NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Sofosbuvir for treating chronic hepatitis C

Response to consultee, commentator and public comments on the consultation on decision to amend the deferred funding

Definitions:

Consultees – Organisations that accept an invitation to participate in the appraisal including the companies, national professional organisations, national patient organisations, the Department of Health and the Welsh Government and relevant NHS organisations in England. Consultees can make a submission and participate in the consultation on the appraisal consultation document (ACD; if produced). All non-company consultees can nominate clinical experts and/or patient experts to verbally present their personal views to the Appraisal Committee. Company consultees can also nominate clinical experts. Representatives from NHS England and clinical commissioning groups invited to participate in the appraisal may also attend the Appraisal Committee as NHS commissioning experts. All consultees have the opportunity to consider an appeal against the final recommendations, or report any factual errors, within the final appraisal determination (FAD).

Clinical and patient experts and NHS commissioning experts – The Chair of the Appraisal Committee and the NICE project team select clinical experts and patient experts from nominations by consultees and commentators. They attend the Appraisal Committee meeting as individuals to answer questions to help clarify issues about the submitted evidence and to provide their views and experiences of the technology and/or condition. Before they attend the meeting, all experts must either submit a written statement (using a template) or indicate they agree with the submission made by their nominating organisation..

Commentators – Commentators can participate in the consultation on the ACD (if produced), but NICE does not ask them to make any submission for the appraisal. Non-company commentator organisations can nominate clinical experts and patient experts to verbally present their personal views to the Appraisal Committee. Commentator organisations representing relevant comparator technology companies can also nominate clinical experts. These organisations receive the FAD and have opportunity to report any factual errors. These organisations include comparator technology companies, Healthcare Improvement Scotland any relevant National Collaborating Centre (a group commissioned by NICE to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups such as the NHS Confederation, the NHS Commercial Medicines Unit, the Scottish Medicines Consortium, the Medicines and Healthcare Products Regulatory Agency, the Department of Health, Social Services and Public Safety for Northern Ireland).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but NICE reserves the right to summarise and edit comments received during consultations, or not to publish them at all, where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would be otherwise inappropriate.

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comments received from consultees

Consultee	Comment	Response
Gilead	Further to our correspondence of 14th November 2014 to Sir Andrew Dillon, a copy of which is attached (Appendix 1), we are writing in response to the consultation on the decision to defer funding for the implementation of NICE guidance recommendation on the use of sofosbuvir following a request from NHS England. As you are aware there have already been a number of delays in the appraisal process for sofosbuvir and further delay to the actual implementation of the final recommendations will cause avoidable harm to patients and increased cost and burden on existing NHS resources. The reasons provided by NHS England to justify delay in implementation of the current Guidance are unsupported by evidence and all information available to Gilead indicates that they are factually incorrect. While without disclosure of the evidence, if any, which has formed the basis for NHS England's submissions, it is difficult for Gilead to respond to this consultation in a comprehensive way, we believe that the concerns expressed by NHS England are based on the predicted implications of the introduction of future treatment regimens, which will permit fully oral interferon-free regimens for the wider majority of Hepatitis C patients - and not on the implications of the implementation of the current Guidance for sofosbuvir. This does not constitute a valid basis for extending the period for implementation of Guidance in accordance with regulation 7(5) of the 2013 Regulations. In contrast to NHS England's assertions, available evidence points to the fact that implementation of the current Guidance is very unlikely to result in substantial numbers of additional patients and will relieve rather than add to the existing burden on Hepatitis C services. **1. <u>Introduction</u>** An extension to the standard 90 day period for implementation of NICE Guidance is permitted only in the specific circumstances set out in regulation 7(5) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 ("the 2013 Regulations") namely:	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	(a) the health technology cannot be appropriately administered until— (i) training is, (ii) certain health service infrastructure requirements including goods, materials or other facilities are, or (iii) other appropriate health services resources, including staff are in place; or (b)the health technology is not yet available in England. Other matters may not lawfully be relied upon to justify delay. Furthermore, while Gilead recognises that the submissions made by NHS England should be taken into account by NICE in making its decision on implementation, the weight to be attached to those submissions will depend on the evidence provided by NHS England in support of its position. In particular it would not be fair, proportionate or rational for NICE to make a positive finding of any of the regulation 7(5) factors and therefore to delay implementation of Guidance based on simple assertion by NHS England (or anyone else) and in the absence of robust evidence. Gilead strongly disagrees with NICE'S preliminary view that the Guidance for sofosbuvir should be delayed by an additional 90-plus days as a result of factors within the scope of regulation 7(5)(a) of the 2013 Regulations. We firmly believe that the matters raised by NHS England and relied upon by NICE are either inconsistent with the requirements of the 2013 Regulations or contrary to the available evidence. Furthermore, NHS England has already had at least 18 months to prepare for the introduction of sofosbuvir treatment. To suggest that they are unprepared now to implement a cost-effective treatment in circumstances where there is an unmet clinical need and therapy has already been introduced in other parts of the UK and across the EU, without the difficulties they identify, is wholly unacceptable. In the consultation document NICE indicates its view that there is a presumption in favour of acceding to the request by NHS England for delay, stating that it *"should be cautious and sure of its judgement before requiring NHS England to provide services that it does not consider that it can provide, or provide safely and efficiently"* and that *"NICE should be wary of substituting its judgement for NHS England's in this respect'.* We believe that this is the incorrect approach as a matter of fairness and does not represent a proper construction of the 2013 Regulations. The points raised by NHS England in their request for delay in implementation of the Guidance for sofosbuvir could equally apply to any Single Technology Appraisal where an innovative technology, representing a step change in treatment, is introduced and NICE should be very cautious about the implications of accepting a request for delay on the basis of what is, at most, insubstantial evidence.	

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	We have provided below specific responses to the following points raised by NHS England and provisionally accepted by NICE as justifying delay in implementing the final Guidance; •the perception that demand for treatment with sofosbuvir following implementation of the current Guidance, will be very substantial •the need to establish a Hepatitis C Network prior to the implementation of NICE guidance on sofosbuvir, In addition to the submissions set out in this letter, we rely on evidence provided by clinicians treating patients with chronic Hepatitis C infection as provided in Appendix 2. For the avoidance of doubt, Appendix 2 contains all statements and correspondence received by Gilead from clinicians, without selection or exclusion. The additional matters raised by NHS England (a) in their letter to NICE dated 19 November 2014 and (b) prior to the meeting of the Appraisal Committee on 10th September 2014 are not addressed in detail in this response document, in view of the fact that they were not seemingly relied upon by NICE and have not therefore formed the basis for NICE'S provisional decision on implementation. **2. <u>Response to the matters relied upon by NICE</u>** **2.1. The demand for treatment with sofosbuvir following implementation of the current Guidance,** *<u>NHS England's position</u>* NHS England have expressed the view that the implementation of the current Guidance for sofosbuvir will result in a huge increase in patients coming forward to be tested and requesting treatment for chronic hepatitis C infection. They state in their letter of 19 November 2014: " *The management and treatment of Hepatitis C is an NHS England priority. The most recent national estimates suggest that around 160,000 adults[1] are chronically infected with hepatitis C (HCV) in England in 2012. Current numbers of patients treated are estimated at 5,000 per year in England - 3% of those currently infected but this will increase rapidly. The CRG Hepatitis C sub group have estimated that 10 - 15,000 people per year may come forward seeking HCV treatment".*	

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	NHS England go on to say: *"Until last year, treatment for HCV has depended on a combination of two relatively low cost drugs - interferon and ribavirin. These have limited efficacy for some large subgroups of patients with Hepatitis C, and for many patients, cause serious side effects. There are other patients who have failed first line treatment who would now be potentially treatable with the new drugs. Patient groups are very aware that new and less toxic drugs will be available soon and there is already reported increased demand for these treatments. Over the next twelve months several directly acting anti-viral agents will be launched into the UK which will have reduced length of treatment, and side effects and increased cure / SVR rates. These drugs have different modes of action to the current treatments and allow for an interferon free (i.e. needleless) treatment strategy".* *Gilead Response* The conclusions NHS England have attributed to the CRG Hepatitis C subgroup have not been published, therefore it has not been possible to understand the basis for the figures quoted by NHS England or to test their accuracy. However, the evidence available to Gilead indicates that, while the implementation of the current Guidance will represent an important development for seriously ill patients with chronic hepatitis C infection, this will not result in a substantial increase in the numbers of patients coming forward for testing and treatment. *Analysis of current Guidance and likely demand* The current Guidance recommends use of sofosbuvir as follows: •In combination therapy with interferon and ribavirin for: • All patients with GT1 o No patients with GT2 • Treatment experienced patients with GT3 and treatment naive patients with cirrhosis • No patients with GT4, GT5 and GT6 •In combination therapy with ribavirin alone (a fully oral regimen) for: • No patients with GT1 • Treatment experienced patients with GT2 and those intolerant or ineligible for interferon • Patients with GT3 who have cirrhosis and are intolerant or	

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	ineligible for interferon • No patients with GT4, GT5 or GT6 In summary the current Guidance for sofosbuvir recommends use as part of a fully oral regimen only for patients with GT2 and GT3 hepatitis C and in limited circumstances. *Evidence from clinicians* Gilead believes, that the Hepatitis C CRG subgroup's estimate of an increase of 10,000 to 15,000 patients is unlikely to be associated with the implementation of this Guidance (which recommends sofosbuvir in combination with pegylated interferon and ribavirin in all but a very limited group of patients), but rather is associated with the introduction of future therapies that allow interferon free options for the majority of patients. This view is supported by the evidence of clinicians provided in Appendix 2; those practising in England who have identified the patients they would treat following implementation of the current Guidance for sofosbuvir and those practising in Scotland who have described the impact of similar recommendations for sofosbuvir issued by the SMC in June 2014. Thus, the evidence of clinicians in England is that whilst the regimens assessed in the current Guidance for sofosbuvir address an important unmet need by providing a high level of efficacy with a shorter duration of treatment, many patients will still wish to defer therapy until additional oral agents are available providing the anticipated fully oral options for more than a very few patients. The evidence from clinicians in England and the experience in Scotland is consistent with that from other European countries where sofosbuvir is available. (Incidentally, it is also consistent with the figures calculated by NICE themselves within the Costing Template prepared for the purposes of implementation of this particular Guidance.) Based on the UK Ipsos HCV monitor database 2013-2014[2] the population of patients with chronic hepatitis C infection in England, may be described as follows : • Approximately 16,000 patients are thought to be 'under treater care' in England of which: •10,516 (66%) are treatment naive and 5,484 (34%) are treatment experienced •3,327 (21%) are cirrhotic and 12,673 are non-cirrhotic (79%) • Approximately 14% are thought to be unsuitable or intolerant to interferon based	

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	therapy. • Approximately 5,500 of those patients thought to be 'under treater care' are currently prescribed Hepatitis C treatment on an annual basis[14] Data on Hepatitis C disease prevalence indicates that patients are affected by hepatitis C genotypes as follows[3]: •45% are genotype 1; •7.3% are genotype 2 (approximately 1,168 patients under treater care in England); •43.8% are genotype 3; •3.9% are genotype 4/5/6 Accordingly, clinician evidence (Appendix 2), is that the patients who will receive treatment in accordance with the current Guidance are patients who have cirrhosis and those who do not have cirrhosis but are eligible for a fully oral interferon-free regimen (i.e. treatment experienced patients with GT2 and those GT2 and GT3 patients who are intolerant or ineligible for interferon). The best estimate we can produce based on the above data constitutes approximately 800 additional patients will satisfy these criteria following implementation of the current Guidance. Those patients who are non-cirrhotic (the majority of patients under treater care) will likely wait to commence treatment until fully oral interferon-free treatment options become available shortly. Patients most likely to opt for treatment at this stage are those with marked extra-hepatic symptoms or those with cirrhosis wishing to reduce their risk of developing cancer during the time required to make all oral treatments available. Even if all cirrhotic patients under treater care came forward for treatment at this stage (3,327[2]), this would not represent an increase in the total numbers of current patients treated over a year (5.500)[14] *Evidence from experience following introduction of Protease Inhibitors* NHS England's statement that *'hepatitis C management has depended on two relatively low cost therapies, interferon and ribavirin',* is factually incorrect. Protease inhibitors, boceprevir and telaprevir were approved by NICE for the treatment of GT1 hepatitis C patients in April 2012 and represented a step change in management of affected patients, (note, the drug acquisition cost of protease based inhibitor regimens range from £22,872 through to £41,210). NHS England has not	

