Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	other
Other role	[redacted]
Location	England
Conflict	no
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	NAT (National AIDS Trust) wishes to comment on the preliminary recommendation not to recommend sofosbuvir in advance of further analyses including a cost-effectiveness analysis with and without HIV co-infection. Â This raises the possibility of approval for mono-infected only should such an analysis not be forthcoming or produce results NICE consider unsatisfactory in some way. Â We note the EASL 2014 full recommendations which state that 'Indications for HCV treatment in HCV-HIV co-infected patients are identical to those in patients with HCV mono-infection' and 'No drug-drug interaction has been reported between sofosbuvir and antiretroviral drugs' [section 4.7]. Â We would also emphasise that people living with HIV are disabled in law under the provisions of the Equality Act 2010. Â We would warn against inequitable and discriminatory provision. Â It would not be acceptable for NICE to refuse effective new HCV drugs to people co-infected with HCV and HIV on the grounds of cost-effectiveness analyses, including on the grounds of the lack of such analyses. Â These drugs are urgently needed for people with these two conditions, each of which can complicate the other.
Date	6/25/2014 8:45:00 AM

Name	[redacted]
Role	NHS Professional
Other role	[redacted]
Location	England
Conflict	yes
Notes	I am a Principal Investigator or Chief Investigator in a number of multicentre Gilead-sponsored clinical trials, including trials of sofosbuvir. I also act as an advisor to Gilead and to many other pharmaceutical companies that have interests in hepatitis treatment.
Comments on individual sections of the ACD:	
Section 4 (Consideration of the evidence)	To demonstrate the benefit of successful treatment we looked at HCV G3 patients treated between 2000 and 2012. The cure rate was 64% (261/408) but only 36% (25/69) in cirrhotic patients. There is a remarkable impact of SVR on transplant-free survival. Of 44 who failed treatment, 20 have died and 14 required transplantation. Only 14/44 (32%) survive without a need for transplantation. Â In contrast, there were 3 deaths during follow-up of the successfully treated group, and none developed liver failure. Transplant-free survival is 84% (21/25).This shows that virological cure has an almost immediate impact on patient survival. There is large cohort of patients in immediate need. The QE hospital clinic has 327 G3 patients. 161/327 (49%) are treatment-experienced. 103/161 (62%) have cirrhosis. 166/327 (51%) are treatment-naÃ¯ve and many have contraindications to IFN. 63/166 have cirrhosis. Overall, we care for 166 cirrhotic G3 patients. A substantial proportion could be cured and would then avoid liver-related death and/or need for transplantation. This cohort of G3 patients is not unique to Birmingham. The potential benefits of sofosbuvir for this population are remarkable and immediate. A reduced need for transplantation would be rapidly apparent, and donor livers would be redirected towards patients who have untreatable liver diseases.
Section 8 (Proposed date of review of guidance)	The committee should consider the wealth of real-life data that could be obtained from the larger Liver Units. In particular, and relevant to the UK population, there are data on treatment outcomes for patients with G3 infection. Also, the impact of treatment, including the reduced need for liver transplantation, must be considered. There is an overwhelming clinical and economic argument in favour of immediate treatment for patients with cirrhosis. Our experience with the routine use of nucleosides to suppress hepatitis B replication is relevant. As a consequence of treatment, hepatitis B associated liver failure has almost vanished as an indication for liver transplantation in Western centres. The number of transplants performed in the UK and USA for hepatitis B associated liver conditions has decreased by two thirds. The same dramatic impact on risk for liver failure and on need for liver transplantation will be achieved by targeting the cirrhotic hepatitis C population for treatment with potent antivirals including sofosbuvir.
Date	6/24/2014 12:22:00 PM

Name	[redacted]
Job description	[redacted]
Email address	[redacted]
Contact number	[redacted]
Role	NHS Professional
Location	England
Organisation	BVHG 'British Viral Hepatitis Group' (sub-section of BASL 'British Association for the Study of the Liver')
Conflict	No
Declaration of interest	[redacted]
Comments on individual sections of the ACD:	
	The British Viral Hepatitis Group and the British Association for the Study of the Liver would like to comment on the Appraisal Consultation Document on Sofosbuvir for treating chronic hepatitis C. We note that specific comments are required: ● Has all of the relevant evidence been taken into account? ● Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? ● Are the provisional recommendations sound and a suitable basis for guidance to the NHS? The provisional outcomes and decisions appear robust and thorough, and we congratulate the NICE committee and Expert Review Group (ERG) on the work done to date. There are however several points that we would like to raise: 1. We believe that Sofosbuvir (SOF) is likely to prove an important antiviral therapy for hepatitis C, given its potency, safety, genotypic activity (particularly across genotypes 1, 2, 4, 5 and 6) and high barrier to resistance. 2. We agree that the lack of comparator arms in the majority of studies is a data gap, which makes it difficult to construct a mixed treatment comparison. Understandably (for the NICE process) this makes the estimation of efficacy and relative benefit difficult to accurately quantify. However it is the view of BVHG and BASL that SOF is a significant therapeutic advance for many patient groups. The increased SVR rates with SOF/PEG-IFN/RBV in naïve genotype 1 patients compared to the results obtained with the current standards of care (PEG-IFN/RBV, or 24-48 weeks of Telaprevir/PEG-IFN/RBV or Boceprevir/PEG-IFN/RBV) are highly unlikely to be biased by patient selection or specific participant characteristics. 3. Inclusion of 48 week IFN-containing or IFN-containing plus DAA control arms would have significantly prolonged the phase 2 and 3 programs and therefore delayed ultimate access to this important medication for patient subgroups in great need. 4. There is a lack of a substantive body of data of efficacy in treatment experienced (TE) patients with genotype 1 infection with or without cirrhosis. The efficacy of SOF/PEG-IFN/RBV for 12 or 24 weeks in TE patients has been modeled, and a

