INTRODUCTION

During the course of the hearings the Inquiry heard evidence from medical experts, as well as from patients and relatives, about the physical and mental effects of Hepatitis C infection and its treatment. The Inquiry also has a considerable body of evidence in the form of statements from patients and their relatives. It is evident that the effects of infection with Hepatitis C vary greatly from one patient to another and that individual patients can experience different effects at different times. The true nature and full extent of these physical and mental effects, and their relationship with the financial and wider social consequences of Hepatitis C infection for patients and their families, can only be appreciated by considering the transcripts of those who gave evidence during the hearings as well as the statements provided by patient and relative witnesses who did not give oral evidence.

1. The physical and mental effects of Hepatitis C infection on patients.

Professor Thomas and Professor Hayes gave evidence about the effects of Hepatitis C infection and its treatment.

The Inquiry heard that 30 per cent of those infected with Hepatitis C will clear the virus within the first three to six months, but that the remaining 70 per cent will experience chronic Hepatitis C infection,\(^1\) although a small number of them will clear the virus spontaneously.\(^2\) Chronic Hepatitis C infection puts patients at an increased risk of developing progressive fibrosis and subsequent cirrhosis, which in turn puts them at risk of developing liver cancer.\(^3\)

The symptoms common in acute hepatitis include influenzal-type symptoms with malaise, muscle pain, joint pain, anorexia and nausea, raised temperature and an ache in the upper

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\(^{1}\) i.e. infection persisting for more than six months - see Transcript 11/10/11 (Day 52): 72(17-18) (Professor Thomas)
\(^{2}\) Transcript 12/10/11 (Day 53): 60(19-22) (Professor Thomas)
\(^{3}\) Transcript 11/10/11 (Day 52): 8(19) to 14(13) (Professor Thomas)
abdomen, many of which are caused by the body producing interferon. Furthermore, the urine can become dark and the stools pale, and the patient can develop itching and become jaundiced. Jaundice is rare in Hepatitis C, but if present lasts one to four weeks and is usually a sign that the patient will improve in the long-term. If the acute infection is mild or asymptomatic, this usually means that there is an increased risk of viral persistence.

Chronic Hepatitis C infection may not be picked up until late-stage disease is reached and a patient shows signs of chronic liver disease or a complication of cirrhosis. Symptoms of liver disease usually appear 20 to 30 years after infection with Hepatitis C, once a patient has developed cirrhosis, and can include lethargy, oesophageal varices, ascites and encephalopathy:

Encephalopathy and ascites indicate that the liver is beginning to fail and that a transplant should be considered. Liver transplantation is also the preferred option for the treatment of hepatocellular carcinoma, but this requires that the tumour is less than a certain size and that there are not more than two or three tumors. Furthermore, Hepatitis C can infect the new liver so it is not a cure. Other treatments include surgery to remove a segment of the liver rather than transplanting it. Segments of the liver can also be destroyed using radiofrequency ablation or chemoembolisation.

The Inquiry heard that Hepatitis C infection is also associated with conditions that are independent of any damage to the liver, including brain fog and mood disorders. Brain fog, or mild cognitive dysfunction, involves a difficulty in concentrating and higher cerebral function generally, and improves when the Hepatitis C infection is treated. It is caused by the Hepatitis C virus infecting and replicating in the brain. This is relevant in relation to treatment for Hepatitis C

4 Transcript 12/10/11 (Day 53): 1(13-24) (Professor Thomas)
5 Transcript 12/10/11 (Day 53): 35(4-19) (Professor Thomas)
6 [PEN.017.1071] at 1081
7 Transcript 12/10/11 (Day 53): 2(1)-5(7) (Professor Thomas)
8 [PEN.017.1071] at 1081
9 Transcript 12/10/11 (Day 53): 5(20-25 (Professor Thomas)
10 Varicose veins in the gullet
11 Abdominal swelling due to the accumulation of fluid.
12 Cognitive dysfunction due to an accumulation of ammonia-like compounds as a result of the liver not functioning properly see Transcript 11/10/11 (Day 52): 123(3-12) (Professor Thomas)
13 Transcript 14/12/11 (Day 78): 89(18-23) (Professor Hayes)
14 Transcript 14/12/11 (Day 78): 90(2) to 91(15) (Professor Hayes) Transcript 12/10/11 (Day 53): 44(10) to 47(12) (Professor Thomas)
15 Transcript 11/10/11 (Day 52): 63(15) to 68(2) (Professor Thomas)
because interferons do not readily cross the blood/brain barrier and the brain therefore provides a sanctuary site where the virus may not be cleared by interferons. Ribavirin, which is used to reduce relapse rate, probably does go into the brain and stops a patient from relapsing by clearing up the second site of replication. In relation to mood disorders, the Inquiry heard that there is a much higher prevalence of depressive disorders in Hepatitis C patients compared with Hepatitis B or other liver disease groups. Professor Thomas explained that the Hepatitis C virus infects monocytes which may settle in the brain where they differentiate into microglial cells which help to clear up any dying cells in the brain. Microglial cells have a very long half-life and when they produce neurosteroids they are involved in the depressive mood mechanism.

