CLAIM # 2101
Province of Infection: Ontario
Province of Residence: Ontario

DECISION

BACKGROUND:

1. The estate of the deceased submitted an application for compensation under the Transfused HCV Plan (the "Plan"), as set out under the terms of the 1986-1990 Hepatitis C Settlement Agreement (the "Agreement").

2. By letter dated April 22, 2004, the Administrator denied the claim on the basis there was insufficient evidence that the deceased's death was caused by HCV.

3. The estate requested that a Referee review the decision of the Administrator.

4. An oral hearing in this matter was held in Toronto, Ontario, on November 2, 2005, at which time it was agreed that additional medical information would be sought. Final submissions were made in writing.

ISSUE:

5. Section 3.07 of the Settlement Agreement provides that a person claiming to be a Family Member of a HCV Infected Person who has died must deliver, to the Administrator, proof that HCV caused the death of the HCV Infected Person. Section 3.07 states:

> A person claiming to be a Family Member, referred to in clause (a) of the definition of Family Member in Section 1.01 of a HCV Infected Person who has died must deliver to the Administrator, within two years after the death of such HCV Infected Person or within two years after the Approval Date or within one year of the claimant attaining his or her age of majority, whichever event is the last to occur, an application form prescribed by the Administrator together with:
>
> (a) proof as required by Sections 3.05(1)(a) and (b) (or if applicable, Section 3.05(3) or (4) and 3.05(5) and (6), unless the

required proof has been previously delivered to the Administrator; and

(b) proof that the claimant was a Family Member referred to in clause (a) of the definition of Family Member in section 1.01 of the HCV Infected Person.

6. The relevant part of section 3.05(1)(a) states:

A person claiming to be the HCV Personal Representative of a HCV Infected Person who has died must deliver to the Administrator ... an application form prescribed by the Administrator together with:

(a) proof that the death of the HCV Infected Person was caused by his or her infection with HCV ....

7. The estates' claim was refused on the basis of Article 3.05(1)(a) as the Administrator found the estate did not meet the criteria for compensation, because there was no evidence to support a finding that HCV caused the deceased's death.

8. The issue to be determined in this matter is, therefore, if the deceased had HCV, did it cause or materially contribute to his death.

FACTS:

9. The following facts were not in dispute:

- The deceased was infected with Hepatitis B for which he was under the care of Dr. S. Chris Pappas, M.D. FRCP;

- the deceased was admitted to Sunnybrook Hospital on June 1, 1990. At that time, he was transfused with 11 units of blood. During the traceback, the donors of 9 units were identified as negative and the donors of two units could not be located. The deceased was subsequently transfused on July 1st, 1992. He was again transfused post-class with 6 units of platelets;

- the deceased died in July 1996 of end stage liver disease. Hepatocellular carcinoma was also present.

EVIDENCE AND SUBMISSIONS:

10. The deceased was tested for the Hepatitis C virus. Specific testing for the infection was done in June and September 1995. These test results indicated that

the deceased had the antibody for HCV, but the PCR testing did not detect the virus at that time.

11. The deceased's physician, Dr. El Kashab, completed the Treating Physician form, indicating he had known the deceased for 2 years. When asked if HCV materially contributed to his death the doctor answered yes and wrote:

> the patient has chronic Hepatitis B – Additional HCV infection contributed to the severity of liver disease and the occurrence of hepatoma which resulted in death.

12. Based on this information, the Administrator obtained an expert opinion. The opinion was dated April 1, 2004, and provided by Dr. Gary Garber, Professor, and head of the Division of Infectious Disease at the Ottawa Hospital.

13. Dr. Garber reviewed the deceased's file, and noted that the deceased's PCR was "negative for hepatitis C" in 1995. He advised that this indicates the "patient was not actively infected with hepatitis C or at a very low grade of infection."

14. Dr. Garber, also noted that the deceased suffered from severe Hepatitis B. It was Dr. Garber's opinion that "with such severe disease in 1990 requiring blood transfusion, the natural history of advanced liver disease would include death from liver failure or hepatocellular carcinoma over time." In addition, Dr. Garber opined:

> There is no material information or evidence to support that Hepatitis C infection contributed to his death as the signs and symptoms of advanced liver disease were already present at the time of his suspected (and not shown) hepatitis C transfusion.