	marketing authorization for TE genotype 1 patients was granted based on these extrapolations. Genotype 1 TE patients without cirrhosis can expect high SVR rates based on the combination of SOF/PEG-IFN/RBV. There is an important need for an effective regimen for these patients. It is believed likely that SOF/PEG-IFN/RBV for 12 weeks will prove relatively less efficacious in genotype 1 patients with cirrhosis and non-favorable IL-28B genotype, particularly in prior partial- or null-responders to interferon. The exact decrement in efficacy is unknown, as is the place of 24 weeks versus 12 weeks of the regimen and the future options for genotype 1 TE patients. 5. The division of patients into cirrhotic and non-cirrhotic groups is a reasonable division based on the sensitivity, specificity, and true- and false-positive rates for cirrhosis of the available non-invasive methodologies, particularly transient elastography (Fibroscan), APRI or ELF testing. Stratifying patients in this manner is, and will remain, standard clinical practice. 6. Similarly the division of patients into treatment-experienced and treatment-naÏve is a standard clinical process and logical for this appraisal. 7. The ratio of men to women in the manufacturer analysis should be adjusted to reflect the gender ratio of HCV infected persons in the UK 8. (continued in separate comment box 2)
	(Continued from comment box 1) 8. We note the detailed cost-effectiveness and economic model structure submitted by the manufacturer and revised by the ERG. A large body of data has been submitted and we trust that we are interpreting the findings correctly. We note particularly the data on extended (24 week) treatments. a. From table 13 the ICERs for SOF for genotype 1 treatment naÏve (TN) SOF/PEG-IFN/RBV 12 weeks interferon eligible (IE) were ~£14,930, ~£11,836 and ~£7,292 versus PEG-IFN/RBV and telaprevir or boceprevir respectively and thus the regimen seems cost effective. However this does not appear to be the case from the figures presented for SOF/RBV for 24 weeks in genotype 1 interferon unsuitable (IU) patients b. No case was made for the cost effectiveness of SOF/PEG-IFN/RBV in TE genotype 1. c. For genotype 2, the ICERS appeared to be within acceptable thresholds for genotype 2 TN IU, TE IE, and TE IU. d. For genotype 3 the ICERS are within acceptable thresholds for 12 weeks SOF/PEG-IFN/RBV in TN IE, and TE IE but were higher for the 24 weeks regimens in the TN IU and TE IU. Thus treatment appeared cost-effective for genotype 3 patients treated for 12 weeks. e. For genotype 4, 5 and 6 similar cost effective ICERs were noted for SOF/PEG-IFN/RBV 12 weeks. 9. The ERG probabilistic sensitivity analysis suggests a high likelihood of the ICER being within the cost effective thresholds: a. For SOF/PEG-IFN/RBV 12 weeks in genotype 1 TN IE b. For genotype 3 TN IE, SOF/PEG-IFN/RBV (12 weeks) (at the Â£30,000 threshold)

	10. We note the trend in the revision table produced by the ERG which in general corresponds to the trend noted above, including table 22 which recalculates the ICERS based on a weighting of 61% men. 11. Thus there are groups that receive 12 weeks SOF/PEG IFN/RBV in whom the ICERS do suggest a cost-effective therapy. 12. In reality the uptake of the less cost-effective regimens with 24 weeks SOF/RBV or PEG IFN/SOF/RBV for genotype 1 infection will be low while waiting for SOF/ledipasvir regimens to become available. The NHS England commissioning process for urgent treatment will provide access for many patients. 13. An exception may have to be found for a small subset of genotype 3 patients who require an IFN-free regimen of SOF/RBV for 24 weeks. 14. In summary we support that SOF should be made available for patients requiring treatment and in whom treatment is cost-effective. 15. We are not in agreement that most clinicians would be likely to utilize 24 weeks of SOF/RBV for G3 patients. Data from the Boson study are not presently available, but it is our view and understanding that the majority of clinicians will likely utilize 12 week PEG-IFN/SOF/RBV for the vast majority of genotype 3 patients, and in the small subset who are truly IU, potentially a 16-24 week SOF/RBV regimen. Many of the latter patients however, unless in urgent clinical need, will probably be advised to await newer treatments rather than utilize prolonged SOF/RBV. 16. For the small subset of genotype 3 TE patients who cannot take IFN, we would strongly encourage discussions with the manufacturer on initiatives such as a cost per SVR, or a charge for 12 weeks of SOF with provision of SOF for 24 weeks 17. (continued in separate comment box 3)
	(Continued from comment box 2) 17. It is unlikely that a large number of patients with genotype 1 will require 24 weeks of SOF and RBV as improved treatments for TE genotype 1 patients are imminent: a. We are aware that SOF and daclatisvir or ledispavir are not considered in this appraisal and the remit and decision problem were to appraise SOF within its licensed indication for hepatitis C. Unfortunately the currently considered data does not take into account near future options which already have a bearing on clinical decision making. Recent phase 3 data has shown that the combination of SOF and an NS5a inhibitor, i.e. SOF/daclatasvir or SOF/ledipasvir, is highly effective in patients with prior non-response to PEG-IFN/RBV or prior non-responders to either telaprevir or boceprevir. b. A 12 week SOF/ledipasvir regimen was effective in > 90% of TE patients, (although prior non-responders with cirrhosis may have benefited from 24 weeks). These data greatly cloud the issue for clinicians who may elect to defer patients for a future non-interferon containing DAA regimen rather than a 24 week SOF + RBV course. Thus the real costs to the NHS are not based on the use of SOF + RBV for 24 weeks but the hopefully similar costs of SOF/ledispasvir for 12