Patients with Hepatitis C can also experience other extra-hepatic manifestations involving multiple organ systems including renal, dermatological, haematological and rheumatological systems. For example, if patients have a genetic predisposition to autoimmune problems such as rheumatoid arthritis and autoimmune thyroiditis, interferon makes those diseases significantly worse. In relation to dermatological conditions, patients with Hepatitis C can experience cryoglobulin anaemia in which blood vessels on the lower parts of the leg become thrombosed giving rise to the appearance of little black nodules which can cause discomfort.

Furthermore, regardless of the degree of liver damage, Hepatitis C can cause chronic ill-health, with decreased quality of life, depression and general malaise. Patients can experience a general reduced mental and physical wellbeing. In addition, when patients start being treated with interferon their quality of life goes down noticeably because of the its side effects.

In addition to liver cancer, Hepatitis C may also cause non-Hodgkins B cell lymphoma, which is a cancer of the lymphoid system, although this is rare.

The Inquiry has heard evidence from patients and their relatives about the appalling physical and mental effects that Hepatitis C has had on them. All of the patients experienced some of the

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16 Transcript 11/10/11 (Day 52): 63(15) to 68(2); Transcript 12/10/11 (Day 53):7(16) to 9(10); Transcript 11/10/11 (Day 52): 67(4-13) (Professor Thomas)
17 Transcript 11/10/11 (Day 52): 65(24) to 66(2); 68(3-14) (Professor Thomas)
18 Transcript 12/10/11 (Day 53): 73(6)-79(11) (Professor Thomas)
19 Transcript 12/10/11 (Day 53): 6(15) to 7(5) (Professor Thomas)
20 Transcript 12/10/11 (Day 53): 7(6-9) (Professor Thomas)
21 Transcript 11/10/11 (Day 52):61(22) to 63(8) (Professor Thomas)
extra-hepatic consequences of Hepatitis C infection. COLIN\textsuperscript{22} has suffered from debilitating aches and pains in his joints and muscles, lethargy and weakness and has also suffered debilitating periods of “shut down” and at times could not get out of bed. GORDON\textsuperscript{23} has suffered from extreme tiredness and from sleep problems. He has difficulty in keeping warm and usually has cold hands and feet. ANNE\textsuperscript{24} has experienced flu-like symptoms, which she has learned to live with, as well as aches and pains. ALEX\textsuperscript{25} has suffered from symptoms of Hepatitis C infection throughout his life but did not previously associate them with Hepatitis C infection. As a child he experienced symptoms of fatigue and would want to stay in bed for a few days. As an adult he has experienced unpredictable but extreme bouts of fatigue, and also feels lethargic, angry and depressed. For years BRIDIE’s\textsuperscript{26} mother had various mood swings, was constantly tired and was frequently in bed. For years she suffered from aches and pains, particularly in her joints, and found it difficult to walk and move. LAURA\textsuperscript{27} experienced feeling generally run down and did not recover here energy levels after having a baby.

For some patients infection has led to liver failure and transplantation and the Inquiry has heard evidence about this from STEPHEN,\textsuperscript{28} COLIN and GORDON. STEPHEN was found to be suffering from liver failure after being rushed into hospital with a variceal bleed, after which he was in a coma for nine days. He was subsequently so weak that he was confined to a wheelchair for two years. Before their liver transplantations STEPHEN and COLIN both suffered episodes of encephalopathy as well as from ascites. Following his liver transplantation STEPHEN developed a heart condition and had to undergo heart surgery and GORDON’S surgery was complicated by a blood clot that had to be removed.

Other patients who are infected will experience these consequences in due course.