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	suggested that the introduction of these treatments required an extended period for implementation or resulted in the increase in numbers of patients presenting for treatment as is now suggested for sofosbuvir. *Evidence from Scotland* Sofosbuvir was appraised by the Scottish Medicines Consortium earlier in this year with guidance issued in June recommending use in patients with genotypes 1 to 6. Use in treatment-naive patients with genotype 2 is restricted to those who are ineligible for, or are unable to tolerate, peginterferon alfa. Use of the 24-week interferon-free regimen of sofosbuvir in combination with ribavirin in patients with genotype 3 is restricted to those who are ineligible for, or are unable to tolerate, peginterferon alfa (SMC Advice Number 964/14). NHS Scotland has a very similar service structure to England and yet has been able to implement broad access to sofosbuvir based regimens within 1 month of the SMC decision to recommend use. Based on Scottish Health protection data 2013,[4] Scotland has approximately 5100 patients under treater care of which in 2013, 1050 were treated. Since positive Sovaldi SMC guidance in June of this year approximately XXXXXXX patients have been initiated on treatment with Sovaldi based regimens over a six month time period[5]. This means that the number of patients treated with a sofosbuvir based regimen over this time period did not exceed the number of patients typically treated over a 6 month period i.e. the availability of Sofosbuvir does not appear to have driven the 2 to 3 fold growth in treatment that NHS England suggest. (Appendix 2) The experience in Scotland has therefore confirmed that a substantial increase in patients presenting for testing and treatment after implementation of this Guidance is unlikely and provides no support for NHS England's concerns. Furthermore, in circumstances where NHS Scotland was able to implement a similar recommendation within a month of issue, the delay proposed by NHS England is unjustified and wholly unacceptable. In summary therefore, while there seems likely to be a substantial increase in patients with chronic hepatitis C infection presenting for testing and treatment once fully oral interferon-free regimens for the predominant non-cirrhotic category of patients are available, Gilead is aware of no evidence which validates NHS England's concerns regarding an increase in numbers following implementation of this Guidance relating to sofosbuvir only, whilst having available substantial evidence indicating the contrary position. **2.2 Need to establish a Hepatitis C network**	

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	NHS England's position NHS England state that there is a need to establish a Hepatitis C Network prior to implementation with this involving the set up a series of centres with the staff and the other resources and systems necessary to provide a multi-disciplinary team (MDT) approach to care. They say in their letter of 19 November 2014: *"A Hepatitis C network model will be formally commissioned comprising specialised centres with a caseload to develop and maintain expertise in the treatment of the condition working in partnership with a range of providers across the health and justice system. The Centres will encompass MDT decision-making by experienced teams on the appropriateness of initiation of treatment or continued surveillance of infected patients. MDT decision-making by experienced teams will support selection of the optimal treatment regimen for each patient. MDTs offer clinical and cost effective prescribing of high cost drug treatments in accordance with NHS England policy/NICE TAs. The network will support access to treatment services locally through formal partnership and outreach models. This will optimise partnership working and utilisation of local expertise in engaging hard to reach groups in completing treatment programmes. NHS England would be required to commission Hepatitis C Networks through a competitive procurement route. This process would take about 9 months. A key part of the model is partnership working and the preferred procurement model would be to allow bidders additional time to develop their proposals jointly with others e.g. prison health, LAs etc.* *Gilead's response* Whilst Gilead welcomes any opportunity to improve the current Hepatitis C service model that may further enhance patient access and outcomes, the submission by NHS England provides no evidence that the proposed Hepatitis C network is required for the implementation of the current Guidance. In particular, whilst a more sophisticated approach may be preferred in the context of the increase in the number of patients with chronic Hepatitis C infection who would be expected to present for testing and treatment after implementation of fully oral interferon-free regimens for the non-cirrhotic group, Gilead believes there is no requirement for this approach for the implementation of the current Guidance relating solely to sofosbuvir - and NHS England has provided no evidence indicating that this would be the case. Importantly we are not aware of any suggestion that implementing this guidance under the current service framework would result in ineffective, unsafe treatment. Currently the majority of hepatitis C treatments (circa 80%) are managed by	

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	approximately 60 tertiary treatment centres across the UK.[6] .We are not aware of any drug or alcohol services initiating hepatitis C treatment without affiliation to one these tertiary centres[6]. (Appendix 2) The current service has historically treated around 5,500 chronic hepatitis C patients on an annualised basis[14] The following two main treatment options providing the standard of care[7]: •Protease inhibitors telaprevir and boceprevir in combination with peginterferon and ribavirin for patients with genotype GT1 for 24 to 48 weeks dependent on patient profile and response. •Peginterferon plus ribavirin (PEG-IFN + RBV) for GT 2 - 6 and GT1 where Pis are contra-indicated for 24 to 48 weeks. Services are therefore already set up to initiate patients on complex therapies involving direct-acting antivirals (DAAs) as well as PEG-IFN and RBV. In order to initiate current NICE-approved therapies, centres already have in place: • The ability to screen for drug - drug interactions (input from speciality pharmacy) •Understanding of resistance considerations for choice of DAA •Ability to use on treatment measurements of response to guide duration (Response guided therapy, RGT) •MDT approach suitable for the prescribing of high cost drugs (treatment with currently NICE approved combinations could cost from £5,000 to £39,000) •Throughout treatment patients must have regular appointments to monitor viral load and safety. In particular Pis have been associated with life- threatening skin reactions and anaemia meaning that rapid referral to dermatology clinics needs to be in place and admissions may be required to manage anaemia The implementation of the current Guidance for sofosbuvir will have the following impact on the Hepatitis C service and is further evidenced in Appendix 2: 1) Reduction in treatment duration of interferon based therapy from 24-48	

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	weeks down to 12 weeks for the majority of patients. The reduction of treatment duration will free- up significant capacity as current treatments require regular checks and interventions. 2) Reduction in time required to manage DDI and resistance profile due to an improved safety and tolerability profile of sofosbuvir vs. majority of existing treatments 3) No need for on treatment viral load testing and adjustments as duration of therapy is ascertained at the start of treatment Therefore for every patient treated it is anticipated that the service capacity required will be substantially lower following the introduction of sofosbuvir. Furthermore, there seems to be no basis for concluding that a service capable of delivering treatment of currently NICE approved options safely and efficiently would not be more than able to implement the current Guidance for sofosbuvir safely and efficiently. NHS England has provided no evidence whatsoever to the contrary or for its conclusion that the introduction of a Hepatitis C network is necessary before the current Guidance for sofosbuvir may be implemented. **2.3 Service implications and sofosbuvir** There are no specific service implications for sofosbuvir. As described in section 2.2 above, treating patients with sofosbuvir based regimens will simplify treatment, reduce pressure on the existing MDT service and significantly reduce impact on current NHS service provision given. Compared with the existing protease inhibitor standard of care sofosbuvir is associated with a: •significantly lower duration of treatment (12 weeks vs. 24 to 48 wks down to 12) •lower number of adverse events leading to increased hospital admissions (e.g.; lower risk of severe anaemia and severe rash) and outpatient stays •lower number of drug-drug interactions to manage In addition there is no requirement for response-guided therapy with sofosbuvir. Patients treated with current standards of care are managed using a response guided therapy approach, where virologic response measured at specific on-treatment time points is used to determine the likelihood of SVR and the required treatment duration (Incivo SmPC[8], Pegasys SmPC[9], Victrelis SmPC[10], Viraferon SmPC[11]). By comparison the high proportion of patients achieving both a rapid virologic response (after 4 weeks of treatment) and an end of treatment response means that on-treatment monitoring of HCV RNA and response-guided therapy are	

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	not required for sofosbuvir-based regimens. This will simplify patient management considerably relative to standards of care and also reduce the need for frequent on-treatment viral load monitoring and clinic visits. The benefits of introducing sofosbuvir within the existing infrastructure are supported by clinical bodies and Dr Michael Jacobs, on behalf of the Royal College of Physicians and a clinical specialist in this appraisal, stated: "*... introduction of sofosbuvir would tend to simplify treatment regimes for chronic HC V infections. Centres with experience in managing patients with Hepatitis C will be able to deliver this intervention without additional training. There is a need to improve accessibility of HCV treatment... and simpler treatment regimes are an important component of this".* Furthermore, as indicated above, two new hepatitis C treatments (boceprevir and telaprevir) were introduced successfully in 2012, without substantial additional investment in infrastructure, supporting Gilead's case that no additional measures are required in order to implement the current Guidance. **3 Impact of delaying implementation** Delaying access to sofosbuvir effectively prohibits those patients who are either cirrhotic or have bridging fibrosis from accessing the best possible treatment now in order to avoid the longer terms complications of this disease. These patients will have no option but to commence treatment using current standards of care (which, as outlined above, are less efficacious, more burdensome to patients and require significant NHS resource given the treatment durations and adverse event profiles). Each of these patients is exposed to an increased risk of liver cancer (approximately 6% per year[12]). This risk is reduced significantly if the HCV virus is removed to around 1% per year[12]. The consequence of this is that for every month that these cirrhotic patients continue untreated, approximately 40 people will develop a preventable cancer that is likely to be incurable. Furthermore every non cirrhotic patient who achieves an SVR is likely to avoid these future complications altogether. The burden placed on these patients is unacceptable when sofosbuvir is available, particularly as the cost of treating these negative patient outcomes far outweighs the shorter term costs for this curative therapy and where sofosbuvir has been demonstrated to be highly cost-effective (NICE provisional guidance). It should be noted: •Liver disease costs the UK National Health Service in excess of £500 million per annum, a cost that is rising by 10% annually[13] •Hospital admissions for hepatitis C-related end stage liver disease and	

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	hepatocellular carcinoma have risen year-on-year, almost quadrupling between 1998 and 2012[14] •Analysis of hospital statistics in England between 2011 and 2012, reveals around half (10,691, 49%) of all recorded hospital admissions for hepatitis C are non-elective (The Hepatitis C Trust. October 2013.). The average cost of a non-elective in-patient admission, including both short and long stays, is £1,436, excluding excess bed days, and £2,052 including excess bed days.[13] Importantly, delaying access for those patients who require treatment now effectively increases future NHS service burden due to the effective 'warehousing' of a significant proportion of patients who would otherwise seek treatment now. In addition, the burden in terms of lifetime tertiary care follow up for patients (who have either progressed to cirrhotic, decompensated cirrhotic or hepatocellular carcinoma health states) should also be considered as there are potentially significant secondary care resource efficiencies and financial savings to be made for the NHS with the introduction of sofosbuvir. In addition, we would like to highlight our concerns that the request from NHS England to extend the implementation period for this Guidance is significantly at odds with the NHS Five Year Forward Review within which Simon Stevens stressed the need for 'getting serious about prevention' and the benefits that this can bring to both patient outcomes and NHS resource over the longer term.[15] Finally and for completeness, whilst we welcome any extension to the NHS England interim access policy regarding access to sofosbuvir it should be noted that this does not provide an appropriate substitute for prompt implementation of NICE Guidance for sofosbuvir (and the 2013 Regulations do not indicate that it does). NHS England's interim policy only covers treatment for those few hundred patients who are already severely decompensated and for whom liver transplant is the only available treatment option. There is no policy in place to treat those patients who could actually avoid these negative outcomes associated with chronic liver disease and reduce future service burden if they were offered treatment now. (i.e. in particular the cirrhotic population and those with bridging fibrosis). **Conclusion** As stated in our introduction there have already been a number of delays in the appraisal process for sofosbuvir and further delay to the actual implementation of the final recommendations will cause avoidable harm to patients and increased cost and burden on existing NHS resources.	