15. In support of its appeal, the estate submitted the TRAN 2 completed by Dr. Pappas, dated February 9, 2004. Dr. Pappas treated the deceased from May 1988 to January 1991. Dr. Pappas also indicated that the deceased's infection with HCV materially contributed to his death. In addition, Dr. Pappas states:

> Exposure to HCV, in the setting of existing chronic hepatitis B may increase the risk of decompensation and the development of heptocellular Ca.

16. Dr. Pappas also provided an accompanying report, also dated February 9, 2004. In that report, he states the deceased was under his care from May 1988 to January 1991. He indicates:

> There were no clinicobiochemical features of his disease to suggest the presence of HCV infection prior to that time, or subsequently, when he was under my care.

17. Dr. Pappas also acknowledged the positive test for the HCV antibody, but that the PCR testing did not detect the virus at that time. Dr. Pappas indicated that:

> This pattern of testing would be compatible with previous HCV exposure and current lack of viral replication in serum. Alternatively but less likely this pattern is compatible with a false positive EIA testing and no previous or concurrent presence of HCV. Finally, it is possible that the PCR HCV-RNA performed at that time was not sufficiently sensitive to detect low level viremia;

18. In response to further inquiries on behalf of the estate, Dr. Pappas, in correspondence dated January 11, 2005, provided the following additional explanation for the deceased's negative PCR results:

> [The deceased's] HCV serology (anti-HCV antibody testing) was clearly positive. Most patients with this positive serology (>75%) are found to have evidence of active HCV infection as evidenced by HCV-RNA testing being positive when it is performed using sensitive accepted methodology. In [the deceased's] case, a far more likely explanation for his HCV-RNA being negative is not the absence of active infection but the performance of insensitive testing (as was common during the time period in question)….

19. Dr. Garber was provided with Dr. Pappas' January 11, 2005 correspondence, and in his March 10, 2005 report in response, addressed the issue of the HCV testing :

> ….The next issue is the fact that the PCR for hepatitis C was negative. As much as it is tempting to question the sensitivity of the testing at that time nonetheless that is the testing that was available and similarly this is the testing that was used as standards for the Compensation Program. Therefore in light that the PCR test was negative, regardless of when he was infected with hepatitis C he did not have active hepatitis C infection. Dr.

> Pappas has agreed that this certainly is a possibility and has brought up the possibility that either the antibody test or the PCR test could have been an error. Regardless, these are the results that we must deal with…

20. The estate points out that Dr. Garber does not directly address the possibility that PCR testing in 1995 was not sufficiently sensitive, and submits he does not fully address the fact that EIA testing was positive, while the accompanying PCR testing was negative. The estate submits that Dr. Garber's conclusion that the deceased did not have active hepatitis C infection is based on a straight reading of the PCR test.

21. The estate maintained that even assuming the PCR test result was correct, there is information that even with a negative PCR test (that is below the detectable level), one can still have active hepatitis C infection. The estate notes that Dr. Pappas points out that even if the deceased did have a low HCV-RNA reading, that could not be detected by 1995 PCR testing (or presumably even more sensitive PCR testing), this does not mean he did not have active hepatitis C infection.

22. Specifically, Dr. Pappas writes in his January 11, 2005 report:

> Furthermore, even if the level of HCV-RNA was low and thus difficult to detect, this does not mean low-grade infection as speculated by Dr. Garber. There is no correlation between HCV-RNA levels and disease severity, particularly in patients with HBV coinfection where, as noted in the provided references, HCV-RNA levels may be depressed by paradoxically disease progression and the risk of decompensation is significantly increased…

23. The estate pointed out that in support of his position, Dr. Pappas provides recent medical research on HBV and HCV co-infection. One of these reports addresses the issue of HCV-RNA levels in HBV-infected patients. The report "HBV Superinfection in Hepatitis C Virus Chronic Carriers, Viral Interaction, and Clinical Course" by Sagnelli et. al. found that HCV detection was often difficult and in fact inhibited in chronic HBV-infected patients:

