(Deputy Minister Letterhead)

CLASSIFICATION

200X-XXX-XXXXX
EKME # XXXXXX

MEMORANDUM FOR THE MINISTER

Epidemic of a Novel, Cancer-causing Viral Disease may be Associated with Wild Salmon Declines in BC

(Information Only / Decision Sought / Signature Required)

Comment [MSOffice1]: Alternative title: Genomic profiles suggest presence of viral disease in wild Pacific salmonids in BC

SUMMARY

A novel viral disease may be a key factor in high variability in performance and general declines in abundance of sockeye, Chinook, and coho salmon in Southern BC. Genomic data from gill, liver and brain tissue elucidated a powerful anti-viral signature in >75% of sockeye salmon returning to the Fraser River in 2005. This signature was associated with high levels of mortality in the Fraser River in 2006. Indications of tumour activity within the "anti-viral" brain profile led to the identification of ocular tumour-like growths in 30-40% of returning adults in 2006. Tumour incidence was increased to 50% of returns in 2008, but declined to less than 20% for fish at the spawning grounds, indicative of tumour-associated mortality in the river. In 2009, a year in which only 1.35 of the estimated 10 million sockeye returned to the river, tumour incidence in returning fish rose to 70% in the ocean, dropping to 50% upon river entry, indicative of tumour-associated mortality prior to river entry. A high incidence of ocular tumours have recently also been discovered in out-migrating smolts of sockeye, coho and Chinook salmon from a wide range of southern BC stocks, with levels declining significantly in the first few months in the ocean (from 40-50% to 10% June-Sept) in all three species. The salmon leukemia virus, the proposed causative agent of plasmacytoid leukemia in Chinook salmon in the late 1980's, is the best fit to the genomic and tumour evidence to date. Establishing a direct link to this virus, obtaining a viral sequence and a tool for molecular screening, and conducting disease challenge and epidemiological research is paramount if we are to establish the potential role of this virus in salmon declines and to develop mitigative measures for control.

Comment [MSOffice2]: decline in tumor prevalence does not necessarily mean fish with tumours died, it could simply mean tumors regressed.

Comment [MSOffice3]: ??? ? Is there strong evidence to directly link tumour decline=mortality?

Background

I. High En-route losses of sockeye salmon stocks returning to spawn in the Fraser River linked to a viral disease signature

Deleted: retroviral disease

- Over the past 12 years, sockeye salmon stocks have experienced unprecedented levels of en-route and pre-spawning mortality during return migration in the Fraser River.

While elevated river temperatures are clearly associated with these losses, there is growing evidence that a novel disease is also impacting survivorship in river. By combining biotelemetry and genomics, the Molecular Genetics lab at PBS identified a viral-response profile associated with poor survivorship of adult migrating salmon in the river. Salmon up to 300 km seaward of the Fraser River carrying this "viral" signature in gill tissue had a 16-times lower probability of arriving to spawning grounds than those carrying a "healthy" signature. There was also an association of the "viral" signature with pre-spawning mortality, with >80% of the pre-spawning mortalities (at spawning grounds) carrying the "viral" signature.

- The "viral" signature has been observed in multiple tissues (gill, brain, liver) and in varying proportions of sockeye salmon in all years in which functional genomics studies have been carried out (2003, 2005, 2006). In 2005, only 26% of returning fish were negative for the "viral" signature in all tissues.
- The genomic profile from brain tissue was highly correlated with the "viral" profile in gill tissue, but also showed a strong stimulation of the sensory region of the brain (visual, olfactory), a more advanced maturation profile, and stimulation of pathways associated with tumour activity. Brain dissections (in 2009) revealed that 30-40% of adult migrating sockeye salmon in 2006 contained tumour-like growths in their optic lobe, a region that was highly stimulated in the brain profiles.
- In 2008, a year of exceptionally high levels of en-route and pre-spawning mortality in the river, brain dissections (in Sept 2009) revealed similar ocular tumours in 50-60% of adult sockeye salmon in the marine approaches and lower Fraser River, but only 20% of fish at spawning grounds (N=250), implicating the potential association of tumours with the extensive en-route losses.
- In 2009, only 1.35 million of the expected 10 million returning Fraser River sockeye salmon arrived at the river. 2009 brain dissections revealed the highest incidence of ocular tumours thus far, with tumours in over 70% of salmon in the marine approaches and 50% in the lower river (N=63). These data imply that the tumours may also be associated with losses of adult salmon in the Strait of Georgia. Estimates put those losses as high as 0.9 million fish.
- The viral-tumour linkage in our data is suggestive of the presence of a virus that can induce cancer; viruses in the retroviral family are most commonly associated with tumours. There are additional elements in the expression signatures that are consistent with a retroviral infection, as a large number of genes associated with retroviral control of host immunity are stimulated. As retroviruses are often vertically transmitted (mother to egg), in September of 2009, we looked to the smolts to see if similar genomic signatures and tumour activity was present in this earlier life-history stage.
- In 2008, 50% of sockeye smolts in the lower river in May and the ocean in June contained the viral-tumour associated brain profile. Incidence for the endangered Cultus Lake stock was 30% in age-1 parr in November and 80% as smolts began their river decent in April. Incidence at Chilko, a large indicator stock for Fraser sockeye, was 50% in smolts leaving the lake. Brain dissections revealed a similar incidence level of tumours, and the presence of tumours in stocks outside of the Fraser River.