2. The physical and mental effects of treatment with Interferon and/or Ribavirin on patients.

\textsuperscript{22} Transcript 13/12/11 (Day 77) (COLIN)
\textsuperscript{23} Transcript 13/12/11 (Day 77) (GORDON)
\textsuperscript{24} Transcript 15/12/11 (Day 79) (ANNE)
\textsuperscript{25} Transcript 10/01/12 (Day 81) (ALEX)
\textsuperscript{26} Transcript 09/12/11 (Day 76) (BRIDIE)
\textsuperscript{27} Transcript 15/12/11 (Day 79) (LAURA)
\textsuperscript{28} Transcript 08/12/11 (Day 75) (STEPHEN)
The Inquiry heard that cirrhosis is considered to be irreversible and has serious complications that can include liver cancer, liver failure and bleeding from oesophageal varices. Preventing cirrhosis prevents these complications and is an important goal of treatment for Hepatitis C.\textsuperscript{29}

In 1986 there were suggestions that interferon might be successful in the treatment of Non-A Non-B hepatitis, but early reports were small and inconclusive in terms of whether or not treatment was doing long-term good.\textsuperscript{30} The first treatment that was shown to be successful in some cases was Alpha interferon, and once the virus had been identified drug trials showed that Alpha interferon alone, three times weekly, appeared effective in clearing the virus in a minority of patients.\textsuperscript{31} Alpha interferon was introduced into clinical practice in about 1991/1992. In about 1995/1996 it was recognised that ribavirin might reduce the risk of relapse and it was introduced into clinical practice some years later, after clinical trials had been carried out. Pegylated interferon, which was longer acting than Alpha interferon, was introduced in the 2000s.\textsuperscript{32}

Antiviral therapy affects a patient’s quality of life and they can experience symptoms such as depression, myalgia, lethargy and influenza-type symptom, similar to those seen in acute hepatitis, which are caused by the body producing interferon.\textsuperscript{33}

Treatment with interferon alone was by way of injection taken three times a week. The side-effects were mainly flu-like symptoms and patients were therefore advised to take it at night with a paracetamol. The side effects of pegylated interferon, which is taken only once a week, are also flu-like symptoms similar to those of interferon alone. However, another less common side effect of pegylated interferon is depression and, occasionally, suicidal ideation. Patients varied greatly in their tolerance of the side effects of interferon and pegylated interferon, with some coping well and being able to carry on their day-to-day living and others finding them so debilitating that they were unable to leave bed, and were incapable of completing the treatment.\textsuperscript{34} The side effects of ribavirin are mainly anaemia.\textsuperscript{35} It is expected that the side effects of the new drugs will be the same, but with additional side effects.\textsuperscript{36}

\textsuperscript{29} Transcript 14/12/11 (Day 78): 83(17) to 84(17) (Professor Hayes)
\textsuperscript{30} Transcript 14/12/11 (Day 78): 48(5-13) (Professor Hayes)
\textsuperscript{31} Transcript 14/12/11 (Day 78): 49(17-17); 51(16-21) (Professor Hayes)
\textsuperscript{32} Transcript 14/12/11 (Day 78): 51(21-25); 53(8) to 54(8) (Professor Hayes)
\textsuperscript{33} Transcript 12/10/11 (Day 53): 35(5-19) (Professor Thomas)
\textsuperscript{34} Transcript 14/12/11 (Day 78): 101(7) to 102(4) (Professor Hayes)
\textsuperscript{35} Transcript 14/12/11 (Day 78): 102(5-6) (Professor Hayes)
\textsuperscript{36} Transcript 14/12/11 (Day 78): 103(24) to 104(2) (Professor Hayes)
Approximately 20 per cent of patients do not manage to complete the treatment, and whether they do or not depends upon the level of support that they can be given. Some patients with Hepatitis C who are feeling well refuse treatment.

During his evidence Professor Hayes emphasised that the people who know the complications of treatment best are the patients themselves.