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	The reasons provided by NHS England to justify delay in implementation of the current Guidance are unsupported by evidence and all information available to Gilead indicates that they are factually incorrect. While without disclosure of the evidence, if any, which has formed the basis for NHS England's submissions, it is difficult for Gilead to respond to this consultation in a comprehensive way, we believe that the concerns expressed by NHS England are based on the predicted implications of the introduction of future treatment regimens, which will permit fully oral interferon-free regimens for the wider majority of Hepatitis C patients - and not on the implications of the implementation of the current Guidance for sofosbuvir. This does not constitute a valid basis for extending the period for implementation of Guidance in accordance with regulation 7(5) of the 2013 Regulations. In contrast to NHS England's assertions, available evidence points to the fact that implementation of the current Guidance is very unlikely to result in substantial numbers of additional patients and will relieve rather than add to the existing burden on Hepatitis C services. In these circumstances, in the absence of any robust evidence supporting NHS England's request for delay and in the context of the presumption under the 2013 Regulations that Guidance will be implemented within the standard 90 day period, Gilead believes that any delay in implementation of Guidance for sofosbuvir would be procedurally unfair, unreasonable and disproportionate. Accordingly any such delay will, in our view, be susceptible to legal challenge.	
British Association for the Study of the Liver and the British Viral Hepatitis Group	Many thanks for allowing the British Association for the Study of the Liver (BASL) and the British Viral Hepatitis Group (BVHG) to comment on the proposal to defer the funding for sofosbuvir for patients with hepatitis C for a further 3 months (as requested by NHS England (NHSE)). We would strongly suggest that this proposal be rejected and detail our arguments below. We fundamentally disagree with the requirement for an extension 'to put in place the resources and arrangements necessary to enable it to effectively implement the recommendations' (paragraph 6). The technology (Sofosbuvir) is less complex than existing therapies in many regards – the lack of response-guided therapy, significantly less toxicity and drug-interactions than presently utilized DAAs, shorter course therapies with significantly better efficacies etc. We do not believe that any significant extra training, staffing or infrastructure are required for existing treatment centres to adopt this technology. We strongly believe that this technology could be safely and effectively adopted immediately within the structures already in place. Further to this we would argue that the issues raised by NHSE in paragraph 7 are	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	not of relevance to the issue. There are indeed areas of complexity in the diagnosis and care of hepatitis C, but this technology will partly relieve and alleviate these, and we do not believe that a delay is therefore warranted or justifiable on these grounds. In paragraph 8 we welcome NHSE's stated intentions to develop more formalized long-term networks for HCV care and treatment. However we would strongly argue that these are not a pre-requisite for the implementation of this technology. There are established and experienced treatment centres/networks already in place that are suitable to allow the use of this technology within approved indications, and already involve the partnerships discussed. Superimposed upon these are the NHSE Sofosbuvir Early Access networks which cover the breadth of England and have proven to function very effectively. Similarly we would welcome the development of a database and dashboard as stated in paragraph 9, but this is not a pre-requisite for delivery or commissioning of this technology. The criteria of who are most in need of earlier treatment and who could have treatment deferred clinically are already well established. All centres already utilise such criteria and have systems to ensure that patients remain under surveillance and recall. Furthermore we find it hard to understand how delaying an evidence-based cost-effective intervention to establish a dashboard to provide evidence of a 'reduction in harm' is logical, when a significant percentage of cirrhotic patients will progress to hepatocellular carcinoma as a result of such delays (Cardoso et al., J Hepatology 2010; Alazawi et al., Aliment Pharmacol Ther 2010). We disagree with the comment that 'providers have stated they would need to increase staff resources' (paragraph 10). It is probable that there will be an increase in demand but we view this as within the capacities of the existing treatment centres and networks. We believe the estimates of potential numbers provided by NHSE to be excessive. The standard of care in many countries is now all-oral DAA therapy (often based of Sofosbuvir) and many patients and clinicians will continue to warehouse patients until such therapies become available. We believe that more realistic total treatment estimates would be 6000 to 8000 patients per annum. Such an increase in demand and treatment should be welcomed - an increase in patients cured will result in decreases in episodes of future hepatic decompensation, the development of hepatocellular carcinoma, and the need for liver transplantation – as confirmed in the NICE analysis of this technology. We are unclear in which way NHSE believes that this technology 'will fundamentally change how we treat those affected' (paragraph 11). Sofosbuvir is a very significant advance but the changes to treatment- and care-pathways are modest and in most regards less significant than the previous introduction of telaprevir and boceprevir	

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	(which were easily instituted within existing treatment centres and networks). We also do not understand NHSE's assertion that sofosbuvir 'may be used inappropriately', as this technology would only be utilized within NICE approved criteria - the NICE process has been robust and the conclusions reached have been evidence-based. NHSE's confirmation of the continuation of the Sofosbuvir Early Access Programme (paragraph 12) is welcome. However the concern of clinicians is those patients who fail to meet the inclusion criteria of this programme but have very significant risks of progressing from significant fibrosis to decompensation and/or the development of hepatocellular carcinoma during the proposed extension of the period of deferment. In summary the strongly held views of BASL/BVHG on the 4 principal reasons presented by NHSE are that: a. The task & finish group's work is not required for the effective implementation of this technology, or compliance with NICE-approved indications and guidance. b. Any increase in demand would be containable within the existing infrastructures and networks, and indeed would ultimately be welcomed to prevent further complications related to hepatitis C and consequent future costly demands upon healthcare resources. We do not agree that such potential increases would place service provision under 'inappropriate levels of stress' or result in 'sub-optimal treatment decisions'. c. Fully established networks would be welcomed but are not a pre-requisite for this, or similar, technologies. The staff and resources required are already in place and are prepared to utilise this technology safely and effectively. d. A national database and dashboard are not in any way pre-requisites for this technology. In fact the only issue we can determine in the implementation of this technology is budget impact – which is not a criterion upon which NICE can consider deferment. We do not believe that any issues related to the potential increase in patient numbers or the establishment of a more formal network amount to a substantive argument that requires further consideration It is our view that any delay in implementing this clinically- and cost-effective treatment is not necessary, and would have a detrimental impact upon patients. Therefore BASL/BVHG would strongly urge NICE to reject this proposal for deferred funding.	

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British Society of Gastroenterology	The British Society of Gastroenterology view is that there is no valid reason to impose further delay on the approval of Sofosbuvir by NICE. The Societies view is that the rationale put forward by NHS England is flawed and will both deny patients at high need therapy and only defer both clinical activity and cost with an even larger potential impact on clinical teams and budgets when approval is granted. It is disappointing that NHS England have chosen this route. They have a very engaged clinical community linking via the Clinical Reference Group and a highly active patient group (the Hepatitis C Trust) with which to interact. All of those partners are fully aware of the immediate challenges NHS England faces with affordability of the new drugs for hepatitis C and that the current NICE guideline will rapidly be superseded by all oral therapy for hepatitis C. In this context we would anticipate that only patients with a pressing need for treatment would wish to take up Sofosbuvir, interferon and ribavirin based treatment at this time. This will limit the budget impact and the service implications. Further active dialogue with the clinical and patient communities by NHS England would have confirmed this. There is also an important principle of the independence of NICE which needs to be taken into account and the view from the British Society of Gastroenterology is that there would need to be very cogent arguments to set a precedent for delay of implementation of NICE judgements, we do not believe this to be the case here. We set out below the specific areas of concern raised by NHS England and the British Society of gastroenterology response. As set out in the letter from NICE the deferred funding period is 3 months unless one of the following conditions applies: a. The health technology cannot be appropriately administered until training is in place; b. The health technology cannot be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities are in place; c. The health technology cannot be appropriately administered until other appropriate health services resources, including staff, are in place; d. The health technology is not yet available in England. Our understanding is that NHS England wish to delay implementation on the basis of points b and c above.	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	NHS England states: "NHS England has confirmed that the treatment of hepatitis C is a priority and notes that 'the *most recent national estimates suggest that around 160,000 adults are chronically infected with hepatitis C (HCV) in England in 2012. Current numbers of patients treated are estimated at 5,000 per year in England - 3% of those currently infected but this will increase rapidly. The CRG (Clinical Reference Group) Hepatitis C sub group have estimated that 10-15,000 people per year may come forward seeking HCV treatment'.* NHS England considers that the arrangements for the care of people living with hepatitis C are complex, involving *'many components of care delivery in different health settings. Commissioners involved in the diagnostic and treatment hepatitis C pathway include 'NHS England Specialised services, Health and Justice, Public Health England, Local Authorities and Clinical Commissioning Groups and Primary Care.'* It considers that the availability of sofosbuvir, and the potential for other treatments to follow, will challenge these arrangements and so it wishes to establish a 'task and finish group' to *'bring together those involved in commissioning services involved in the Hepatitis C pathway to clarify responsibilities and to agree a coherent set of priorities'.* It anticipates that this group will complete its work by the end of March 2015 and that the actions which arise from it will be implemented in the 2015/16 financial year." **The British Society of Gastroenterology responds:** There is no controversy at all as to clinical priorities for treating patients with hepatitis C with a broad clinical consensus that those with significant liver disease and those who have failed previous therapy and who fit within the NICE guidance should receive therapy as the initial priority. To delay treatment for these groups is unreasonable and runs the risk of patients developing decompensated cirrhosis and cancer with their associated costs, morbidity and mortality which would be avoided in the very significant proportion who will be cured of their HCV infection with Sofosbuvir based therapy. The principle of the task and finish group is strongly supported by the British Society of gastroenterology with a clear remit to consider other groups who may be at a lower clinical priority and decide a further roll out of treatment based on affordability and benefit. The short-term availability of non-interferon containing regimens mean that the uptake of sofosbuvir, interferon and ribavirin in other patient groups at lower short term risk of serious liver disease related adverse events will be relatively low. **NHS England states:** NHS England intends to commission a series of *'Hepatitis C Networks'*, consisting of specialist centres which will each manage a caseload of patients, working in	

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	partnership with other providers of care in the NHS and in the justice system. The initiative would provide a centralised resource for patients whose care '*occurs as an adjunct to the delivery of other services including HIV, drug and alcohol, sexual health and prison health services, as well as from within gastroenterology and specialist hepatology services'.* Each centre will have a multi-disciplinary care (MDT) team which *will 'support selection of the optimal treatment regimen for each patient.* NHS England estimates that it will take 9 months to establish these centres, with the process allowing for candidates to build partnerships with NHS, local government and prison health services. **The British Society of Gastroenterology responds:** NHS England has already commissioned hepatitis C networks for the Early Access Programme, MDTs are in place with strong links to the services mentioned by NHS England above. The EAP has shown both that the care delivery via these networks is effective and outcomes are excellent. There is no practical reason why the existing centres cannot broaden their remit and take on assessment of patients in those higher risk groups referred to previously. The British Society of Gastroenterology remains in full support of the further development of hepatitis C treatment networks in the future. **NHS England states:** NHS England also intends to establish a database to 'support development of a national database of treatment and collection of outcomes to inform future treatment and commissioning of clinically effective care. It argues that the slow development of liver diseases means that some patients don't need immediate treatment, on clinical grounds, but that any decision to delay treatment would need to be supported by *'robust surveillance and recall systems which are not yet in place'.* It says that *'a national Dashboard is already being developed for 2015/16 that will provide evidence of the reduction in harm from increased treatment of hepatitis C'* but gives no other information about how long it might take to fully implement its plans. systems necessary to provide a multi-disciplinary team approach to care. **The British Society of Gastroenterology responds:** Patients have already elected to delay treatment in significant numbers through shared decision making and all treating centres have details and local recall systems to ensure such patients can re-engage when more effective therapy is available. There is no need for a national database to enable this particular immediate function and indeed the prospect of rolling out such a national database to all treating centres is a major undertaking which would seem unlikely to be complete and fully functional in the medium term. A far more realistic approach is to again utilise the existing database used to monitor outcomes of therapy in the EAP,	