	weeks (and perhaps, in rare cases, for 24 weeks). This should be taken into account when weighing up the costs to the NHS. Indeed the NHS has already put in place interim commissioning arrangements for SOF plus an NS5a inhibitor, for example ledispasvir, for patients at significant risk of death or irreversible damage. 18. Some potentially important data is missing from the document ‘ specifically further data on HIV co-infected individuals (1910 study). 19. The value of cure in patients without cirrhosis but with symptoms of hepatitis C will need to be addressed by NICE and by NHS England and commissioners in Wales. 20. The public health benefits of cure ‘ preventing onward transmission ‘ should be addressed in future appraisals. 21. The shorter duration of treatment for higher SVR rates is a great advantage in the clinical management of patients. The reduced number of interventions, including monthly visits, and reduced need for ancillary measures for managing side effects, particularly anaemia and cytopaenias, will be significantly advantageous. 22. (continued in separate comment box 4)
	(Continued from comment box 3) 22. The relative lack of significant drug-drug interactions is also a significant advantage for SOF, particularly in those with multiple co-morbidities. 23. An important issue is that of specific subgroups who are sociologically disadvantaged. The Consultation Document comments that access for such patient groups is related to implementation and not a technology appraisal. However we believe that the shortened treatment durations and markedly improved adverse event profiles in certain subgroups significantly impact on certain disadvantaged groups, for example people with injecting drug use and therefore acknowledgement and some discussion of this would be appropriate. Another example is those in offender institutions (e.g. prison), where oversight from healthcare staff may be less than other settings, and where patient transfers may significantly impact on the ability to complete prolonged treatment regimens. It may be appropriate to allow or direct clinicians to consider these factors when deciding on treatments. 24. Lastly it is gratifying that recognition has been taken of the patient representatives and potential patient voice. Though this should not directly affect the decisions of the NICE committee it is important to appreciate the context - SOF is the first new agent for G2 and G3 patients in over 15 years, and therefore the first new hope to some patients who have failed or been intolerant of previous standard-of-care; and, though the SMC decision-making process is different from NICE, patients may find it hard to understand discrepancies of guidance (and ultimately access) across borders within the UK. We would like to strongly urge the committee to allow clinicians in England and Wales to have access to SOF as part of our

	increasing armamentarium for battling hepatitis C; something which ultimately will bring significant health benefits and cost-savings to the NHS. The drug is cost-effective for many patients, and negotiation regarding the costs of exceptional use of SOF/RBV for 24 weeks, particularly in genotype 3 TN or TE IU patients, could be sought from the manufacturer. We thank the committee again for the opportunity to comment, and congratulate them on the work completed to date.
Date	2014 07 02

Name	[redacted]
Job description	[redacted]
Email address	[redacted]
Contact number	[redacted]
Role	NHS Professional
Location	England
Organisation	[redacted]
Conflict	Yes
Declaration of interest	
Comments on individual sections of the ACD:	
	Thank you for asking me to comment, as part of BASL (the British Association for the Study of the Liver). I have reviewed the documents in detail. My comments have been amalgamated into the comment submitted jointly by the British Viral Hepatitis Group (BVHG) and BASL
	Please se
Date	2014 07 02

Name	[redacted]
Job description	[redacted]
Email address	[redacted]
Contact number	[redacted]
Role	[redacted]
Location	England
Organisation	[redacted]
Conflict	No
Declaration of interest	
Comments on individual sections of the ACD:	
	Our comment is based on feedback from the HIV/Hep C community. 1. We note that the cost of the drug may be prohibitive for the NHS under current austerity. We also note the debates in the US on cost. This is a commerical product however we are deeply disappointed at the manufacturers cost for this drug. 2. We are aware of those loving with HIV/Hep C who have passed away given intolerance to current interferon based medical approaches. Including those for whom current interferon based treatment has been unsuccessful. 3. One of the major reasons for intolerance is the mental health impact to those under an interferon based approach. Some with HIV may already have poor mental health and interferon/ribavarin therapy simply worsens the situation. 4. Using a interferon/ribavarin may impact on HIV therapy. Forcing a change bringing about additional complications and side-effects at a time patients have to deal with impact of Hep C therapy. 5. We are aware of patients holding off on treatment until new therapies with less side-effects are introduced. For some this maybe due to intolerence of existing therapies or that work/life is delicately balanced already and the risk of side-effects of interferon/ribavarin. Especially the mental health issues. A risk factor. 6. When considering cost, NICE ought to assess the efficacy of the drug, adherence to therapy, impact to mental health compared with existing therapies, impact on highly stigmatised and marginalised patients and as a therapy for those unable or unsuccessful on interferon/ribavarin. 7. The HIV community and BHIVA are well placed to advise on the benefits of therapies here given experience of HIV therapies in the past. 8. We call on the manufacturer to realise it has a societal obligation as well as a commercial obligation and out to

	consider cost. 9. At the very least, cost issues aside. It has to be cost effective to treat people with and have Sofosbuvir available to those unable to tolerate current treatments. 10. NICE ought to consider that in arming health professionals with a suitable armoury of medication. Costs are saved over the medium to longer term by less infection being transmitted. There is an over arching Public Health factor here. On a personal level, I hope those whom are close to me, living with Hep C, and unable to undergo interferon/ribavirin therapy. Will have the option of sofosbuvir to aid and 'cure' there condition, improve there wellbeing and mental health but moreover make the contribution to society they feel unable to currently undertake. We are not a medically based organisation. However we campaign to fight the stigma associated with Hep C infection and ensure all therapies are available to those who need them. By far the biggest problem we see is the impact on mental health and those around sufferers who proffer support.
Date	2014 07 03