The Inquiry has heard evidence from a number of witnesses about their experiences of the effects of treatment with interferon and/or ribavirin. STEPHEN underwent treatment with Alpha interferon and ribavirin and after about six months of treatment felt generally unwell and tired and was unable to concentrate. He experienced severe nose bleeds, loss of appetite, thinning of his hair, severe muscle cramps, insomnia, nausea and vomiting and had to stop working. The treatment was unsuccessful. COLIN underwent two courses of treatment. The first was with interferon and ribavirin and within three weeks of starting treatment the side effects were so bad that he was completely bedridden. He felt unwell and experienced joint aches and pains, muscle weakness, and felt completely washed out, weak and exhausted. He had to stop the treatment after 12 weeks. His second course was with pegylated interferon and ribavirin treatment and within hours after taking the first dose he started experiencing the same side effects he had experienced with the previous treatment. After two weeks he was also experiencing chest tightness, palpitations and widespread aches and pains, with lower back pain and earache. His haemoglobin levels and neutrophil counts were also low. As a result of the side effects he had to stop treatment. GORDON also underwent two courses of treatment for Hepatitis C. The first course was with interferon and he felt substantial fatigue and flu-like symptoms and he ached and felt generally miserable. He also suffered from a skin rash. During the course of the treatment he found day-to-day living a struggle but continued to work. He was still Hepatitis C positive after five months so treatment was stopped. During his second course of treatment, which was with pegylated interferon and ribavirin, he suffered substantial fatigue and flu-like symptoms, nausea, headaches, aches and stiffness in his knees. He passed out on two occasions and also developed a rash which needed attention by a dermatologist. His haemoglobin levels fell and he experienced shortness of breath. During the treatment his body weight fell from 63 kilograms to 56 kilograms. The treatment was unsuccessful. ANNE

37 Transcript 14/12/11 (Day 78): 97(1-8) (Professor Hayes)
38 Transcript 14/12/11 (Day 78): 77(21) to 78(3) (Professor Hayes)
39 Transcript 14/12/11 (Day 78): 101(7-14) (Professor Hayes)
40 Transcript 13/12/11 (Day 77): 35(10); 37(11) (COLIN)
underwent two courses of treatment for Hepatitis C. The first was with interferon during which she experienced flu-like symptoms, headaches, cramps in her legs, tiredness and slight hair loss. She put on about half a stone in weight and became hypothyroid and has had to take thyroxine ever since. Her second course of treatment was with interferon and ribavirin. Her treatment impacted on her personality, and she experienced extreme symptoms of anxiety and anger. She saw a psychiatrist who confirmed the diagnosis as interferon-related depression and she was started on antidepressant therapy, which she continues to take. She also suffered intense physical side effects. She had continuous flu-like symptoms, her temperature fluctuated, and she suffered from a cough for six weeks followed by a chest infection for four weeks. She had a dry mouth and dry skin and suffered from alopecia. She experienced poor concentration, insomnia and vivid dreams. She lost her appetite and lost about four pounds. She also experienced extreme fatigue. By the time she finished the treatment the virus was already detectable. ALEX underwent a course of interferon treatment when he was only eight years old. He was given injections three times a week by the local nurse and was sick nearly every time he was injected. He was tired from the start of the treatment and withdrew into his shell. He hated receiving injections and during his interferon treatment he was injected three times a week by the local nurse. At the time he was also on prophylactic treatment for his haemophilia. Alex would feel sick and drained after his interferon injections but disliked going to hospitals so much that he would down play any illness. The treatment was unsuccessful. LAURA underwent two courses of treatment for Hepatitis C. The first course was with interferon and while on the treatment she felt extremely tired, generally miserable and depressed, ached physically and had no appetite. She also suffered from headaches and thinning of her hair. She did not respond to the treatment and it was stopped. During her second course of treatment LAURA was constantly tired and irritable. She experienced slight aches and pains in her shoulders and flu-like symptoms. She had headaches and lost weight. The treatment was successful.

Other patients who have acquired Hepatitis C through their treatment with blood and blood products have already suffered similar effects in their attempts to rid themselves of Hepatitis C, and although the side effects of treatment can vary in severity and nature from one patient to another, they all impact on a patient’s quality of life and can be completely debilitating.

3. The personal and social consequences of Hepatitis C infection for patients and the stigma associated with Hepatitis C infection.
4. The personal and social consequences of treatment with Interferon and/or Ribavirin for patients.

and

5. The personal and social consequences of Hepatitis C infection for patients’ families.

and

6. The personal and social consequences of treatment with Interferon and/or Ribavirin for patients’ families.

The Inquiry heard evidence from patients and their relatives about the personal and social consequences of Hepatitis C infection, and it is apparent that Hepatitis C is a disease that affects not only individuals but also their families.

It affects the quality of patients’ lives and their ability to carry out activities which they were previously able to enjoy. It prevents them from progressing in their careers or from pursuing careers which they might otherwise have chosen, and can force them to stop working when they would prefer to continue. It affects patients’ relationships with their families, and can prevent them from forming relationships and engaging in social activities which they might otherwise engage in. It can cause patients to feel isolated and reluctant to tell people about their infection due to the stigma associated with it. Hepatitis C also affects family members who are required to assist patients when they are unable to care for themselves, which can involve having to take time away from their own employment or stopping work altogether. Children suffer as a consequence of not having a parent who is able to spend time with them.