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	HCV UK. This has been highly successful and would fulfil the immediate need. **NHS England states:** *'historic low uptake of both testing and treatment means that providers have stated they would need to increase staff resources particularly specialist pharmacy and nurse specialist support in order to treat the expected increase in demand'.* **The British Society of Gastroenterology responds:** We do not agree that the historic rate of testing is low. The Health Protection Agency data show that testing has improved immensely in the past 5 years and now runs consistently at about 10,000 per annum and it is likely that more than 50% of infected people have been identified. Treatment rates were increasing up to the time that new treatments came on the horizon when patients more frequently chose to defer therapy. It is therefore incorrect to suggest treatment rates are low because of lack of capacity in the treatment system. In addition, Sofosbuvir treatment for most patients initially will involve interferon therapy but this is for a 12 week period only. As stated earlier, the numbers of patients who will chose to take therapy is likely to be relatively small. The existing staff currently providing therapy are well used to managing interferon related side effects which are not added to by the use of Sofosbuvir. The average duration of interferon based therapy currently is around 30 weeks across all genotypes. Cutting this to 12 weeks per patient means that automatically the capacity to treat patients with the same medical and nursing infrastructure will increase. This means without any additional infrastructure we could increase treatment numbers to cope with the initial demand, pending the outcome of the task and finish group and further NHS England investment in treatment delivery infrastructure to meet the future demand they refer to.	
British HIV Association and British Association for Sexual Health and HIV	The British HIV Association (BHIVA) represents health-care professionals and community members involved in the care of people living with HIV-infection including those coinfected with HIV. The British Association for Sexual Health and HIV (BASHH) membership includes medical practitioners, other healthcare workers, scientists and epidemiologists working in sexual health. The Advisory Committee had access to the BHIVA Guidelines for the management of hepatitis viruses in adults infected with HIV (*HIV Medicine* (2013), **14** (Suppl. 4), 1–71) and members of BHIVA and the British Association of Sexual Health and HIV (BASHH) were involved in the original sofosbuvir consultations. BHIVA and BASHH strongly disagree with the NHS England request to defer funding of sofosbuvir, and the rationale on which this request is based, for the	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other

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	following reasons: ▪ The role of sofosbuvir in hepatitis C management and the need for this new agent has been agreed – this is simply a request to delay access to an approved drug ▪ Concerns regarding hepatitis treatment networks are unfounded since NHS England has already 'designated' viral hepatitis treatment centres and most regions have responded by creating new networks or strengthening those already in place. The sofosbuvir expanded access programme (EAP) demonstrated clearly the effectiveness of these networks and that the infrastructure required to start using sofosbuvir is already in place. ▪ There is a huge need for sofosbuvir and there will undoubtedly be some increase in prescribing activity but this does not necessarily translate to an over-burdening of staff and services. Most of the patients currently in need already access specialist services on a regular basis for monitoring and management of complications. Those patients who are still being treated with the limited options we have available require frequent visits for additional monitoring, symptom control, dose adjustment and prescribing of complex supportive treatments. We have the capacity to manage complex patients and complex treatments so we also have the capacity to manage increased prescribing of a shorter, simpler and better tolerated treatment such as sofosbuvir. ▪ Any short-term increase in clinic/staff time (and we emphasise that we believe the service we represent have the structure, flexibility and capacity to manage this) will be more than counterbalanced by a reduction in monitoring and complications. ▪ We disagree with the notion that making sofosbuvir available would increase numbers coming forward to test for HCV. For HIV-infected patients in the UK, about 90% have already been tested for HCV (UK CHIC Cohort, unpublished data) and guidelines suggest annual testing. ▪ The uptake of sofosbuvir treatment, as per the draft guidance, would not be as high as projected by NHSE; most patients with mild liver disease would prefer to wait for IFN-free therapy. It would be unjustifiable to delay therapy for those with more severe forms of liver disease (Metavir F3/F4) any further. In the context of HIV co-infection these patients would be at significant risk of disease progression in the next 6-9 months. ▪ We would welcome the development of a dashboard and database but do not accept that this should in any way delay access to sofosbuvir. Most clinics already have very robust monitoring and recall systems, particularly for patients with advanced liver disease (as evidence by the rapid and efficient uptake of sofosbuvir within the EAP). To put patients at risk of harm	facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	while insisting on systems to measure reduction in harm seems counter-intuitive at best. There are a significant number of patients who did not quite meet the criteria for the EAP who will progress rapidly. ▪ Since the sofosbuvir EAP closed in November 2014 we have no access to treatments outside of those already approved for use. This leaves non-genotype-1 patients and 1st generation protease inhibitor failures NO ALTERNATIVE TREATMENT OPTIONS. To delay access to sofosbuvir when there is simply no other option for many patients is unethical and unsafe. Whilst we applaud the NHSE for promising to re-institute expanded access to treatment for the sickest patients (de-compensated cirrhosis, Child-Pugh B/C), this still leaves many with advanced fibrosis 'at risk' whilst we delay therapy further and may require more to have access to IFN-free therapy when the programme gets underway after the delay because IFN would be contraindicated in those having progressed to CP-B/C disease or having had a de-compensation event. ▪ Boceprevir and telaprevir are associated with a high risk of adverse events resulting in extra visits, extra treatment, excess cost and suboptimal patient experience. In addition they are licensed only for genotype-1 infection leaving no available DAA for patients infected with other genotypes ▪ Patients are at risk of disease progression while access is delayed. Patient co-infected with HIV and hepatitis C experience a faster rate of disease progression and we believe that to condemn patients. Particularly those with already advanced liver disease, to further delay is simply unacceptable. ▪ Interactions between hepatitis C drugs and drugs used to treat HIV and HIV-related co-morbidities are complex and potentially dangerous. Sofosbuvir has minimal interaction potential including no interactions with HIV drugs so will reduce complexity, improve safety and increase access to hepatitis C therapy for co-infected individuals. The group would also like to confirm its endorsement of the comments that are being submitted by Mr [redacted] on behalf of HIV i-Base. We strongly urge NICE to reject the notion of delaying implementation of this very important guidance and stay with the time-lines promised so that we can prevent harm to vulnerable groups of patients, especially those with HCV/HIV co-infection.	
British Liver Trust	**Liver Disease a Priority?** The NHS Outcomes Framework 2014/2015, Domain 1 – Preventing people from dying prematurely, prioritises liver disease as an improvement area and acknowledges that liver disease is a major cause of death. This is also reflected in	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section

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	the Public Health Outcomes Framework 2013- 2016 (4.6).[i] Public Health England's Hepatitis C Annual Report[ii] highlighted that hospital admissions from hepatitis C-related end stage liver disease have risen from 608 in 1998 to 2,390 in 2012, while deaths have risen from 98 in 1996 to 428 in 2012. Liver transplants first registrations, where post-hepatitis C cirrhosis was an indication for transplant, have quadrupled from 45 in 1996 to 188 in 2013. Therefore the British Liver Trust contends that if liver disease is a stated priority then all interventions that address this improvement area should be mandated for funding, especially when the 'cure' rates (sustained viral responses) as demonstrated with new hepatitis C treatments are high. **Justifiable Reasons for Funding Exemption?** The Secretary of State[iii] and the Health and Social Care Act 2013 set the deferred funding period for a NICE technology appraisal at 90 days from its issue. This has been iterated in the Explanatory Memorandum to the National Institute for Health and Care Excellence (constitution and functions) and the health and social care information centre (functions) regulations 2013[iv]. Regulation 7 makes 'provision that requires the NHS Commissioning Board, clinical commissioning groups and, with respect to their public health functions, local authorities to comply with a NICE technology appraisal recommendation following a direction of the Secretary of State.' This regulation also underpins the NHS Constitution[v] right to "drugs and treatments that have been recommended by NICE technology appraisal guidance for use in the NHS, if your doctor says they are clinically appropriate for you." A requirement to fund treatments recommended by NICE technology appraisal guidance previously applied to primary care trusts. This provision reflects the Government commitment to replicate the effect of the funding direction in the new NHS structures. It is the position of the British Liver Trust having analysed NHS England's arguments that there are no viable reasons for an extension to this mandatory 90 days. We would emphasise that: 1. Sofosbuvir is both a clinically and cost-effective intervention for the treatment of hepatitis C[vi] and has met the NICE TAs affordability criteria.	7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	2. The resources and arrangements for safe delivery of treatment are already in place as a result of the availability of telaprevir and boceprevir. Both these interventions have been funded by the NHS since they received NICE TA approvals in early 2012. It is therefore not the case that 'Until last year the treatment of hepatitis C has depended on a combination of two relatively low cost drugs – interferon and ribavirin'. 3. There is considerable experience in the clinical trial use of sofosbuvir and other new hepatitis c treatments to ensure robust utilisation. 4. Sofosbuvir has been used in excess of 500 patients since the publication of the interim commissioning policy in April 2014[vii] by specialised centres that have effectively monitored sofosbuvir' s availability. Therefore the British Liver Trusts contends that NHS England's arguments do not satisfy the exemption criteria as defined in paragraph 2b and c of NICE's consultation document and that the mandatory funding of 90 days should be upheld. It is of great concern that lives will be lost if NHS England are allowed to delay treatment with sofosbuvir any longer.	
Department of Health	Ministers strongly believe that clinically and cost effective drugs should be available to patients who will benefit. However, we also recognise that the new hepatitis C treatments are expected to lead to a significant increase in the numbers of patients presenting for treatment, which could have significant service implications. We agree with NICE's assessment that NHS England has put forward a valid case for deferring the funding period to allow time to prepare for and put in place the necessary systems and mechanisms to implement NICE's recommendations effectively. It is important to note that Ministers' support for the proposed extension is on the understanding that NHS England will use this interim period to prepare and implement, from the end of July, an active programme to ensure that eligible patients are able to access these drugs promptly according to their clinical need. Clearly, it is also vital that patients at urgent need of treatment should not be denied treatment during this interim period. It will be important that NHS England's interim plans for the period prior to August 2015 ensure that patients with the greatest need can continue to access appropriate treatment without undue delay.	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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Haemophilia Society	The Haemophilia Society were very pleased to hear that NICE had recommended Sofosbuvir for a variety of genotypes and circumstances. We are very concerned to hear that NHS England had requested an extension to the usual 3 month funding period. We accept the arrangements for people living with hepatitis C are complex, however there does not appear to be sufficient evidence to suggest that NHS England could not, if it chose to do so implement the funding for Sofosbuvir using existing treatment pathways for patients already identified as having hepatitis C. The evidence provided by NHS England tell us that - the Task and finish group will be completed by the normal deferred funding period. **This should not be a reason for delay** - NHS England anticipate a substantial increase in patients seeking active treatment, due to public awareness campaigns. **If NHS England do not start public awareness campaigns until they are fully resourced to deal with new diagnosis and returning patients, this risk could be mitigated allowing current patients access to treatment immediately through their existing treatment pathways, placing a moderate increased burden on NHS staff who currently treat people with hepatitis C, which should be manageable.** - NHS England wish to test assumptions on the long term cost effectiveness of treatment via a new Network. **This is not within the remit of NHS England as NICE have undertaken an HTA** - NHS England require a dashboard and national database. **This is a reasonable and positive step, but should not be a reason to delay treatment. Data can be collected from first prescription for retrospective entry into a database. For the bleeding disorder community data could potentially be collected via the National Haemophilia Database to enable accurate collection from day one and later transferred to any specific hepatitis C database.** NICE state that they should be cautious and sure of its judgement before requiring NHS England to provide services it does not consider it can provide, or provide safely and efficiently. NHS England does not believe it has in place the arrangements it considers necessary to provide Sofosbuvir. **There is nothing to suggest Sofosbuvir cannot be provided safely, so the argument must be on the ground of efficiency, with careful consideration of public campaigns and record keeping it is not unreasonable to expect NHS England to provide an efficient service to enable immediate access to Sofosbuvir for patients already**	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	in the treatment pathway and gradually expand services and resources to meet demand as it increases over time. You also ask if a decision to extend the deferred funding period until 31 July 2015 could have any adverse impact on people with a particular disability or disabilities. **The Haemophilia Society believes a delay in access to treatment would have a significant adverse impact on the haemophilia and other bleeding disorder patient population who have a diagnosis of hepatitis C. Every patient from this community who has hepatitis C was infected via their NHS treatment between 1970 and 1991 and so have had chronic hepatitis for a minimum of 23 years.** The World Health Organisation states A significant number of those who are chronically infected will develop liver cirrhosis or liver cancer. Of those with chronic HCV infection, the risk of cirrhosis of the liver is 15–30% within 20 years. **In light of this there is a strong possibility that that more people with haemophilia and other bleeding disorders will progress from chronic hepatitis to cirrhosis or liver cancer during the delayed funding period. These people will not be eligible for treatment under NHS England interim commissioning policy until their disease has progressed. If treatment were prescribed with no delay they may be prevented from progressing to the advanced stage of hepatitis C.** **Additionally we would ask NICE and NHS England to consider that for the haemophilia and bleeding disorder patient population, once a patient has progressed to requiring a liver transplant their requirement for Factor replacement treatment cost would significantly outweigh the costs of treating the wider haemophilia and bleeding disorder hepatitis C infected patient population with Sofosbuvir immediately.** **In conclusion The Haemophilia Society do not believe NHS England has provided sufficient evidence to justify an extension of the deferred funding period and that NICE should reject this application.**	
Hepatitis C Trust	**Background** 1. Under Regulations[1] made under the Health and Social Care Act 2013, NICE is required to specify, in the guidance that results from a technology appraisal, the period within which the funding necessary to enable its recommendations to be applied must be made available (the 'deferred funding period').	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions)