Name	[redacted]
Job description	[redacted]
Email address	[redacted]
Contact number	[redacted]
Role	[redacted]
Location	England
Organisation	Addaction
Conflict	No
Declaration of interest	
Comments on individual sections of the ACD:	
	Addaction believe that better HCV treatment options are needed, including oral treatments with good tolerability that are more suitable for use in a community setting. Hepatitis C can be cured and the current treatments available are not having a significant impact on hepatitis C as a serious public health issue. The newer treatments such as Sofosbuvir offer the option of oral treatment which are easier to take, treat in a shorter period and may have less side effects. Economic modelling has shown that without treatment for HCV, quality of life decreases and the cost of management increases as the disease progresses. All available evidence points to it being more cost- effective to treat patients for HCV than to manage the effects of liver disease progression. If the infected population is left untreated, the number of patients with severe HCV-related disease will continue to increase and represent a substantial future burden on healthcare resources. This can be mitigated by increasing treatment uptake, which will have the greatest impact if implemented quickly. Drug treatment is not the only element of treatment which needs to be up scaled, opiate replacement treatment (OST), needle syringe programmes, care pathways need to be improved so that people are able to access treatments easily. However access to sofosbuvir and the new treatments for all groups of patients is vital to be able to reduce the burden of hepatitis C. Addaction has developed a BBV strategy that looks at ways in which drug treatment services could develop existing best practice models, so that more people are tested for hepatitis C, and more are referred into treatment. Sofosbuvir would support this strategy. The hepatitis C virus (HCV) is a potentially fatal infection that causes cirrhosis in about 20% of those infected for 20 years (Seeff 2009) and in a higher percentage in those infected for longer. Up to 4% of those with cirrhosis will develop liver cancer. Currently there is treatment available that can cure the infection in about 70% of those infected, thereby greatly reducing the risk of cirrhosis, liver cancer and death. End-stage liver disease caused by hepatitis C is now the leading indication for liver transplant. Sofosbuvir could increase the amount of people who could potentially be cured.

	Approximately 90% of chronic HCV infections acquired in the UK are among people who inject drugs (PWID) or who have injected drugs in the past (Harris et al., 2012). Drug services have played the major part in diagnosing these people with most services being commissioned to offer at least 90% of their service users a test for hepatitis C. Of these, all should be referred to see a consultant at their local hospital. HCVAction conducted a survey amongst 15 randomly selected drug services in the UK in 2013. The study showed an estimated 30% of patients referred for continuing management of their condition attended hospital appointments for further management of their hepatitis C and therefore that 70% did not. The challenges faced by this particular demographic include psychological barriers to attending hospitals, often based on perceptions of a requirement to undergo tough treatment regimes or the need for a biopsy. The introduction of treatment regimes such as Sofosbuvir that are easier to adhere to, and with greater successful outcomes, would contribute to our patients overcoming these barriers. Addaction would like to ask the NICE committee to include the evidence and expert opinions presented in this consultation response when making their final decision on sofosbuvir. We believe that the public health impact of hepatitis C and the opportunities to eliminate the disease should be considered in this appraisal.
Date	2014 07 04

Name	[redacted]
Job description	
Email address	[redacted]
Contact number	[redacted]
Role	[redacted]
Location	England
Organisation	London Joint Working Group on Substance Use and Hepatitis C
Conflict	Yes
Declaration of interest	The LJWG are funded by AbbVie, RBP, Merck, BMS, Gilead Sciences, and Janssen [redacted]
Comments on individual sections of the ACD:	
	Sofosbuvir Appraisal Consultation: Response by the London Joint Working Group on Substance Use and Hepatitis C 4th July 2014 Public Health impact of Hepatitis C Overall there are 215,000 individuals living with chronic HCV infection in the UK. Injecting drug use is the most common route of transmission in the UK accounting for more than 90 per cent of new infections. People who inject drugs represent a population who find it difficult to access traditional models of care. 'Research indicates that PWID (people who inject drugs) are interested in HCV treatment uptake and have rates of viral clearance comparable with other populations. Current injectors are not precluded from HCV treatment access ..... yet uptake rates are substandard'. Reference: Barriers and facilitators to hepatitis C treatment for people who inject drugs. WHO. Harris, Martin, Rhodes June 2012 190,000 PWID are infected with HCV. There is a greater uncertainty over number of ex injectors. Among non-injectors about 40% is among migrants. So estimates suggest that 90% of HCV acquired in UK was through injecting. Reference ' Eliminating HCV within a generation: HCV prevention and treatment of PWID. Matt Hickman LJWG symposium EASL 2014 The appraisal consultation document could consider examining the benefits of treating active injecting drug users with effective anti-viral therapy and thereby reducing onward transmission. 'In London an estimated 34,000 people with a history of injecting drugs have hepatitis C - yet only about 800 people (2%) a year receive treatment. Not only does this represent a major health inequality but it is also a false economy in terms of NHS resources.' Reference: Tackling the Problem of Hepatitis C, Substance Misuse and Health Equalities: A Consensus for London. London Joint Working Group on Substance Misuse and Hepatitis C, Health