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41 See for example STEPHEN; ANNE
42 See for example GORDON
43 See for example ALEX
44 See for example GORDON; COLIN; LAURA
45 See for example COLIN; ANNE;
46 See for example ANNE;
47 See for example ALEX;
48 See for example ALEX
49 See for example ANNE; ALEX; STEPHEN;
50 See for example STEPHEN; BRIDIE
51 See for example COLIN
due to illness. Other family members can suffer from anxiety and depression as a consequence of having a loved one who is ill.

In his evidence Professor Hayes acknowledged that there are a number of areas of stigma associated with Hepatitis C infection, which will differ from centre to centre. The majority of patients with Hepatitis C will have acquired it through drug misuse so people being treated at mixed clinics are likely to feel more stigmatised than, for example, patients being treated at haemophilia centres. Furthermore, it is common for people who are referred with abnormal liver function tests to have been cautioned about their GP about drinking too much alcohol, when they insist that they are almost tea-total, because alcohol is such a common cause of abnormal liver function tests. Many patients with liver disease can feel stigmatised about things, but those infected through blood and blood products are very different populations compared to those who have acquired Hepatitis C through intravenous drug misuse, so there is a great deal of potential for misunderstanding and stigmatisation.

7. The financial consequences of Hepatitis C infection, treatment with Interferon and/or Ribavirin, and liver failure and transplantation for patients and their families.

In our submission the evidence before the Inquiry from patients and their relatives clearly indicates that Hepatitis C infection has far-reaching financial consequences. Patients experience diminished earnings and earning capacity, and their Hepatitis C infection impacts upon their employability, portability of employment, possibility of promotion and their ability to pursue studies with a view to a career. Patients are forced to sell their businesses due to ill health and their homes due to financial concerns. Many patients and their families have found themselves forced to rely on State benefits in order to survive. Hepatitis C infection also affects the ability of patients to obtain life insurance, mortgage protection insurance or travel insurance, or being required to pay significantly higher premiums in order to obtain such insurance. Patients and their relatives also have to pay expenses associated with travel and accommodation while attending hospital for treatment. Patients can require domestic assistance, aids and equipment

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52 See for example STEPHEN; COLIN  
53 See for example COLIN; GORDON  
54 Transcript 14/12/11 (Day 78): 104(3) to 105(9) (Professor Hayes)  
55 This evidence includes the evidence heard during the oral hearings, the witness statements that are before the Inquiry and eight questionnaires from case studies on the financial consequences of Hepatitis C infection that have been provided to the Inquiry.
and additional expenditure for utility bills, in particular due to needing additional heating to keep warm.

It is important that all of these features of the financial consequences are recognised and acknowledged in the final report.

8. The effectiveness of Interferon and/or Ribavirin in the treatment of Hepatitis C infection.

Professor Hayes gave evidence about the effectiveness of treatment for Hepatitis C infection. Interferon monotherapy had success rates of about 10 to 20 per cent. This was improved to about 20 to 40 per cent with the introduction of ribavirin. With pegylated interferon and ribavirin this was improved to about 50 per cent with genotype 1 and to over 70 per cent in genotype 3. These figures take into account people who fail to complete treatment because they cannot tolerate the side effects, and have been borne out in clinical practice.

He also pointed out that once a patient has cirrhosis they are unlikely to be cured of Hepatitis C with treatment, partly because they are likely to have had it for a long time and partly because they don’t tolerate the complications of treatment in conjunction with the problems of cirrhosis.

Future treatments for Hepatitis C include protease inhibitors, which are expected to increase the response rate in patients with genotype 1 Hepatitis C to around 80 per cent, although the side effects are likely to be more severe than those experienced with interferon and ribavirin.