[1] 'The National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013'

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	(Responses in bold)The Hepatitis C Trust is already extremely perturbed that budgetary impact has turned 'within' three months to 'no earlier than' three months. This is a subversion of the intention of the Act. We fully believe that the requested delay would prevent anyone accessing the new technology for a full six months. 2. This deferred funding period is 3 months unless one of the following conditions applies: a. The health technology cannot be appropriately administered until training is in place; **This does not apply as Sofosbuvir plus peginterferon/ribavirin is less complicated to administer than either Telaprevir or Boceprevir plus peginterferon/ribavirin which is the current standard of care for genotype 1 patients and therefore routinely administered** b. The health technology cannot be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities are in place; **Telaprevir or Boceprevir plus peginterferon/ribavirin which is the current standard of care for genotype 1 patients is currently routinely administered. Networks will provide a better system but are clearly not a requirement for this particular technology** c. The health technology cannot be appropriately administered until other appropriate health services resources, including staff, are in place; **Telaprevir or Boceprevir plus peginterferon/ribavirin which is the current standard of care for genotype 1 patients is currently routinely administered. Sofosbuvir is less complex then Boceprevir or Telaprevir and allows for shorter duration treatment so there will be significant extra capacity in the current system** d. The health technology is not yet available in England. **It is available** 3. NICE has completed its appraisal of sofosbuvir, which has a marketing authorisation for the treatment of chronic hepatitis C, in combination with	and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	other medicines. The Final Appraisal Determination will be released to consultees, for appeal, in December. It recommends the use of sofosbuvir in specified circumstances (Appendix A). 4. The text in italics is taken from the letters to NICE from NHS England (Appendix B). **Request to vary the deferred funding period from NHS England** 5. NICE has received a request from NHS England (Appendix 2) to extend the deferred funding period. The request has been made in the context of a likely significant demand for treatment, and the knowledge that a number of other treatments, currently being appraised by NICE, may become available during 2015. NHS England has confirmed that the treatment of hepatitis C is a priority and notes that 'the *most recent national estimates suggest that around 160,000 adults are chronically infected with hepatitis C (HCV) in England in 2012. Current numbers of patients treated are estimated at 5,000 per year in England - 3% of those currently infected but this will increase rapidly. The CRG (Clinical Reference Group) Hepatitis C sub group have estimated that 10-15,000 people per year may come forward seeking HCV treatment'.* **As far as we are aware the CRG estimate is for *interferon-free therapy* which is such a game-changer for patients that significantly increased demand is likely. This appraisal on the other hand considers mainly Sofosbuvir plus peginterferon/ribavirin. Given the imminent arrival of interferon-free therapy we cannot conceive of such a level of demand for this technology. Only those likely to need or particularly want treatment now are likely to come forward. As per 2c above there will anyway be extra capacity in the existing system.** 6. NHS England considers that it needs more time than the standard 3 month period allows in order to put in place the resources and arrangements necessary to enable it to effectively implement the recommendations in the appraisal. **NHSE has known of this technology for at least 18 months.** 7. NHS England considers that the arrangements for the care of people living with hepatitis C are complex, involving *'many components of care delivery in different health settings. Commissioners involved in the diagnostic and treatment hepatitis C pathway include 'NHS England Specialised services, Health and Justice, Public Health England, Local Authorities and Clinical Commissioning Groups and Primary Care.'* It considers that the availability	

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	of sofosbuvir, and the potential for other treatments to follow, will challenge these arrangements and so it wishes to establish a 'task and finish group' to *'bring together those involved in commissioning services involved in the Hepatitis C pathway to clarify responsibilities and to agree a coherent set of priorities'.* It anticipates that this group will complete its work by the end of March 2015 and that the actions which arise from it will be implemented in the 2015/16 financial year. **NHSE is right about the complexities of care for people with hepatitis C. However, the delivery of this technology and the need for a delay do not involve commissioners of diagnostics nor do they involve upcoming technologies. Commissioning is happily centralised in specialist commissioning and health and justice. We are delighted that the Task and Finish Group has been established but the fact that the arrangements it recommends (for example improved pathways) will not start being introduced until 2015/6 will ensure that treatment numbers remain low during the period for which this delay is sought. This is therefore a good argument against the need for delay.** 8. NHS England intends to commission a series of *'Hepatitis C Networks'*, consisting of specialist centres which will each manage a caseload of patients, working in partnership with other providers of care in the NHS and in the justice system. The initiative would provide a centralised resource for patients whose care '*occurs as an adjunct to the delivery of other services including HIV, drug and alcohol, sexual health and prison health services, as well as from within gastroenterology and specialist hepatology services'.* Each centre will have a multi-disciplinary care (MDT) team which *will 'support selection of the optimal treatment regimen for each patient.* NHS England estimates that it will take 9 months to establish these centres, with the process allowing for candidates to build partnerships with NHS, local government and prison health services. **We strongly welcome the establishment of networks which we consider will improve access to treatment and the best possible care under expert supervision for patients. They will be badly needed when a whole range of new technologies becomes available over the next two years. Here we are discussing a delay for one new technology that will largely replace a more complicated treatment regimen so it cannot be argued that this is needed for this technology. Even were networks to be essential for this technology, NHSE has had a proposal for these networks (the service specification) for a year and it has still not been signed off by CPAG. It would be unconscionable that patients should**	

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	be made to wait simply because NHSE has dragged its feet. 9. NHS England also intends to establish a database to 'support development of a national database of treatment and collection of outcomes to inform future treatment and commissioning of clinically effective care. It argues that the slow development of liver diseases means that some patients don't need immediate treatment, on clinical grounds, but that any decision to delay treatment would need to be supported by *'robust surveillance and recall systems which are not yet in place'.* It says that *'a national Dashboard is already being developed for 2015/16 that will provide evidence of the reduction in harm from increased treatment of hepatitis C'* but gives no other information about how long it might take to fully implement its plans. **A database is essential. It is quite extraordinary and unacceptable that this does not exist. For years, high cost drugs for hepatitis C have been commissioned without any data requirements. NHSE has known about the impending arrival of even more expensive drugs and is still only 'intending' to establish a database. Apparently NHSE considers this very important now that it wants a delay but until now has not considered it important enough to do anything about. Patients cannot be asked to wait for reasons like this.** 10. NHS England argues that *'historic low uptake of both testing and treatment means that providers have stated they would need to increase staff resources particularly specialist pharmacy and nurse specialist support in order to treat the expected increase in demand'.* No indication of the number of staff involved has been provided, although they appear to be associated with the proposed network centres. **Yet again, what on earth has testing got to do with it? Testing is not suddenly going to increase because of this TA. As stated in 5 above there is no expected increase in demand for *this* technology. Even if there were, there will be extra capacity amongst specialist nurses because of the shorter treatment duration. We cannot comment on specialist pharmacy but would want to see evidence of this.** 11. NHS England concludes its case for a variation to the deferred funding period by stating that it *'believes that the introduction of new Hepatitis C treatments will fundamentally change how we treat those affected. However, in order to ensure that the services we provide are both fit for purpose and can deliver these new treatments that ensure best outcomes for our patients we feel it is imperative that we are given sufficient time to implement the strategy outlined above before we are required to fund drugs that may be*	

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	used inappropriately and to ensure systems are in place to collect outcomes data to inform future. **Interferon-free therapy will indeed fundamentally change how we treat people. This technology is not interferon-free. This delay is requested for a particular technology not 'new treatments'.** 12. NHS England has confirmed that it will continue to approve the use of sofosbuvir for those in immediate and urgent need of treatment during the deferred funding period. This will happen under the terms of the interim commissioning policy which is currently in place.[2] **We are delighted to hear this and wish to applaud NHSE for its Early Access Scheme which has undoubtedly saved lives (and as it happens money).** **Consideration of the request** 13. NHS England has set out 4 principal reasons why it considers a variation to the deferred funding period is justified: a. The need to complete the work of the 'task and finish' service redesign group. **This is not necessary for the current technology** b. A substantial demand for treatment with sofosbuvir, which it anticipates will increase further, as patients who have not sought active treatment in the past will come forward, and which will be increased further by new patients identified through public awareness campaigns and screening of high risk groups, which have either been initiated or which are planned. **There is no evidence for this and, while interferon remains part of treatment extremely unlikely. What new public awareness campaign is being planned for the next 6 months? This is the best kept secret in the NHS. Opt-out testing in prisons will increase diagnosis as it gets rolled out *over the next two years*.** c. The need to establish a Hepatitis C Network, which will involve setting up a series of centres with the staff and the other resources and systems necessary to provide a multi-disciplinary team	

[2] Interim Clinical Commissioning Policy Statement: sofosbuvir + daclatasvir/ledipasvir +/- ribavirin for defined patients with Hepatitis C. NHS England

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	approach to care. **This is important for 'new treatments' but not necessary for this one** d. The establishment of a national database and dashboard to monitor and support individual care. **This is important but not necessary and could easily have been put in place when hepatitis C treatment became part of specialised commissioning two years ago.** 14. NHS England does not refer to the incremental budget impact of treating patients with sofosbuvir. Estimates of this vary because it is not clear how many patients will come forward for treatment. In addition, although it cannot be a specific consideration in this decision, the widening of treatment options, should forthcoming appraisals of other new treatments for hepatitis C have positive outcomes, will lead to increasing numbers of patients seeking and receiving treatment. **The Hepatitis C Trust objects in the strongest possible terms to any attempt to introduce budget as a factor. If we are going to change our healthcare resource allocation model to one based on the arbitrary consideration of this year's budget, then this should be debated nationally, preferably through an election manifesto. Either NICE has a mandate to decide resource allocation or it doesn't.** 15. NHS England is clearly concerned about its ability to make sofosbuvir available in the way it considers necessary for planned, efficient and properly audited care. It has advised NICE that *'an end date of August 2015 fits in with (our) timescales to support implementation'*. 16. In considering the argument for establishing the Network, NHS England say that they intend to *'… test some of the assumptions on the long term cost effectiveness of treatment and the impact this has on current costs in the acute sector of treating Hepatitis related liver failure'.* NICE does not agree that any further analysis of the cost effectiveness of the use of sofosbuvir is required and its consideration of the case for extending the deferred funding period takes no account of it. 17. The argument for a delay, based on the need to establish a national database and dashboard is not supported by a timescale. In addition, it appears that the dashboard component is, in any event, already being put in place. The consequences of not having the database at the same time as	