Comment [MSOffice4]: Sinc e the abnormalities observed in the brains have not been confirmed to be tumours it would be better to use the word "anomalies" thoughout

Comment [MSOffice5]: ?

Comment [MSOffice6]: With out histology of the brain adnormalities this statement is highly speculative

Comment [MSOffice7]:

These data imply that the viral infection associated with tumour activity is already active in natal rearing areas; hence, there is the potential for the virus to impact survivorship in all stages of salmon development.

- Ocular Tumours were also observed in coho, Chinook, and sockeye smolts sampled in the ocean in June and Sept/Oct of 2008 and 2009 (N=400). For each species in each year, there was a notable decline in tumour incidence from June to Sept/Oct (average 40% incidence in June, 10% in Sept/Oct). This data indicate that the tumours are associated with early ocean mortality in all three species.
- Importantly, in all three species, tumours were found in a wide range of stocks rearing in the Strait of Georgia. These data imply epidemic levels of disease in southern BC and Washington.

II. The Salmon Leukemia Virus causing Plasmacytoid Leukemia—Best link to the genomic evidence, but not yet confirmed

- There is strong evidence to suggest that the genomic profiles and tumours observed in all three salmonid species are linked to Plasmacytoid Leukemia (PL), a disease that is purported to be caused by a Salmon Leukemia Virus (SLV). This relatively unknown virus was associated in the 1980's through 1990's with mortalities in cultured Chinook salmon in fresh and saltwater in BC and potentially associated with mortalities of Coho in a BC enhancement hatchery. Moreover, challenge studies showed a high susceptibility of Chinook, sockeye and coho salmon to the virus, low susceptibility of Atlantic salmon, and no measurable effect on Rainbow trout. Most importantly, the virus is associated with ocular tumours in a proportion of affected fish.
- SLV causes severe anemia (also called Marine Anemia), with primary infections involving the kidney and spleen. In advanced infections, proliferating plasmablasts move into secondary organs, including liver, pancreas, intestine, gill and brain. Involvement of secondary organs varies among individuals.
- In 1991, 6% of wild Chinook salmon in the Strait of Georgia were positive for PL/SLV (N=116), and 0% of sockeye were positive (N=150). If the viral-tumour profiles described herein are PL/SLV, incidence levels in the wild are presently an order of magnitude higher, with >75% of sockeye and Chinook salmon affected. Most notably, this is the time-period during which behavioral shifts, highly fluctuating losses, and large-scale declines in southern BC stocks of sockeye, Chinook and coho salmon have occurred.
- Linkages of SLV with our genomic and physiological data are thus far indirect but strong
    - Genomic signatures indicative of retroviral activity and tumourogenicity
    - Incidence of ocular tumours (predicted originally from brain profiles)
    - Involvement of gill, brain and liver but not muscle tissue
    - Pale gills, enlarged spleen/kidney
    - Disease in Chinook, coho and sockeye salmon, three species susceptible to PL

Comment [MSOffice8]: Such clinical signs are observed for a multitude of diseases and are not strong evidence solely associated with SLV.

Comment [MSOffice9]: Has anyone looked at Atlantic Salmon brains for similar abnormalities? Is it possible that such brain anomalies do indeed exist in farmed Atlantics but that no one has looked?

