval validates the choice of 2% as a delisting criterion. Since we have already sampled over 700 reference fish and over 450 far field and urban fish with a combined tumour prevalence of under 2%, we can use the combined sample size from these two groups (rounded to 1,150) as our “background prevalence” sample size for determining significant differences at the AOC locations. In order to clarify further fish tumour impairment discussions of the AOCs, this 1,150 fish data base with the assigned 2% tumour prevalence will be referred to in the rest of this report as the Impairment Criterion (IC) data base. In creating a contingency table for Fisher’s exact test, the IC number for fish with neoplasms would be (2% x 1,150) or 23 and the IC number for normal fish would be (1,150 – 23) or 1,127. A hypothetical site having a hundred fish sample and a 5% liver tumour prevalence would have a P value (used to detect a statistically significant difference between liver tumour prevalence (%) in an AOC and reference criterion of 2%; should be less than 0.05 or 5% for significance) of 0.06, which is not statistically significant.



**Figure 1. Bootstrapped 95% confidence interval (0.73 to 1.5% as indicated by the two vertical lines) determined for the liver tumour prevalence of bullhead at reference locations. This confidence interval was estimated using 10,000 iterations.**

### Determination of BUI Status

The Bay of Quinte AOC samples were taken in 2004 and 2005 from the Trenton waterfront, Belleville waterfront, and at Deseronto. The more contaminated Trenton location had a bullhead liver tumour prevalence of 4%. There is no statistically significant difference between liver neoplasm prevalence in the Bay of Quinte and that of the delisting criterion of 2% based on reference sites in the Lower Great Lakes (see the Great Lakes Fish Tumour database for all the raw data) (Table 5). Given the data set, the tumour rate would need to be at least 6% in the Bay of Quinte AOC to be statistically different from the reference criterion of 2%.

Thus the delisting criteria has been met and the status of the Fish Tumours or Other Deformities beneficial use for the Bay of Quinte can now be changed to 'not impaired'.

**Table 5. Canadian AOCs with completed surveys (sub-locations and multiple year samplings combined) with sample sizes, ages, gender percentage, neoplasm numbers and prevalence, and significantly differences (S), or not (N), from the impairment criterion.**

Exposed Site	Sample Size	Median Age	% Female	Neoplasm # (%)	P Value	Significance
Wheatley Harbour	100	7	47%	4 (4%)	0.27	N
Niagara River	101	5	50%	3 (3%)	0.47	N
Hamilton Harbour	200	8	48%	11 (5.5%)	0.013	S
Toronto and Region	213	7	45%	8 (3.8%)	0.14	N
Bay of Quinte at Trenton	100	5	42%	4 (4%)	0.27	N
St Lawrence River	100	5	46%	2 (2%)	1.0	N

### **Recommendation**

Based on the above review, the conditions in the Bay of Quinte AOC show that the “Fish Tumours or other Deformities” BUI should be considered as not impaired in the Bay of Quinte AOC.

### **Future Monitoring Requirements**

A review of sediment data for the Bay of Quinte (Golder 2012) indicates that with respect to contaminants, only a few areas along the urbanized waterfronts have elevated levels of some metals and organic substances, and concentrations of these contaminants are decreasing compared to historical levels. The older, deeper sediment contains higher levels of contaminants than the surficial sediment.

A comprehensive survey of sediment undertaken in 2013 at 20 Belleville waterfront sites showed that although PCBs and PAHs can be found along the waterfront, there were no sites where the levels of PCBs exceeded the Canadian Federal Probable Effect Level and no sites where PAHs exceeded the Canadian Federal Severe Effect Level (MOECC 2014).

A more recent sediment survey at the Trent River mouth undertaken by Environment Canada (Marvin 2015) shows that PCDD/F concentrations and corresponding TEQs are relatively low, compared to PCDD/F concentrations in typical Lake Ontario sediments and sediments previously sampled near the mouth of the Trent River in 2008 and 2011. All TEQ concentrations were below the CCME Canadian Federal Probable Effect Level (PEL, 21 pg/g TEQ); in fact all TEQ concentrations were less than half the PEL value (Marvin 2015).

The recent assessment of the Beneficial Use #4 Fish Tumours or Other Deformities for the Bay of Quinte Area of Concern which focuses on liver assays in Brown Bullheads collected at the Trenton and Belleville waterfronts in 2013 show that although contaminant levels in Brown Bullheads from Trenton remain elevated, fish from Belleville have intermediate values and are not statistically different from the reference site. Over all, the consumption restrictions have been improving in recent years as contaminant concentrations in fish have declined appreciably over the past decade (Ridal, 2014).

Thus it is likely that current levels of fish tumours are the same, or have decreased, in the Bay of Quinte since the fish tumour assessment was undertaken. Thus no future monitoring is required.

## **Glossary**

**Basophilic:** Relating to tissue components that stain readily with basic dyes used for microscopic examination.

**Cholangiocellular:** Pertaining to the bile ducts.

**Clear cell:** A type of cell, especially a neoplastic one, which does not take on a color with the ordinary tissue stains used for microscopic examination.

**Eosinophilic:** Containing the White blood cells eosinophils. The cytoplasm (the fluid environment inside the cell) of eosinophils is filled with coarse, refractile granules that stain intensely with acid dyes.

**Epithelia:** Membranous tissue covering internal organs and other internal surfaces of the body.

**Epizootics:** An epidemic outbreak of disease in an animal population.

**Etiology:** The cause or origin of a disease.

**Far field site:** Far field site is generally further downstream of the exposed site and is often used to look for improved fish performance with dilution of the contaminant source.

**Fibrosus:** A proliferation of fibrous connective tissue that occurs normally in the formation of scar tissue to replace tissue lost through injury or infection.

**Foci:** Plural of focus. The origin or centre of a disseminated disease.

**Hepatic:** Having to do with the liver.

**Hepatocellular:** Of or pertaining to the cells of the liver.

**Medaka:** A small Japanese fish (*Oryzias latipes*) commonly found in rice fields and often used in biological research.

**Myxozoan parasite:** The Myxozoa are a group of parasitic animals of aquatic environments.

**Necropsied: Autopsy:** An examination and dissection of a dead body to determine cause of death or the changes produced by disease.

**Neoplasia:** The process of abnormal and uncontrolled growth of cells.

**Neoplastic:** An abnormal new growth of tissue in animals or plants; a tumour.

Papillomas: A benign tumour growing exophytically (outwardly projecting) in finger-like fronds.

Preneoplastic: Before the formation of a tumor.

Reference Site: A sampling site selected for its relatively undisturbed conditions, generally upstream of the exposed zone in a river system. It is a specific locality which is unimpaired or minimally impaired and has habitat similar to that of the exposed zone. At sites within a lake, a Reference site is a site as similar as possible to the Exposure Zone except for the presence of the contamination source.

Retrovirus: Retroviruses belong to the Retroviridae family of viruses. The genetic material of retroviruses consists of ribonucleic acid (RNA), instead of deoxyribonucleic acid (DNA). Retroviruses are known to lead to certain types of cancers.

Vacuolated: Formed into or containing one or more small membrane-bound cavities within a cell.

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