9. The effects of exposure to multiple strains of Hepatitis C.

Professor Thomas indicated that it is not uncommon for persons with haemophilia to have more than one genotype of the Hepatitis C virus and said that this can be relevant to treatment. In this regard he indicated that in patients carrying more than one genotype of Hepatitis C, particularly haemophiliacs who may also have Hepatitis B, viral interference can occur whereby the

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56 Transcript 14/12/11 (Day 78): 93(8-16) (Professor Hayes)
57 Transcript 14/12/11 (Day 78): 95(24) to 96(7) (Professor Hayes)
58 Transcript 14/12/11 (Day 78): 87(9-24) (Professor Hayes)
59 Transcript 12/10/11 (Day 53): 51(15) to 53(17) (Professor Thomas)
replication of one virus suppresses the second virus. Consequently that it may not be realised that the second virus is there until the first virus clears up.60

He also testified that, although he was not aware of any data, it would be reasonable to deduce that, in relation to persons with haemophilia who were repeatedly exposed to Hepatitis C through treatment with concentrates, they might reach a point where they were unable to clear the virus spontaneously and go on to develop a chronic condition.61

Professor Thomas said that it is not known whether or not the rate of progression of liver disease is increased by the fact that a patient is infected with more than one genotype of the Hepatitis C virus. He nevertheless suggested that it may be more difficult for a patient’s immune system to cope with continually being presented with variations of a virus, which could give rise to immune exhaustion, where the immune system starts to make less antibody.62

10. The level of information, support and counselling previously and currently available to patients infected with Hepatitis C through blood and blood products, and their families and the differences between centres.

and

11. The effect that the level of information, support and counselling has had on the ability of patients and their families to cope with Hepatitis C infection and its consequences.

In our submission it is clear from the evidence provided to the Inquiry by patients and their relatives that there is a general feeling of dissatisfaction about the level of information, support and counselling that has been made available to them over the years. Very little information about the disease and its treatment was communicated to them and they have consequently felt as though they did not understand very much about it.63 They were also offered very little in the way of

60 Transcript 11/10/11 (Day 52): 60(12) to 61(16) (Professor Thomas)
61 Transcript 12/10/11 (Day 52): 61(3-18) (Professor Thomas)
62 Transcript 12/10/11 (Day 53): 29(13) to 30(20); Transcript 11/10/11 (Day 52): 70(3-23) (Professor Thomas)
63 Transcript 10/01/11 (Day 81): 28(17) to 29(13); 56(12-21), 87(19-25) (ALEX); Transcript 13/12/11 (Day 77): 123(25) to 124(4) (GORDON); Transcript 15/12/11 (Day 79): 83(11) to 84(6), 87(16) TO 88(8). 90(4) TO 91(8) (ANNE); Transcript 09/12/11 (Day 76): 71(5-12) (BRIDIE); Transcript 13/12/11 (Day 77): 25(2-8) (COLIN)
support and counselling. In this regard the Inquiry heard about how the concept of counselling differs between patients and medical practitioners and that medical practitioners view it essentially as the giving of information. The lack of information, support and counselling is discussed more fully in our submission on Topic C5(c).

In our submission the lack of information, support and counselling has contributed significantly to the uncertainty and anxiety that patients and their relatives have experienced in trying to cope with the widespread and devastating consequences of Hepatitis C infection. In our submission patients and their relatives would clearly have benefitted from additional support and counselling, beyond the mere provision of information. Furthermore, the fact that patients were infected through medical treatment will undoubtedly have made it more difficult for them to come to terms with their infection, and this could have been made easier with the necessary support.

12. **Lessons and implications that can be identified, and recommendations that can be made for the future, arising from the Inquiry’s consideration of Topic C6.**

Recognition needs to be given to the wide-ranging and devastating consequences that Hepatitis C infection has on patients and their families, and acknowledgement given to the impact that the circumstances of their infection has had on them, when consideration is given to their ongoing treatment and care.

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64 Transcript 09/12/11 (Day 76): 18(19-23) (BRIDIE); Transcript 10/01/11 (Day 81): 30(18) to (31(3), 39(23) to 40(1), 45(24) (ALEX); Transcript 13/12/11 (Day 77): 125(5-7), 151(17-21) (GORDON); Transcript 15/12/11 (Day 79): 68(25) to 69(8) (LAURA); Transcript 15/12/11 (Day 79): 83(11) (ANNE); Statement of Core Participant: PI119JP at paragraph 17; Statement of Core Participant: PI066MF at paragraph 11; Transcript 12/01/12 (Day 84): 40(23) to 41(7) (Professor Nathanson) Transcript 14/12/11 (Day 78): 65(6) to 67(4) (Professor Hayes)

65 Transcript 13/12/11 (Day 77): 20(3-7); 24(20) to 25(8) (COLIN); Transcript 09/06/11 (Day 30): 114(22-35) (DAVID); Statement of Core Participant: PI066MF at paragraph 11; Transcript 14/12/11 (Day 78): 65(6) to 67(4) (Professor Hayes)