- Location of disease, in stocks that rear in the Strait of Georgia, incidence in fresh and saltwater
- Percentage involvement of secondary tissues similar to histological observations. In 2005, multiple tissue profiles of the same fish showed 40% of sockeye salmon with viral profiles in liver, 30% in brain, and 20% in gill tissue. Importantly, only 26% of fish were negative in all three tissues. Given that these are all secondary organs, we predict that rates of infection could exceed 90%.

III. Next Steps

- Evidence from genomics research indicates a possible linkage between environmentally-induced disease associated with the Salmon Leukemia Virus and episodic mortality in sockeye, coho, and Chinook salmon both in freshwater and saltwater environments. This disease and current environmental conditions may be major factors in the fluctuating annual returns and general declines in abundance of many stocks of Pacific Salmon species in Southern BC.
- Most of the previous data on the disease and associated mortality comes from cultured fish, because these fish are in captivity and can be observed when they become sick. In wild fish, we don't observe mortality events (especially in the ocean) because the fish simply disappear. There is no regular disease/fish health screening on wild salmon. Evidence from culture operations indicates that the presence of viral infection does not necessarily cause high levels of mortality, but that infected fish become sick and may suffer mortality when they are stressed.
- Atlantic salmon, the key farmed salmonid species in BC, is not highly susceptible to SLV. The size of the Chinook aquaculture industry in BC is very small but this species is highly susceptible.
- At the present time, we do not know how long this disease has persisted in southern BC. It is possible that this virus has been endemic within the region for decades, but the incidence of disease and mortality has increased due to enhanced stress from shifting environmental conditions. Environmentally enhanced levels of disease may also have served to spread the virus to a wider array of species and stocks. It will be important that we build a better understanding of the epidemiology of this virus and resultant disease if we are to develop appropriate mitigative strategies for control.
- Mitigative actions may be possible for fish reared in hatcheries. Broodstock screening for the virus may be possible once we obtain a DNA sequence of the virus. Husbandry practices could also be improved to minimize horizontal transfer of the virus. Anti-viral treatments for eggs may also be effective.
- Given the indirect evidence that this disease is most virulent when salmon are stressed, management of wild fish will require that we develop a better understanding of the link between the viral-associated disease and the environment (e.g. temperature, salinity, food availability). Once these relationships are better understood, regular screening of smolts and adults and tracking of environmental conditions would allow

managers to adjust escapement estimates according predicted mortalities associated with this disease.

- New genomics tools enabled the work that has been conducted to date that reveals the potential involvement of SLV with current poor survival of salmon in southern BC. Viral diseases are among the most elusive of all pathogenic diseases, because they are difficult to detect and identify, their virulence can depend upon the level of stress of the fish, and because they tend to weaken immunity and increase the susceptibility of fish to other pathogens and to predation. Genomics can also contribute to the rapid development of new molecular approaches allowing full characterization of the virus, determination of its relationship with fish abundance, and strategies for mitigation.
- If SLV is confirmed as a major factor in salmon declines, it may mean that Pacific salmon in southern BC are experiencing a significantly altered environment. A better understanding of the underlying reason for the variable but generally low levels of survival in salmon will facilitate better management of the resource and possibly ease tensions among user groups.
- Given the cultural and economic importance of Pacific salmon in BC, these preliminary findings need rapid confirmation/refutation. A research plan has been developed and could be conducted by Pacific region DFO scientists.

Analysis / DFO Comment

- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

…/2

Recommendations / Next Steps

- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
- XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

Claire Dansereau

_____

I concur,
Gail Shea **(*this part only if for decision*)**
Minister, Fisheries and Oceans

Attachment (1) **(*if applicable*)**
Description of the attachment(s) **(*if applicable*)**

Officers / DGs / ADMs / initials of the admin clerk or typist

Government of Canada
Fisheries and Oceans

MECTS # 200X-XXX-XXXXX
EKME # XXXXXX
FILE / FICHIER #

To:
Pour Claire Dansereau Date:

Object: **TITLE**
Objet:

From / De: DG

Via: ADM / SMA

☐ Your Signature Votre signature	☐ Information
☐ For Comments Observations	☐ Material for the Minister Documents pour la Ministre

Remarks:
Remarques:

DISTRIBUTION

Drafting Officer/ Rédacteur: OFFICER (TEL #)/DIR/DG
C:\DOCUMENTS AND SETTINGS\TROTTIERS\DESKTOP\TEMPLATES\TRANSMITAL SLIP (BILINGUAL) - FICHE DE TRANSMISSION (BILINGUE).DOC