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	the dashboard are not made clear. 18. The work of the task and finish group is likely to be completed within the normal deferred funding period. 19. NHS England's case for an extension to the deferred funding period therefore needs to be considered against criteria b) and c) as set out in paragraph 2, above. It is clear that criterion d), the non-availability of the technology, does not apply. It is possible that criterion a), relating to the need to provide training, may also apply to staff working the proposed Network centres. However, the substance of the case for delay appears to relate to the organisational and staffing arrangements for the Network. 20. The question as to whether an extension to the deferred funding period is warranted appears to turn on whether either, or a combination of a substantial volume of patients seeking access to sofosbuvir, and the need to establish the Hepatitis C Network (with or without the database and monitoring function) amount to a substantive argument. Patients who consider that they can benefit from treatment now, supported as they may well be by their clinicians, may not wish to wait for treatment even though they may recognise the benefits of their care being part of a nationally-networked service. NHS England, on the other hand, will argue that it has a responsibility to manage its resources efficiently in the interests of both current and future patients. 21. It is clear that sofosbuvir marks a step change in the treatment available to patients with hepatitis C. NICE has recommended its use, with some restrictions because it is clinically and cost effective. Having done so, the Institute should be cautious about introducing any delay in patients gaining access to treatments from which they may benefit. However, it should also avoid placing the NHS in a position of confronting a significant tide of expectation from patients for access to care which they do not feel equipped to provide. That would risk sub-optimal treatment decisions and may place current service provision under an inappropriate level of stress. 22. The responsibility for securing care for the NHS in England rests with NHS England. NICE should be cautious and sure of its judgement before requiring NHS England to provide services that it does not consider that it can provide, or provide safely and efficiently. In effect, NICE would have to conclude that NHS England was mistaken. NHS England has indicated that it does not currently have in place the arrangements that it considers necessary for sofosbuvir to be provided. Its position, in setting out what it believes it needs to do to put the necessary arrangements in place, has	

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	credibility. NICE should be wary of substituting its judgement for NHS England's in this respect and so it therefore proposes to grant an extension to the deferred funding period until 31 July 2015, under criteria b) and c) in paragraph 2 above. **The Hepatitis C Trust strongly opposes a delay for all the detailed reasons given above. We believe that no single justification presented by NHSE holds up to scrutiny. We therefore believe that the real reason is that NHSE fears it cannot afford the 'new drugs'. We believe this fear is unjustified in the case of Sofosbuvir and that the demand for an interferon-containing regime will be nowhere near what NHSE has indicated and will be affordable. Unfortunately this TA comes against the backdrop of a need to make savings to the specialised budget. While we have every sympathy for the difficulties NHSE finds itself in, we cannot let hepatitis C patients get picked on in this way. This is a largely marginalised population who have been consistently under-prioritised (that we treat just 3% each year is a scandal) and it is hugely ironic that NHSE is seeking to delay introduction of a technology that offers very high rates of *cure.* This is not a technology that prolongs life by a few months or is merely palliative. It cures people. For good.** **In summary:** **1. There is no evidence this delay is necessary** **2. Delays cannot and must not be granted for budgetary reasons**	
HIV i-base	Thank you for the opportunity to comment on the request by Public Health England (PHE) or an extended time for the sofosbuvir approval process. We would like to express concern for any further delay and would therefore register an objection to allowing this extension. 1) There has already been sufficient time for PHE to prepare for use of sofosbuvir. The timeline both development of new drugs and the approval process itself has been not only well publicised but keenly followed by patients, doctors, nursing staff and presumably other NHS departments. The i-Base submission for sofosbuvir approval highlighted the urgent need by people living with hepatitis C and especially for those coinfected with both HIV and HCV. Further delays to this essential new medicine are not acceptable.	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services

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	2) There is no logical way that patients who already have a clearly unmet need will be helped by a further delay in access, even when PHE suggest that continued use may be possible. The level of need for sofosbuvir, detailed in earlier submissions, is not only acknowledged by PHE but is recognised as being one that will be taken up immediately. The solution to a pressing demand for a new medicine cannot be helped by further delay in access. 3) We are concerned that a simpler treatment is being blocked based on an unjustified fear of a "potential challenge". NHS England appear to be overcomplicating the issues related to similar treatment in order to avoid providing better treatment. Health care support needed to prescribe sofosbuvir is significantly more simple than current treatment. It will require less intensive support and care than previous treatment. The treatment period is shorter and the treatment itself has far fewer side effects and other complications. We believe that PHE are over-stating and over complicating the need for staff training. Our experience is that clinics, certainly for people with HIV/HCV coinfection, are already well-prepared to provide wider access and that this approval process is in fact the rate-limiting step. 4) Availability of additional new medicines should also not be a reason to delay access to current new options. If, and when, new drugs become available, the situation may or may not be different based on cost and price. This will continue to be a moving target for several years. It is not reasonable to force patient to continue with suboptimal treatment options because of hoped for future medicines. European treatment guidelines already recognise DAA combinations as the standard of care. 5) Patients should not be made to wait further while NHS England develop new services. If NHS England are falling behind in their timeline for planning, this should not be an excuse to change the standard regulatory timeline for drug approval. 6) Broader access to effective treatment is not dependent on establishing a new network for aftercare. The data supporting the effectiveness clearly argue against this suggestion. An end date of August 2015 is completely unacceptable. PHE and NICE should be ashamed to be suggesting this. In summary, we are concerned at further extension to the predetermined timeline for	resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	the decision on approval.	
Liver4Life	While we understand that NHS England may not be able to put in place its plan for HCV Networks, and its 'task and finish' plan, and appears to be concerned that the introduction of Sofosbuvir will make the treatment of HCV more difficult, we would like to disagree. The development of Sofosbuvir will mean that the treatment of people affected by HCV will be simpler to treat, not more difficult. This will be due to the reduction in side effects, and also the reduction in the treatment period. From a patient perspective, NHS England's plan to delay the implementation will cause additional stress to individual patients, who have been waiting for this treatment to be released. The treatment of HCV does not just remove the risk of onward transmission and halt the progression of liver disease, but can be a point of change for patients to also change the way they live their lives. We also feel that the existing clinical structure of the NHS can deliver the treatment without delay. The existing structure currently offers triple therapy to all available patients, and this treatment is more difficult to manage than Sofosbuvir treatment, and therefore we strongly disagree with the proposed delay in making this treatment available. Finally we feel that this may be about the cost implications to NHS England's 2015 budget, rather than the ability of the NHS to deliver Sofosbuvir safely and effectively. The majority of hepatologists have been waiting for these drugs for many years, and are keen to use them, as the benefits to patients are obvious. We believe NHS England is worried about the number of treatments offered in the first year, rather than the impact it will have on patients and their families.	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.
NHS England	In October 2014 NHS England wrote to you requesting a waiver on the 90 day implementation of the NICE TAs for Sofosbuvir (mainly in conjunction with pegylated interferon) (ID654), and for Simeprevir (in conjunction with pegylated interferon and ribavirin) (ID668). Since then there have been a number of changes in the progress of new drugs for treating hepatitis C, and in the agreement of NHS England interim policies. There have also been further discussions with the clinicians on the Clinical Reference Group HCV subgroup. In the light of these changes NHS England would like to provide further information in support of a waiver for the NICE TA on Sofosbuvir.	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health

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	NHS England has, since the previous letter, approved an interim policy document for the use of simeprevir in conjunction with pegylated interferon and ribavirin, for introduction early in 2015. This policy has dealt with the concerns about the introduction of this drug, and there is no longer a need to delay implementation of NICE TA ID668. NHS England still believe that a delay in implementation of NICE TA ID654 (Sofosbuvir) is required to allow necessary infrastructure to be put in place to ensure equity of access to treatment and quality of care. This is in accordance with the requirements of the Health and Social Care Act 2012 and The National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013. b. The health technology cannot be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities are in place; NHS Capacity to deliver implementation of the guidance Although the new drugs for treating hepatitis C infection are less toxic than earlier regimens, selecting the most appropriate agents and course length remains highly complex. It is therefore important that expert clinicians are involved in prescribing decisions (while maintaining local delivery of care). NHS England is committed to putting appropriate systems in place to ensure that patients get the best quality of care, which we believe will be best provided by a combination of a network model and clinical guidelines. The networks will encompass MDT decision-making by teams experienced in the treatment of hepatitis C and in the appropriateness of initiation of treatment or continued surveillance of infected patients. MDTs including experienced clinicians will support the best quality of clinical care, and allow the most clinically and cost effective prescribing of high cost drug treatments in accordance with NHS England policy / NICE TAs. These innovations will take some time to develop and implement. The network model will also ensure better equity of access. Many patients with chronic hepatitis C infection come from marginalised groups who do not engage well with health care, and there is a risk that without proper structures in place a significant proportion of patients in need will not get access to care. Mechanisms are needed to encourage outreach and engagement with patients outside traditional health care settings: these will be much easier to set up as part of formal clinical networks than with uncoordinated local commissioning. It is recognised that treatment with new drugs could be introduced without such systems, but this is likely to disadvantage many patients. At the same time NHS England recognises that there is a substantial group of patients (mainly but not exclusively those with cirrhosis) who run the risk of serious harm if treatment is delayed. Patients with compensated HCV-related cirrhosis have	technology cannot be appropriately administered until ‘certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place’. Please see section 5 of the Final Appraisal Determination.

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	a significant risk of developing hepatocellular carcinoma, or decompensated liver disease; this risk can be reduced dramatically by successful antiviral treatment. By these means patients at greatest need will get rapid access to the best possible therapy, while a delay in implementation of NICE guidance will allow systems to be put in place to provide the most equitable and effective treatment for those patients who have less severe disease and so less urgent need for treatment. The procurement advice to NHS England is that a competitive procurement route would be required to commission Hepatitis C Networks. This process would take about 4 to 5 months to complete. A key part of the model is partnership working and the preferred procurement model allows bidders the opportunity to develop their proposals jointly with others e.g. DGHs, prison health, LAs etc. The network proposal includes costings to support the need to increase core staff and to facilitate network partnerships and co-ordination of care. As you will know, there IS a range of very promising developments in the treatment of hepatitis C expected in the near future, and we do have a concern that implementation of all new treatments should be managed holistically so as to leave clinicians with a coherent set of guidelines covering the full range of new and existing treatments, rather than being potentially distorted by the order in which products come to market. We are concerned that there are potential ethical difficulties if we cannot take an overview of all available and soon to be available treatments. We would suggest that the availability of additional new treatments which are known to be coming to market, and the associated policy and decision making clinical networks, amounts to “health service infrastructure” without which implementation of a recommendation for Sofosbuvir in isolation would be problematic. In order to ensure that the services we provide are both fit for purpose and can deliver these new treatments that ensure best outcomes for our patients we feel it is imperative that we are given sufficient time to implement the networks outlined above, before we are required to fund drugs that may otherwise be used inappropriately (having regard in particular to the need for specialist expertise and the imminent arrival of further new treatments for hepatitis C). This will also ensure systems are in place to collect outcomes data to inform future clinical practice. We are not making a case not to commission Sofosbuvir or Simeprevir prior to your recommendation taking effect. In recognition of the delay in implementation publication of the guidance if the waiver is granted NHS England will expect to have interim policies in place from April 2015 to cover key patient groups. In summary NHS England will: • Fast track for approval the service specification allowing the formation of clinical networks for the management of hepatitis C infection, and take the steps necessary to implement the specification within the 2015-16 year; • Fast track for consideration by April 2015 for approval of an interim policy	