	Service Journal, 2011
Comments on individual sections of the ACD:	
	Visconti also showed the cost effectiveness of treating PWUD despite the inclusion of reinfection and lower compliance patients. Reference: Visconti A, Doyle J, Weir A, Shiell A, Hellard M. Assessing the cost-effectiveness of treating chronic hepatitis C virus in people who inject drugs in Australia. J. Gastroenterol. Hepatol. 2013; 28: 707'16. Martin wrote about the cost-effectiveness of providing antiviral treatment for injecting drug users (IDUs) as compared with treating ex/non-IDUs or no treatment. 'Despite the possibility of reinfection, the model suggests providing antiviral treatment to IDUs is the most cost-effective policy option' Reference: The cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations. Martin, NK, Vickerman, P. University of Bristol Hepatology, vol 55., pp. 49-57 She also writes that direct acting anti-virals will soon be available with very high SVR rates (>90% for all genotypes), a short duration of 8-12 weeks, high barriers to resistance and low toxicity. 'This could lead to dramatically higher uptake rates, particularly among PWID'. Reference: How cost-effective is hepatitis C virus treatment for people who inject drugs? Natasha K Martin, Peter Vickerman, Alec Miners and Matthew Hickman. J. Gastroenterol. Hepatol. 2013; 28: 707'716. Within the overall population of people with hepatitis C 'just 28,000 people received treatment between 2006 and 2011. That means only 3% of the people chronically infected with hepatitis C are accessing treatment each year'. Reference: A hepatitis C story worth telling. Helen Harris, 30 June 2014. Gov.UK blog Public Health Matters. https://publichealthmatters.blog.gov.uk/2014/06/30/a-hepatitis-c-story-worth-telling/
Comments on individual sections of the ACD:	
	The Hepatitis C Trust report 'The Uncomfortable Truth: Hepatitis C in England' highlights that the virus affects the poorest in society who account for almost half of all hepatitis C hospital admissions. In addition, deaths and hospital admissions for hepatitis C-related end stage liver disease and liver cancer have nearly quadrupled in the last 15 years. Reference: Public Health England. Hepatitis C in the UK: 2013 report. July 2013. http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317139502302

	In 2010/11 alone, up to Â£22 million was spent on emergency hospital admissions caused by potentially avoidable hepatitis C complications. Reference : Calculation based on data from: Pgs. 8, 21: Payment by Results team, Department of Health. Reference costs 2011-12. November 2012. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/127112/2011-12-reference-costs-publication.pdf; The Hepatitis C Trust. Hepatitis C in England: The State of the Nation ' Technical Appendix. August 2013. http://www.hepctrust.org.uk/News_Resources/resources/reports Professor [redacted], Consultant Hepatologist [redacted], said: "It is a travesty that increasing numbers of patients on our wards are dying from hepatitis C when so many with early liver disease can be cured and protected from liver damage."• Modelling work shows that there will be a significant long-term increase in liver disease morbidity and mortality if hepatitis C treatment rates are not increased. Radical change to current practice including the introduction of the newer oral treatments can avert over 5,000 liver deaths in England alone and prevent over 1,000 liver transplants. At the LJWG EASL symposium 2014 Professor [redacted] spoke about a scale-up to treating 20 per 1000 PWID annually could reduce prevalence by nearly 70% in 15 years, and a further scale-up to 40 per 1000 PWID annually could reduce prevalence by over 90%, from 25% in 2012 to less than 3% in 2027. He discussed DAAs possibly more than halving the prevalence. Despite the availability of NICE recommended therapies for some years the treatment of patients with HCV in England remains sub-optimal. Reference: Journal of Hepatology May 2014: Increased uptake and new therapies are needed to avert rising hepatitis C-related end stage liver disease in England: Modelling the predicted impact of treatment under different scenarios. Ross J. Harris, Helen Harris DOI: 10.1016/j.jhep.2014.05.008
	If we continue with our current level of treatment, the 215,000 individuals living with chronic HCV infection in the UK will impose an increasingly heavy clinical and economic burden. Increasing the number of people cured of hepatitis C would represent a significant step towards the aim expressed in NHS England's and PHE's outcome frameworks of reducing the burden of liver disease. Professor [redacted] from [redacted] spoke at the International Liver Congress about better treatment options being needed, including oral treatments with good tolerability that are more suitable for use in a community setting. Prevalence and transmission of hepatitis C in people who use drugs can be reduced by scaling up hepatitis C treatment, in combination with effective opioid substitution therapy, alongside needle exchange services.