> The inhibition exerted by HBV on the HCV genome also has been shown in chronic HBV/HCV concurrent infection. In our previous Italian multicenter study on patients with chronic hepatitis, **the prevalence of those with HCV-RNA in serum was significantly higher in the group with HCV infection alone (90.7%) than in those with chronic HBV/HCV concurrent infection (65.2%).** [emphasis added]

24. The estate pointed out that the above indicates that HBV infection can actually suppress the detection of HCV by inhibiting the production of HCV-RNA. It submits that the deceased's chronic HBV infection could certainly have played a role in the detection of HCV-RNA in his serum, and sufficiently explains why the deceased tested positive for HCV under EIA testing, and negative under PCR testing.

25. The estate maintained that the above demonstrates convincingly that the deceased was co-infected with HCV. The estate points out that the EIA test showed a positive result, and the negative PCR tests can be explained by sufficiently insensitive testing at the time, as well as by recent medical evidence that demonstrates that HBV infection renders HCV detection more difficult.

26. In his January 11, 2005 report, Dr. Pappas states:

> It is based on this peer-reviewed medical literature and my clinical experience and opinion that on the balance of probability HCV infection did materially contribute to [the deceased's] death.

27. The estate pointed out that this is contrary to Dr. Garber's finding that the deceased's death could have been caused by HBV infection alone, referred to in paragraph 14.

28. Dr. Garber details further in his March 10, 2005 report:

> The natural history of advanced hepatitis B infection, even if medically stabilized would be ultimate deterioration over time and this is the group that is at risk of developing hepatocellular carcinoma and death. In fact, the course of his disease and his demise in 1996 would be completely compatible with his hepatitis B disease independent of whether he had hepatitis C or not….

29. Dr. Garber goes on to state in his concluding paragraph:

> Considering that his deterioration and ultimate death is completely compatible with Hepatitis B infection alone, there is no evidence to support the fact that active Hepatitis C infection materially contributed to his death. To conclude otherwise in the absence of any evidence that there is active Hepatitis C infection is purely speculative.

30. In response to the point that the deceased was already suffering from advanced liver disease due to HBV infection, Dr. Pappas points out that the deceased's disease and ultimate death still may have been caused or exacerbated by subsequent HCV infection:

> …In reference to Dr. Garber's observation that the signs and symptoms of advanced liver disease were already present at the time of the deceased's HCV infection, the point is not that they were present but rather whether the HCV superinfection materially contributed to the deceased's death. Patients may have signs and symptoms of advanced liver disease but remain compensated with adequate liver function until another event, such as HCV superinfection, supervenes and leads to liver decompensation and death.

31. In the vein of HCV superinfection on an HBV-infected patient, Dr. Pappas points to medical literature which finds that HCV and HBV co-infected patients carry a much higher risk of cirrhosis and hepatocellular cancer than those infected with HCV or HBV alone. For instance, in one published article, Chun-Jen Liu et. al find:

> …Moreover, the HCV- and HBV-coinfected patients have been shown to carry a significantly higher risk of developing cirrhosis or hepatocellular carcinoma than those with HCV or HBV infection

alone.

32. Further, in a study of chronic HBV-infected patients, Liaw YF et. al. found that acute HCV superinfection led to "a significantly higher cumulated incidence of cirrhosis (48% at 10 years) and hepatocellular carcinoma (14% at 10 years, 21% at 15 years, and 32% at 20 years) than acute HDV superinfection or active chronic hepatitis B."

33. Therefore the estate maintained that the added factor of HCV superinfection significantly increases the incidence of hepatocellular cancer over HBV infection alone.

34. Dr. Garber agreed that the effect of HCV infection on an HBV-infected patient can be extremely grave:

> ...I agree with Dr. Pappas that co-infection clearly can be problematic and in one of his references it clearly shows how more rapidly a hepatitis C infected patient will deteriorate when they get active hepatitis B. This [is] why vaccination with hepatitis B is virtually mandatory in anyone found to be hepatitis C infected.

35. The estate maintained that there is significant evidence to demonstrate that the deceased did have HCV infection, in addition to chronic HBV infection.