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	document (currently under development) to provide oral antiviral therapy to all cirrhotic patients (plus a small number with severe non-hepatic complications of HCV); • Bring together as soon as possible a clinical body that will publish (non - statutory) clinical guidance to ensure the populations with the greatest need receive early treatment and that all patients receive the most appropriate and cost-effective therapy. This will incorporate both NICE guidance and any published NHS England interim clinical policies; and • Implement the NICE TA ID654 on Sofosbuvir within 180 days of publication of the guidance, allowing treatment to be expanded to a wider group of patients. NHS England requests that NICE: • Agree to a waiver in the implementation of NICE TA ID654 as previously requested; and • Include reference in their TA to the clinical guidance produced on behalf of NHS England to ensure that as far as possible all clinicians follow a national standard of care. These proposals have the full support of the NHS England Clinical Reference Group subgroup on hepatitis C infection.	
NHS England Clinical Reference Group	Thank you for asking for my comments on the NHS England application for a deferral of implementation of the NICE Technology Appraisals (TA) for simeprevir and sofosbuvir. The CRG HCV subgroup has discussed this request at some length. While there is some variation in detail of opinion, not one of the clinicians on the group supports the request for a delay in either TA. It is important when considering these NICE TAs to remember that they deal almost entirely with interferon-based therapy. Adding sofosbuvir or simeprevir to pegylated interferon is certainly a step forward, but it is not the paradigm change that all-oral regimens have brought to treatment in some other countries. A significant proportion of patients who are eligible for treatment under these two NICE TAs may well opt instead to wait for more effective and more tolerable regimens, and the demand is unlikely to be as high as has been suggested. **Simeprevir** Simeprevir is perhaps the more straightforward of the two drugs to deal with. Simeprevir plus pegylated interferon and ribavirin (Sim/P/R) is a regimen whose time has largely come and gone. There are relatively few patients (perhaps a few hundred across the country) for whom this treatment is still appropriate (although some of the expert clinicians on the subgroup do not believe that it has any application at all now). These are patients with relatively mild disease due to genotype 1 or 4 virus, who have made an informed decision not to wait for more tolerable and effective oral treatments. The HCV subgroup submitted an interim policy document to NHS England in May 2014 recommending the use of Sim/P/R	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	(at which point uptake may have been greater); this interim policy has now finally been approved by NHS England and should be implemented soon. The policy allows use of Sim/P/R in patients with genotype 1 (not genotype 4) infection, in accordance with the simeprevir licence. It is therefore similar to the NICE TA, except for the g4 indication. The main argument from NHS England for an extension of the NICE implementation period from 90 to 180 days is that it will take this time for systems to be put in place to deliver Sim/P/R treatment. Given that uptake for this regimen is likely to be low, and for those patients in whom it is used it will be a direct replacement for telaprevir/P/R or boceprevir/P/R (both of which have longer courses and more side effects than Sim/P/R) we do not envision any difficulty for current providers in delivering the new treatment immediately. NHS England have already approved a policy very similar to the NICE TA, to be delivered through existing systems, so it is puzzling that they do not think that the NICE TA can be delivered through the same route. The HCV subgroup was not unduly concerned about the clinical impact of a delay in implementation of the simeprevir TA because of the NHS England interim policy allowing its use (and the view of some members that it should not be used at all). However for a small group of patients with genotype 4 infection (almost exclusively Egyptian) a deferral would mean further delay in access to therapy. Genotype 1 patients (largely Caucasian) would be eligible for treatment now, while the genotype 4 patients would face a wait of several months. **Sofosbuvir** The arguments around sofosbuvir and pegylated interferon (plus or minus ribavirin) – Sof/P/R – are more complex. As with Sim/P/R many patients, especially those with mild disease, may choose to wait until all-oral regimens are available. However patients with stable cirrhosis, who are at risk of decompensation or hepatocellular carcinoma, may decide (after discussion with their clinicians) that it is better to have treatment now than delay. This is especially true for those with genotype 3 infection. There is therefore more urgency to get availability for this combination, and there is currently no interim policy to supply it through NHS England (apart from the highly restricted early access programme for sofosbuvir plus ledipasvir in decompensated liver disease). It is difficult to predict the number of patients who will opt for treatment with Sof/P/R rather than waiting, but it will not be nearly as many as the 15 000 quoted by NHS England (this figure was based on an estimate of the number that might come forward for all-oral treatment). NHS England have requested a delay in implementation on the ground that it will be impossible to get a delivery system for Sof/P/R in place within 90 days of the NICE TA publication, but it will be possible in 180 days. This proposed delivery system is based on the idea of a centrally-commissioned service run through	

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	networks of specialist providers. The majority of the clinicians on the HCV subgroup remain of the opinion that the best way to deliver hepatitis C services in England is indeed through this network model. However this is not the only model of delivery, and is certainly not an absolute requirement for getting treatment to patients. The members of the HCV subgroup believe that current resources and delivery systems are adequate to provide safe and effective treatment for those patients who will opt for treatment with Sof/P/R. The HCV subgroup submitted a completed proposal for a HCV Service Specification to NHS England (including the establishment of the network model) in December 2013. This specification remains under consideration by NHS England, and has yet to be approved. The HCV subgroup has asked why, if it is thought to be essential for service delivery, this specification has not been approved and adopted already. Sof/P/R is a regimen that will have limited appeal to many patients, who will wish to wait for all oral treatment. It may however be life-saving for some people who have cirrhosis, and are at risk of rapid disease progression without treatment. A further 3 month delay may have a significant effect on the outcome for a small group of patients. This is amplified by the fact that many clinicians have held off treating some of these patients for many months already in anticipation of NICE approval of the new drugs. Given that the clinicians on the HCV subgroup can see no practical difficulty in delivering the treatment straight away (accepting that the current model is not the one that most would ideally like to see in place), and that there is no guarantee from NHS England that a better system will be put in place in the near future, there is a strong argument for making these drugs available as soon as possible, and not delaying further. In summary, the unanimous view of the clinicians on the HCV subgroup (made up of representatives from the HPB and ID CRGs) is that: Sof/P/R is an important new therapeutic choice, and may be life-saving for a small number of patients; Sim/P/R may be useful in a minority of patients with mild disease; Current services will be able to deliver these treatments safely and effectively to the number of patients likely to opt for the new interferon-based regimens; There are no grounds (under the terms of the Health and Social Care Act 2013) for NICE to delay implementation of its guidance beyond the 90 day period specified.	
Positively UK	Positively UK is responding to the application from NHS England for an extension to	Comments noted. Following consideration of comments received on the decision to amend the

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	the deferred funding period for sofosbuvir in chronic hepatitis C.
	
	While we fully understand the reasoning set out by NHS England, we do not support their case and believe there is evidence to support 'fast-track' access to sofosbuvir for key populations. Our arguments are as follows:
	
	• NHS England cite the introduction of the Dashboard and Database. However the Dashboard will go live by March 2015 the time sofosbuvir would be available. The Database will require longer and there is no timeframe set for this, nor, knowing the trouble with introducing new IT systems, that a database will be in place by the estimated time of late 2015. We are also of the opinion that awaiting the introduction of a database should not negatively impact upon achieving the optimum health of people with Hepatitis C.
	• NHS England cite the need to implement a Hepatitis C Network Model. There is no indication that this will improve patient care for those already tapped into care, and waiting could detrimentally impact upon the health of key populations with Hepatitis C.
	• Awaiting the implementation of a Hepatitis C Network Model is contradictory to the argument to defer funding for sofosbuvir. One case made by NHS England is that there will be increase in demand and this will impact up capacity, however it is also clear that there are hard-to-reach groups and it will take the establishment of the network and time to reach these populations. Again this should not negatively impact against those already accessing care and treatment for Hepatitis C.
	• We understand provider capacity may be an issue that needs addressing. However we believe this can be addressed by introducing a **'fast-track'** mechanism and would ensure key groups receive access to key groups. We define these groups as:
	
	  ○ Patients with advanced liver disease e.g. liver fibrosis and NHS England also recognises the need to support this cohort
	
	We would further add
	
	  ○ People co-infected with HIV; there is evidence that co-infection
		deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	with HIV and Hepatitis C damages the immune system and faster liver disease progression ○ Gay men and people who use drugs who are disproportionately affected by Hepatitis C ○ Patients where current treatments are having a detrimental impact on either or both physical and mental well-being. This cohort can be identified by the consultant currently providing care and we believe that the patient and healthcare are best placed to determine this We make the recommendations based on ensuring we promote the best well-being of patients l with Hepatitis C and obtain optimum health outcomes without delay. We are also aware that progression to advanced liver disease for some cohorts may be rapid and that treatment is less effective in administered late; people co-infected with HIV are particularly affected with accelerated liver disease. The consultant must have the ability to treat the patient with sofosbuvir now, or opt for another treatment as they come online. Finally we need to consider of issues of treatment as prevention and the disproportionate burden upon the gay community and people who use drugs of Hepatitis C. In treating these patients, we will reduce the onward transmission of Hepatitis C. Finally we must consider the potential impact of Pre Exposure Prophylaxis, (PrEP). Although PrEP is still in the trial stages there are calls for a rapid implementation following the success of trials in the UK. Implementation of PrEP will result in a cohort of predominantly gay men using treatment as prevention over condom use, and this again will increase the risk of transmission of Hep C within the gay community.	
Royal College of Pathologists	"It is disappointing that NHS England has to apply for a deferral in the implementation of a NICE recommendation. There are in existence many Hepatology centres and networks within England that are able to deliver interferon based therapy efficiently to patients. It is difficult to see why additional effort over 9 months is required to set up the necessary infra-structure to implement a NICE recommendation, which is still largely based on a combination therapy of the new drug sofosbuvir with interferon/ribavirin with a limited number of patients eligible for	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions)

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	interferon free therapy. The need for setting up a database is acknowledged, but this should not take up to 9 months to set up. We believe that the new service provision could be set up at a much shorter time frame. There should also be an interim plan to continue to allow patients with advanced disease to be prioritised for access to the new drug without waiting for the whole infra-structure to be set up."	and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.
Royal College of Physicians	The RCP is grateful for the opportunity to respond to the above consultation. In doing so, we have liaised with our experts in gastroenterology, hepatology, infectious diseases and genito-urinary medicine. We would like to make the following general and specific points as well as endorsing the submission of the British Society of Gastroenterology (BSG). **General comments (also submitted to the similar request regarding simeprevir in combination with peginterferon alfa and ribavirin for treating genotypes 1 and 4 chronic hepatitis C [ID 668])** We believe that a range of contributory factors means that NHS England Specialised Commissioning is facing huge financial issues and is therefore not able to afford the services it has taken on. Hepatitis C presents a particular problem. New treatments are available which are highly effective, demonstrably cost-effective yet unaffordable - the introduction of sofosbuvir, simeprevir, and daclatasvir has already caused significant issues in the US. It is our opinion that NICE is likely to recommend the use of these drugs as: • the treatments are highly cost effective (preventing the development of very costly liver disease) • 'affordability' does not fall under NICE remit. However, the NICE consultation on sofosbuvir has already been extended twice and there have been very significant changes made between the first and the second ACD. The final TA has still not been published (the original date was September). A waiver has now been requested on the implementation period for the NICE guidance for sofosbuvir and for simeprevir - increasing it to 180 days from publication. This request has been made on the grounds that the introduction of the new therapies is not clinically possible without the establishment of formal clinical	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	networks defined by a national service specification. Our experts do not agree with this stance for several reasons: **Simeprevir** - the case of simeprevir is the more straightforward than sofosbuvir. NHSE has approved (and indeed has fast-tracked) a policy for the use of simeprevir, which will be in place by late December 2014. This policy essentially allows the same use of simeprevir as the NICE TA, with the exception of use in genotype 4 virus (which makes up a tiny fraction of cases in England). If this policy can be introduced immediately without the need for a service specification then we see no reason why the NICE TA should be delayed. We are aware that NHSE have had the proposed service specification since December 2013. The specification has not been approved to date, and we do not feel it any more likely to be in place at 180 days than it is at 90 days. If the specification is considered essential for the development of new treatments we wonder why this has not been given greater priority? **Sofosbuvir** - The situation with the sofosbuvir TA is more complicated, yet many of the same points above apply. Overall, we are unaware of any expert clinical opinion that says that the NICE TA could not be implemented immediately, using available resource. We therefore do not see this as a valid reason for delaying the implementation of NICE guidance on these drugs. It is important to set these issues in the context that we are already lagging behind much of the developed world in our treatment of HCV. The disputed NICE TAs are still for interferon-based combinations, which have been in widespread use in the US for at least 6 months. NICE will not be reporting on interferon-free regimens (which are the standard of care in many countries) until the middle of next year. **Specific comments** The introduction of sofosbuvir does mark a significant advance in the treatment of chronic hepatitis C infection. However, the current NICE consultation relates to treatment with sofosbuvir in combination with pegylated interferon (with a few exceptions for subgroups of genotype 2 and 3 disease where it is recommended without interferon). This is very different from the paradigm shift in treatment seen in the United States and a number of other European countries, where for some time treatment has been available using sofosbuvir in combination with other potent oral anti-viral drugs such as simeprevir and daclatasvir. These all-oral treatments are better tolerated, simpler to administer, and have generally better success rates than	