	At the International Liver Congress 2014 [redacted] from PHE presented on how standard treatment (peg interferon and ribavirin) is achieving 37% SVR for genotype 1 and 70% non 1, with a worse outcome for older patients and those with more advanced disease and that improved treatments over next 5 years could achieve 90% SVR rate, 60% in cirrhotics. [redacted] went on to say that treatment regimens with good safety/tolerability profiles that can be rolled-out in community settings will be key. Reference: 'Increased uptake and new therapies urgently needed: Modelling the predicted impact of treatment under different scenarios'. Ross Harris Dr. Helen Harris Immunisation, Hepatitis and Blood Safety Department CIDSC, PHE, London. LJWG symposium International Liver Congress 2014.
	Dr [redacted] spoke at the International Liver Congress in 2014 about the new DAA's being improved treatments, with better cure rates, fewer side effects and shorter treatment increasing treatment eligibility. Hepatitis C can be cured and the current treatments available are not having a significant impact on hepatitis C as a serious public health issue. The newer treatments offer the option of oral treatment which are easier to take, treat in a shorter period and may have less side effects. Reference ' Eliminating HCV within a generation: HCV prevention and treatment of PWID. Matt Hickman LJWG symposium EASL 2014 Hospital admissions and deaths from HCV-related end-stage liver disease and HCC increased almost four-fold in the UK between 1998 and 2011, from 612 to 2,268 and 98 to 381 respectively. In an article in the HSJ 2014 Dr Steve Ryder and Dr John Dillon speak about a cure with a 74 per cent reduced risk of all-cause mortality and a 94 per cent reduction in the risk of liver-related mortality or transplantation and cancer. Dr Stephen Ryder and Dr John Dillon wrote in the HSJ in 2014 'increasing treatment numbers in this way will reduce healthcare costs by an estimated Â£852m between 2013 and 2030.' Reference: 'Eradicating hepatitis C is a realistic aim' By Stephen Ryder and John Dillon HSJ 2014
Comments on individual sections of the ACD:	
	Scotland: Hepatitis C drug Sofosbuvir approved for use on NHS The Scottish Medicines Consortium (SMC) decided the high cost of offering sofosbuvir to patients was outweighed by its effectiveness. It is estimated 50,000 people in Scotland have hepatitis C. A statement by the SMC said: "The consortium accepted sofosbuvir for restricted use because it is effective and addresses an unmet

	treatment need." It will be available for patients with genotypes of the disease from one to six. Reference: http://www.bbc.co.uk/news/uk-scotland-27762181 9thth June 2013
	Treating cirrhotic and not non- cirrhotic There is a benefit of treating people just pre-cirrhosis reducing the HCC risk and this is not considered in the 'cirrhotic/non-cirrhotic' model. Hospital admissions and deaths from HCV-related end-stage liver disease and HCC increased almost four-fold in the UK between 1998 and 2011, from 612 to 2,268 and 98 to 381 respectively. Reference: 'Eradicating hepatitis C is a realistic aim' Stephen Ryder and John Dillon HSJ 2014 The presence or absence of cirrhosis creates diagnostic problems also because of the unreliability of fibro scan and serum marker method. This could mean that people who are being considered for the newer treatments will be referred for biopsy and this can deter patients from engaging in assessment and treatment in specialist services. Many patients with hepatitis C complain of extrahepatic manifestations like severe fatigue and excluding patients with mild hepatitis C and extrahepatic manifestations from sofosbuvir and permitting only those with cirrhosis (who may be asymptomatic) to access the drug (or vice versa) will be clinically difficult to implement. Dr [redacted] looked at 3 cohorts of people who use drugs (PWUD's) never injectors, current injectors and former injectors and concluded that 'Early treatment is more cost effective than late treatment (at compensated cirrhosis) for all cohorts'. Reference: How cost-effective is hepatitis C virus treatment for people who inject drugs? Natasha K Martin, Peter Vickerman, Alec Miners and Matthew Hickman. J. Gastroenterol. Hepatol. 2013; 28: 707'716.
	Cost effectiveness of treatment It has been highlighted in the appraisal that treatment for 24 weeks with sofosbuvir would not be cost effective. There are very few pegylated interferon intolerant patients many can tolerate a shorter duration of interferon thus that the majority of patients will be treated for 12 rather than 24 weeks. If the infected population is left untreated, the number of patients with severe HCV-related disease will continue to increase and represent a substantial future burden on healthcare resources. This can be mitigated by increasing treatment uptake, which will have the greatest impact if implemented quickly.

	The total additional cost for implementing rapid complete coverage was estimated at Â£1460 million (95% CrI 1170’1890) over the next 30 years. These are substantial costs; however, the total healthcare cost of the HCV-infected population over the next 30 years under current treatment levels was estimated to be Â£4680 million (95% CrI 3770’5900). Therefore, although treatment costs are substantial, they are still relatively small compared to the total cost of disease burden. Reference: Journal of Hepatology May 2014: Increased uptake and new therapies are needed to avert rising hepatitis C-related end stage liver disease in England: Modelling the predicted impact of treatment under different scenarios. Ross J. Harris, Helen Harris DOI: 10.1016/j.jhep.2014.05.008 Economic modelling has shown that without treatment for HCV, quality of life decreases and the cost of management increases as the disease progresses. All available evidence points to it being more cost- effective to treat patients for HCV than to manage the effects of liver disease progression. Reference: Public Health Report on Commissioning of HCV services in London for People who Inject Drugs. Author Abigail Knight. London Joint Working Group on Substance Use and Hepatitis C and NHS NW London. Health Service Journal April 2013 The LJWG would like to ask the NICE committee to include the evidence and expert opinions presented in this consultation response when making their final decision on sofosbuvir.
Date	2014 07 04