36. Further, the estate submitted that the medical evidence demonstrates that Hepatitis C infection significantly increases the chances of hepatocellular cancer in patients with Hepatitis B, and that consequently, the deceased faced a markedly higher chance of liver cancer and death.

37. The estate maintained that the evidence of the deceased's HCV infection (in particular the positive EIA test), coupled with the unrefuted medical evidence that HCV/HBV co-infection leads to a high incidence of hepatocellular cancer, supports a finding that the deceased's death was caused by HCV infection.

38. The estate also pointed out that in order to succeed, it is not required to prove the deceased's death was caused solely by HCV. Rather the legal test is whether HCV materially contributed to his death. Consequently, the estate argued that Dr. Pappas' failure to state that HCV was the sole cause of the deceased's death does not disentitle his estate from compensation by the Fund.

39. The estate also submitted that while the literature does not make specific reference to the deceased's case, it still is helpful in understanding the scientific underpinnings of Dr. Pappas' opinion, and should be given significant weight in a decision-making process that requires a comprehension of complex medical

processes.

40. The estate also submitted that in considering the evidence, I ought to give significant weight to the reports provided by Dr. Pappas. The estate pointed out that Dr. Pappas is an expert in the field of liver disease, and is currently the Clinical Research Director at the Texas Liver Institute at St. Luke's Episcopal Hospital in Houston, Texas. He has also published extensively on matters relating to liver diseases and their treatment.

41. The estate also noted that in addition, and perhaps more importantly, Dr. Pappas was the deceased's treating physician for nearly three years, and as such had close knowledge of the deceased's health and medical history.

42. The Administrator maintained its position that there was insufficient evidence to conclude the deceased had the HCV virus at or before the time of his death. The Administrator further maintained that the estate has failed to establish that the deceased's death was caused by HCV.

ANALYSIS:

43. Article 3.05(1)(a) of the Agreement requires, as a threshold test for a claim, proof that a deceased's death was caused by his or her infection with HCV.

44. The estate, therefore, must establish that the deceased's death was caused by his infection with HCV. As stated by Arbitrator Outhouse, in Decision 157:

> The burden is on the Claimant to establish, on the balance of probability, that the death of the Primarily Infected Person was caused by HCV infection. Such proof is not required to be absolute but must meet the civil code balance of probabilities.

45. As the estate must establish that the deceased's death was caused by HCV, the first fact which must be established is that the deceased had the HCV virus at some time prior to his death, and not simply the antibody. However, as pointed out by Dr. Garber, in his April 1, 2004 correspondence, the PCR negative testing indicates that the claimant was not "actively infected with Hepatitis C or a very low grade of infection".

46. As pointed out by counsel for the Administrator, the absence of the virus or alternatively a low grade of virus strongly militates against the estate establishing, on a balance of probabilities that the deceased's death was "caused by his or her HCV infection".

47. Dr. Pappas, in his correspondence of January 11, 2005 did ultimately suggest that the "far more likely" reason for the negative result of the PCR HCV-RNA test was insufficient sensitivity to detect low level viremia. However, he does not explain his departure from his earlier correspondence.

48. Specifically, in his initial report of February 9, 2004, Dr. Pappas suggested three possible interpretations of the test results. It is apparent that at that time, he was of the view that the most likely explanation was that the testing indicated exposure, but with a current lack of viral replication in serum (i.e. no virus). He indicated that it was only "possible" that the PCR HCV-RNA performed at that time was not sufficiently sensitive to detect low level viremia.

49. While Dr. Pappas indicates that his subsequent view, set out in his January 11, 2005 correspondence, is based on a review of the medical literature and his experience, it is not apparent why his evaluation of the likelihood of the PCR HCV-RNA testing not being sufficiently sensitive to detect low level viremia changed from a "possibility" to "far more likely."

50. Further, while the literature submitted by Dr. Pappas, and relied on by the estate, indicated that 75% of those with positive serology (ie. the antibody) are found to have HCV, this provides little assistance to the estate, as there is no way to determine whether the deceased comes within that group, or the remaining 25% . In other words, it does not assist in determining whether the deceased had the HCV virus. Even if the test performed on the deceased was inadequate or insensitive, this would not prove that the deceased had the virus.