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	regimens that still rely on sofosbuvir in combination with interferon. The estimate of 15 000 patients being treated annually quoted by NHS England is made in the context of all-oral therapy being available, and is likely to be a significant over-estimate if the only treatment available still includes interferon. (Many physicians and patients will choose not to take up treatment with Sofosbuvir as part of an interferon-containing regimen, and will choose to wait for all oral therapy). The true figure is difficult to estimate, but is probably 6 -8 000 patients per year (compared with a historical rate of about 5 000 per year). Course length for sofosbuvir-containing regimens is shorter than for previous treatments (with pegylated interferon/ribavirin +/- 1st generation protease inhibitors), and side effects are dramatically reduced. The amount of clinical input for each patient will therefore be significantly reduced, and it is likely that existing treatment services will in general be able to cope with the predicted level of treatment demand that would follow implementation of the Sofosbuvir NICE TA. One particular group of patient will gain significant benefit from treatment under this NICE TA: patients with advanced liver damage due to hepatitis C genotype 3 infection. Published and ongoing studies demonstrate that the addition of Sofosbuvir to interferon and ribavirin, including treatment of patients who have failed prior dual therapy with interferon and ribavirin, will result in a high cure rate for patients with established cirrhosis. Successful treatment will prevent liver failure, reduce the risk for liver cancer, and substantially reduce the need for liver transplantation in this population. Delaying treatment by contrast will result in avoidable harm to a proportion of these patients. The availability of sofosbuvir for treatment of hepatitis C genotype 3 infection represents the first improvement in treatment for the last 15 years. The best way of delivering a high quality service for patients with hepatitis C infection is through managed networks based around specialist centres. The formal proposal for a Service Specification based on this principle was submitted to NHS England in December 2013, and remains under consideration. The request for deferral by NHS England is in part predicated on the assumption that this Service Specification is accepted and prioritised by CPAG, and that specialised centres will be commissioned and functioning by August 2015. In fact, there is no certainty that it will be approved by the Specialised Commissioning Oversight Group (SCOG). Even if the Service Specification is eventually approved it is unlikely to be done in time for the 2015-16 commissioning round, and NHS England have made it clear that new services will only be commissioned 'in year' in exceptional circumstances. The request for deferral of sofosbuvir treatment on the grounds that a reliable and functioning new delivery structure will be in place by August 2015 is therefore based	

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	on a series of assumptions and aspirations rather than by fact. NICE will judge the request for deferral on four specific criteria. The responses to these are as follows: *a. The health technology cannot be appropriately administered until training is in place;* All the centres likely to be using sofosbuvir plus pegylated interferon have been treating patients with pegylated interferon in combination with ribavirin, boceprevir, and telaprevir for some considerable time. They therefore already have staff trained and experienced in the use and monitoring of interferon and ribavirin. Sofosbuvir has very few significant side effects or drug-drug interactions (certainly fewer than the 1st generation protease inhibitors), and many of the centres will already be using sofosbuvir under the early access programme. For those centres that do not have previous experience of sofosbuvir the additional training required will be minimal. *b. The health technology cannot be appropriately administered until certain health service infrastructure requirements including goods, materials or other facilities are in place;* As discussed above, all treatment for hepatitis C infection would be better managed through clinical networks. This would allow for universal quality standards, equity of access, and better data collection. However, there is no absolute requirement for these networks, and there is as yet no guarantee from NHS England that it will commission them anyway. Some informal networks already exist, the current system of treatment delivery is adequate (at least in the short term), and the absence of universal clinical networks should not prevent the most urgent patients from receiving treatment as soon as possible. *c. The health technology cannot be appropriately administered until other appropriate health services resources, including staff, are in place;* Given the estimated level of demand for the treatment regimens covered by the NICE TA (i.e. predominantly sofosbuvir in combination with pegylated interferon), the shorter courses of these regimens compared with first generation protease inhibitors, and the relative simplicity of monitoring patients on sofosbuvir compared with other drugs, the current levels of human resource and facilities should be	

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	adequate to deliver the proposed treatments. Approximately 5 000 patients per year are being treated successfully with far more complex and lengthy drug regimes, and there is no reason to think that a moderate increase in numbers being treated will be unmanageable. *d. The health technology is not yet available in England.* This criterion is not relevant to the current consultation. Overall, the facts do not support the NHS England case for an increase to the implementation period for this NICE TA.	
Royal College of Nursing	The RCN is in agreement that the demand for Hepatitis C treatment will increase significantly in the context of availability of next generation therapies, which will change the landscape of Hepatitis C over the next 12 month period and beyond. We are however as a country already well behind in terms of identification of HCV and treatment numbers. In view of this there are many existing and emerging examples of excellent innovative service delivery, the best provision of which is delivered as close to the patient as possible. There are a number of documents relating to minimum service specifications for HCV treatment delivery. Many hospitals reach these specifications and prior to the early access scheme (EAS) were delivering HCV treatment with high standard auditable outcomes being demonstrated. This pathway continues for standard of care therapy (Pegylated interferon, ribavirin and for some addition of Boceprevir or Telaprevir). Unfortunately for many centres not involved with the EAS there have been a proportion of patients unable to, or unwilling to travel to specialist centres to have their treatment instigated and monitored. For some patients a door to door journey to receive their hepatitis C treatment, may be in the region of 2 hours travelling time each way, not accounting for poor transport links in some areas. This has made the EAS a postcode lottery of treatment for some individuals. The proposal of NHS England developing further specialist treatment centres providing a centralised resource for patients is but an extension of the EAS and being put in place predominantly for budgetary reasons. Many of the centres	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	currently running EAS programmes are 'holding patients' for newer therapies and some centres have an extremely large number of patients waiting. In addition the centres involved with EAS are also centres collaborating with the HCV registry which opens up access to clinical research that many other hospitals cannot gain. Again this raises concerns regarding access and equity to treatment giving some patients' excellent access to trials and depriving others. In particular the intravenous drug using HCV population appear to be most disadvantaged currently. In fact they should be one of the most important groups to treat as the most health gain will be achieved due to the reduction in the incidence of HCV. With regards to the need for increasing staff and resources we have to remember that in fact the clinical delivery of newer therapies will be much easier with significantly fewer side-effects to monitor, less time on treatment for patients and less intervention with clinic appointments. Even in the patients with established cirrhosis where complications may be more frequent this is no different to complications seen with cirrhosis in previous therapies and continued close liaison with tertiary centres will remain important. With regards to potentially deferring patients with mild disease to await therapy consideration should be taken with regards to previous NICE documentation and recommendations (NICE technology appraisals TA106). The suggestions made by NHS England may lead to further health inequalities with regard to parity and equity of access to the recommended contemporary treatment modalities. It is vital that treatment can be offered as close to the patients home as possible. If hospitals can offer a set specification standard for HCV treatment they should be allowed to deliver HCV treatment. Serious consideration by NHS England to expand the number of treating centres is vital. Data could be fed back to a regional HCV network for monitoring and audit. The networks responsibility would be to develop treatment guidelines on appropriateness of therapy and compare outcome data to national standards. As the health service infrastructure and facilities are most definitely in place, and we do not believe otherwise. We believe that NHS England should not be driving the NICE mandate to decide on treatment in this way. To be able to have such dramatic results in Sustained Viral Response (SVR) with Sofosbuvir, and the impact this will have on QALYs for patients will end up being a huge cost savings to the NHS with reduced problems of cirrhosis/HCC and liver	

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	transplantation – We don't think it makes sense to delay treating hepatitis C with Sofosbuvir.	
UK Clinical Pharmacy Association Hepatology and Gastroenterology Group	We as the UKCPA Hepatology and Gastroenterology Group would like to comment on the document circulated on the 21st November entitled; *Sofosbuvir for treating chronic hepatitis C [ID654] .Consultation on decision to amend the deferred funding*. As stakeholders in the awaited NICE appraisal for sofosbuvir we were disappointed to see a request from NHSE to defer the funding of sofosbuvir at this very late stage of the process. We would ask that NICE consider the following in its decision making of this request **Cost of not treating patients with fibrosis** The suitable patient criteria for the NHSE Early Access Scheme for sofosbuvir was explicit and only those with Childs Pugh B and above were eligible. We are concerned that a large number of patients who did not fit the criteria for the scheme such as those with F3-F4 fibrosis will continue to advance towards cirrhosis whilst waiting for sofosbuvir to be NICE approved and funded. It is widely clinically acknowledge and supported by a robust evidence base that the presence or absence of cirrhosis has a clinically significant effect on the probability of achieving a sustained viral response. If we wait for patients to become more advanced in their stage of liver disease before treating their hepatitis C then we increase the likelihood of treatment failure and hence the overall cost burden to the NHSE. **Cost of not treating cirrhotic patients** Although reference is made to extending the NHSE early access scheme we have yet no clarity on the specifics relating to this and whether it will broaden the patient criteria to include those with mild/moderate disease. However if the scheme is not extended and/or the patient numbers are strictly capped then there inevitably will be a number of cirrhotic patients who will not be in a position to be treated. The cost modelling is available which indicates that the cost burden of patients with cirrhosis is significant. The sooner an intervention is made in a patient with hepatitis C then the lower the overall	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.

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	cost impact and importantly the greater the improvement in a patient's quality of life. **Waiting for specialist teams and networks to be assimilated** We welcome and fully support the comments made in point 10 of the document referencing increasing specialist pharmacist support to assist in the seamless delivery of sofosbuvir. However we do not feel the latter should be used as a time-limiting factor in terms of gaining access to sofosbuvir. The UKCPA Gastroenterology and Hepatology Group consists of a large number of pharmacists who are involved in the delivery of hepatitis C treatments and provides consistent support and education to its service users. This delivery of education can be tailored to meet increased interest and demand. **Services are 'fit for purpose'** Whilst we as a group acknowledge the reference made in point 11 around service pathways being 'fit for purpose' we would equally acknowledge that this is an unusual statement due to hepatitis C service pathways being in place for many years. These pathways have enabled patients to be successfully treated. Although national figures suggest we are treating < 5% of the infected population this is not solely due to services not being fit for purpose but due to multi-factorial logistical issues such as screening/diagnosis rates and centre capacities. We support the increased focus on solidifying these service pathways but would highlight that this will be a long term project and one that should not limit the introduction of sofosbuvir. In summary; we support the creation of a robust and integrated hepatitis C delivery pathway as is outlined in the circulated document but would ask NICE to consider the points made above and to reconsider NHSEs request to defer funding. We would also ask you to take into account broadening the early access patient criteria if the decision is to approve NHSEs request. If funding is deferred then enabling a broader population to be treated via early access would be well received by this group.	

Comments received from commentators

Commentator	Comment	Response
Foundation for Liver Research	My main comment is that it is very, very, unlikely that patients with genotype 1 infection will accept treatment with Interferon along with Sofosbuvir. There were dozens of papers at the recent American Association for the Study of Liver Diseases (AASLD) conference in Boston showing excellent clearance results could be obtained with short periods of treatment using oral agents alone. These agents do not give the side effects of Interferon. I refer to Simeprevir, Daclatasvir, the new AbbVie agents and the drug Harvoni that Gilead are introducing as a single pill combining Sofosbuvir with Ledipasvir. All these drugs I imagine will be coming before NICE, or are in the process of so doing, for approval in the NHS. I would strongly recommend therefore that NICE consider all these agents together as an approach for treatment of hepatitis C that will be acceptable to patients. Interferon is unlikely to be used in the future because of the side effects and with the longer duration of therapy needed. Yes, NHS England have to come up with an organisation that can ensure equitable availability of these agents throughout the country and also the monitoring of costs and efficacy, which surely should be done through specialist commissioning.	Comments noted. Following consideration of comments received on the decision to amend the deferred funding, the NICE Guidance Executive has agreed to an extension to the deferred funding period, to 31 July 2015, granted under section 7(5a)[ii and iii] of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013; the health technology cannot be appropriately administered until 'certain health service infrastructure requirements including goods, materials or other facilities are, or other appropriate health services resources, including staff are in place'. Please see section 5 of the Final Appraisal Determination.
Merck Sharp and Dohme	No comment	Comments noted.

[i] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf
[ii] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/337115/HCV_in_the_UK_2014_24_July.pdf
[iii] http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4075686.pdf
[iv] http://www.legislation.gov.uk/uksi/2013/259/pdfs/uksiem_20130259_en.pdf
[v] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/170656/NHS_Constitution.pdf
[vi] http://www.nice.org.uk/guidance/indevelopment/gid-tag445/documents
[vii] http://www.england.nhs.uk/wp-content/uploads/2014/04/sofosbuvir-pol-stat.pdf