Name	[redacted]
Job description	[redacted]
Email address	[redacted]
Contact number	[redacted]
Role	Patient
Location	England
Organisation	[redacted]
Conflict	No
Declaration of interest	A few years ago I was on a committee funded by Gilead looking at patient education in HIV.
Comments on individual sections of the ACD:	
	The UK-CAB is a national HIV treatment advocacy organisation that has more than 600 community members and that links more than 100 HIV organisations. It works to educate people with HIV, advocates and supporters on health and treatment issues about HIV infection.[1] We were extremely disappointed that the committee does not seem to understand the paradigm shift in treatment of HCV and appears stuck in an outdated mindset that permeates the appraisal document. In the interferon era genotype 1 was harder to treat, genotypes 2 and 3 were treated exactly the same and HIV coinfection reduced response rates. These premises are all incorrect for interferon free regimes and should be abandoned; genotype 1 will have a much wider range of highly effective treatment options than all other genotypes; genotype 3 requires a longer treatment regime to genotype 2 and coinfection is no longer relevant to treatment response .[2] This submission contains an interferon regime and a DAA regime but both are treated within this outdated mindset. We were disappointing that Gilead did not appear to provide sufficient data for a cost-effectiveness assessment in HIV/HCV coinfection for treatment of genotypes 1, 4, 5, 6. The submission includes a use with Pegylated Interferon for these genotypes and started when it was still thought to be a relevant criterion for treatment response. The extraordinarily high cost of Sofosbuvir is also very concerning given the large numbers of people with this condition and the decreasing funding of the NHS. A sensible and sustainable price for Sofosbuvir would lead to the curing of many more people with HCV in the UK and elsewhere. The treatment response rates for HIV coinfection may be the same with DAAs as for HCV monoinfection but the natural history of the disease remains different with accelerated progression to hepatocellular carcinoma [3,4] and higher mortality rates [5,6] than HIV or HCV monoinfection. For this reason of faster progression to illness and death it is relevant to think about people

	coinfected with HIV as an important sub-group. However any cost effective treatment for HCV monoinfection will inevitably be even more cost-effective in those with HIV because of this accelerated natural progression. The rate of HCV infection amongst people with HIV is over 22 times [7] that of the general population [8] and increasing with the ongoing epidemic of sexually transmitted HCV infectious amongst gay men with HIV .[9] It is very concerning that a lack of data is the reason for delaying a decision about all use of Sofosbuvir. There is always going to be a lack of data in aspects of hepatitis C treatment (e.g. acute HCV infection or treatment of genotypes 5 and 6) and a lack of data should not be a reason to delay all access or provide inequitable access without a verifiable justification. The treatment of Genotypes 2 and 3 with Sofosbuvir and Ribavirin are discussed together even though they have different response rates necessitating different durations of treatment (see Fission and Fusion trial data). The trial looking at 24 weeks of treatment for Genotype 3 (Valence) does have some methodological problems but it was perfectly clear that 12 weeks was insufficient for Genotype 3 and it would have been wholly unethical to continue the trial merely to re-prove this. The evidence it provides may not be quite as solid as a double-blinded RCT but it would be wrong for the committee to ignore it and downgrade the evidence because the trial managers acted ethically. The committee should look at cost effectiveness of treatment for these two genotypes separately, at 12 weeks of Sofosbuvir and Ribavirin for genotype 2 and 24 weeks of sofosbuvir and Ribavirin for genotype 3. HIV coinfection is not relevant to the response rate of Sofosbovur and Ribavirin for genotypes 2 and 3 and there is no reason for the lack of data about this to be used to delay access.
	Currently NHS England has agreed to provide Sofosbuvir to patients that are at “significant risk of death or irreversible damage within the next 12 months...• . [10] This is a vitally important step but still leaves the large majority of people with HCV unable to access the drug before the committee makes its recommendation. Sofosbuvir with Pegylated Interferon and Ribavirin for people with genotype 1, 4, 5 and 6 provides a significantly reduced duration of an arduous treatment and a simpler regime than is the current standard of care. Sofosbuvir with Ribavirin for people with Genotype 2 will make a huge difference in terms of the likelihood of success, tolerability and duration of treatment over the current standard of care. Sofosbuvir with Ribavirin for people with genotype 3 provides a treatment that lasts as long but with far fewer side-effects allowing them to work and live more easily while on treatment.
	References 1. http://www.ukcab.net/ 2. European Association for the Study of the Liver (EASL). Recommendations on treatment of hepatitis C. April 2014. Available at: http://files.easl.eu/easl-recommendations-on-treatment-of-hepatitis-C/index.html (Accessed on July 1, 2014). 3. Clifford GM, Rickenbach M, Polesel J et al. Influence of

	HIV related immunodeficiency on the risk of hepatocellular carcinoma. AIDS 2008; 22: 2135’2141. 4. Kramer JR, Giordano TP, Souchek J, Richardson P, Hwang LY, El-Seraq HB. The effect of HIV coinfection on the risk of cirrhosis and hepatocellular carcinoma in U.S. veterans with hepatitis C. Am J Gastroenterol 2005; 100: 56’63. 5. Tedaldi E, Peters L, Neuhaus J et al. Opportunistic disease and mortality in patients coinfected with hepatitis B or C virus in the strategic management of antiretroviral therapy (SMART) study. Clin Infect Dis 2008; 47: 1468’1475. 6. van der Helm J, Geskus R, Sabin C et al. Effect of HCV infection on cause-specific mortality after HIV seroconversion, before and after 1997. Gastroenterology 2013; 144: 751’760 7. Turner J, Bansi L, Gilson R et al. for the UK Collaborative HIV Cohort (UK CHIC) Study. The prevalence of hepatitis C virus (HCV) infection in HIV-positive individuals in the UK ‘ trends in HCV testing and the impact of HCV on HIV treatment outcomes. J Viral Hepat 2010; 17: 569’577 8. http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/HepatitisC/GeneralInformation/ 9. Peters L, Mocroft A, Soriano V et al. Hepatitis C virus reappearance in HIV-infected patients with spontaneous HCV-RNA clearance. J Hepatol 2009; 50(Suppl 1): S155. 10. Interim Clinical Commissioning Policy Statement: Sofosbuvir + Daclatasvir/Ledipasvir +/- Ribivirin for defined patients with Hepatitis C. April 2014 Reference: NHS ENGLAND A02/PS/b
Date	2014 07 04