51. Further, there appears no clinical indication that the deceased had the HCV virus. Dr. Pappas treated the deceased from 1988-1991, but indicates that during his treatment he observed no "clinicobiochemical features of his disease to suggest the presence of HCV infection…"

52. Dr. Garber also indicated there is nothing in the deceased's condition that suggested his disease progression was related to anything other than HBV. Rather, he notes there is no indication of the deceased having HCV during his illness. In particular, he notes that after the transfusion there is "no evidence over the next three months that there was a change in his liver function test or his clinical condition suggestive of an acute hepatitis C infection."

53. Dr. Garber also notes in his March 10, 2005 report, that Dr. Pappas refers to significant clinical changes occurring when a mono infection becomes co-infection, yet no clinical changes were present in the case of the deceased. Rather, as pointed out by counsel for the Administrator, the evidence suggests that there were no clinical indications that he had the virus, which is consistent with the negative test result.

54. Consequently, I find there is insufficient evidence to conclude the deceased had the HCV virus at or before his death.

55. Notwithstanding this finding, I will also address the issue of whether HCV, if the deceased were indeed infected, materially contributed to his death.

56. The estate is correct in pointing out that the test in determining whether a deceased's death was caused by his or her infection with HCV is whether HCV materially contributed to the death.

57. As indicated earlier, Dr. Pappas' original opinion was simply that "it is **possible** that underlying chronic HCV infection contributed to his increased risk of developing decompensated liver disease and/or heptoma in the setting of established chronic HBV infection". [emphasis added]

58. While Dr. Pappas subsequently indicated, in his January 11, 2005 correspondence, that "on the balance of probability HCV infection materially contributed to the deceased's death, " this is not based on any clinical evidence regarding the deceased. Rather, this opinion is based on "published information describing the complex clinical relationship between HCV and HBV infection."

59. As submitted by Counsel for the Administrator, the literature alone does not create "probable grounds" – at least not without some evidence to establish the deceased meets some personal criteria evidenced in the literature. In fact, the literature, by its own admission, is not authoritative. Rather, in the article submitted by the estate, titled "HBV Super Infection and Hepatitis C Virus Chronic Carriers – a Viral Interaction and Clinical Course" the authors state:

> very little is known about HBV/HCV acute concurrent infection because only a few case reports are available in the literature. Also, little is known about HBV acute infection when it develops in HCV chronic carriers, but the few case reports published on the topic suggest an association with a severe clinical presentation.

60. It is worth noting again that Dr. Pappas did not witness any clinical presentation when he treated the deceased. Consequently, while Dr. Pappas was the deceased's treating physician for almost three years, his opinion that HCV materially contributed to his death appears to be based on statistical probability set out in limited literature which itself is non-conclusive, rather than anything he observed that was particular to the deceased's circumstances.

61. In contrast, Dr. Garber, quoted in paragraphs 28 and 29 above, indicates he has

been unable to detect any basis on which to suggest that HCV played any part in the death of the deceased, and that the course of his disease and his demise would be completely compatible with his Hepatitis B disease, independent of whether he had Hepatitis C or not. He points out there is no evidence to find that active Hepatitis C infection materially contributed to the deceased's death, and suggests that to conclude otherwise is purely speculative.

62. For the reasons set out above, I prefer Dr. Garber's view that there is nothing in the deceased's death that can be attributed to the HCV virus. Combined with the absence of compelling evidence that the deceased was infected with HCV, I find there is no evidence on which I could conclude that HCV materially contributed to his death.

DETERMINATION:

63. In light of the reasons set out above, I find the estate has not established on a balance of probability that the deceased's death was caused by HCV.

64. Accordingly, I find that the Administrator correctly determined that the estate of the deceased is not entitled to compensation pursuant to the Agreement, as there is insufficient evidence to demonstrate that his death resulted from his having been infected with HCV.

65. The decision of the Administrator to deny the estate of the deceased compensation pursuant to the Hepatitis C 1986-1990 Class Action Settlement Agreement is upheld.

DATED AT TORONTO, THIS 21ST DAY OF JULY, 2005.

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Tanja Wacyk, Referee