Name	[redacted]
Job description	[redacted]
Email address	[redacted]
Contact number	[redacted]
Role	Voluntary Sector
Location	England
Organisation	[redacted]
Conflict	Yes
Declaration of interest	Positively UK receives monetary and in-kind support from Gilead Sciences amounting to approximately Â£20,000 per annum.
Comments on individual sections of the ACD:	
	Positively UK supports over 1,000 people living with HIV every year, many with co-infection with Hepatitis C. HIV and Hep C are both stigmatized conditions. People living with these conditions must adhere strictly to medications, and HIV will result in people being diagnosed early and with greater prevalence of co-morbidities such as cardiovascular disease. We want to ensure people living with HIV, and with Hep C, have access to the best quality care for the best quality of life. While we note NICE's appraisal and the Patient groups consulted stated how sofosbuvir would encourage people to seek diagnosis and treatment and we support this assertion. Clinical specialists while rightly raises concerns over small patient numbers and cohorts in trials and robustness of the mixed treatment comparison, however in some cohorts it would lead to better sustained virological response. The Scottish Medicines Consortium in its assessment raised the same concerns as the NICE appraisal. However Scottish Medicines Consortium concluded that Sofosbuvir should be licensed but for restricted use - notably with restrictions on genotype 2 and 3. We would urge NICE to re-consider its recommendation for sofosbuvir in treating chronic Hep C in adults and include in the recommendation a guide to the limits and restrictions for its use. In doing so NICE will be extending patient choice, promoting the quality of life of people living with Hep C and promoting access to testing and treatment. We also seek to tackle disparities in quality of healthcare across England and across the UK, and believe licensing of sofosbuvir will provide equity of care across the UK.
Date	2014 07 04

Name	[redacted]
Job description	[redacted]
Email address	[redacted]
Contact number	0121 449 4405
Role	Patient
Location	England
Organisation	[redacted]
Conflict	No
Declaration of interest	
Comments on individual sections of the ACD:	
	BASELINE www.baseline-hiv.co.uk is a community magazine for people living with HIV and HIV/hepatitis C coinfection. We believe sofosbuvir, in its shorter duration offers people with hepatitis C a major advance in treatment and will increase the uptake of treatment. We are aware that NHS England recently approved funding for sofosbuvir in England and Wales significantly at risk of dying or needing a liver transplant and that there are a number of clinical trials, though perhaps small in number, detailing the efficacy of sofosbuvir across of range of sub-populations including people with HIV and people with advanced liver disease including cirrhosis. The current standard of care for HCV involves 24-48 weeks of therapy with RBV and peg-IFN, which has to be injected and is associated with significant side effects. This treatment course is sometimes extended to 72 weeks among people who live with both HIV and hepatitis C. The current standard of care often causes people to lose time from work and people often report lingering toxicity for months or years after taking the treatment. Historically being HIV positive has been associated with a reduced likelihood of SVR with RBV and peg-IFN treatment. With sofosbuvir-based treatment this is no longer the case. The playing field among mono-infected and co-infected patients has been leveled HIV should no longer be a barrier to access to new hepatitis C medicines. Sofosbuvir is a major advance for people with hepatitis C as it offers treatment of shorter duration and with a significantly better tolerablity profile. Historically treatment uptake of hepatitis C medicines has been very poor. We believe that an advance such as sofosbuvir has the potential to increase the likelihood that a patient will take up the offer to initiate treatment. And we believe this could play an important role in reducing

	hepatitis C incidence and onwards hepatitis C transmission since coinfected individuals are more likely to sexually transmit hepatitis C. We believe that people with HIV and hepatitis C are more easily identified (or are already identified as they are receiving HIV care with regular hepatitis C testing in clinic) and constitute a great target population in which the eradication of hepatitis C could be demonstrated to be possible. We believe the cost of not treating a coinfected individual with sofosbuvir is much higher than treating in view of the high proportion of patients who will develop the complications associated with cirrhosis, need liver transplantation, or treatment for liver cancer, and we reflect on the shorter time often seen for these states to occur among coinfected people. HIV is no longer a barrier to treatment response with new medicines like sofosbuvir. Recent guidance from the European Association for the Study of the Liver (EASL) states that it is no longer acceptable for people with HIV coinfection to be treated any differently to people with hepatitis C monoinfection. By NICE denying access to people with HIV we believe this would be inequitable. Sofosbuvir has already been approved by the SMC and we believe that should it not be approved in England for all patients we believe this will be inequitable. We also believe it should be patients' decision when they access treatment, that patients should not have to wait to be cirrhotic to access treatment and that the decision to start should be made by the patient and their physician should be able to offer treatment if the patient wants it, if that treatment has been shown to be effective and cost-effective. The over-arching desire among the patients we work with is for a short-course tolerable dual tablet-based therapy that is highly effective. We believe sofosbuvir to be the drug that brings these desires a huge step closer to being a reality.
Date	2014 07 04