# Professional organisation statement template

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

**About you**

**Your name:** [redacted]

**Name of your organisation: Association of Clinical Microbiologists**

**Are you (tick all that apply):**

- a specialist in the treatment of people with the condition for which NICE is considering this technology? No
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)? No
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? No
- other? (please specify): Provider of laboratory services to support the diagnosis and follow up and monitor the treatment of hepatitis B infected patients on antiviral therapy

**What is the expected place of the technology in current practice?**

How is the condition currently treated in the NHS?
I am not involved in the treatment of patients with hepatitis B, but am involved in the diagnosis and follow-up of patients with that condition.

Is there significant geographical variation in current practice?
I have no knowledge of the geographical variation in practice, although it is likely that in the first instance it is more likely that a patient would be treated if they were under the care of a specialist liver unit which has taken part in the clinical trials of the drugs.

Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?
I am not involved with these discussions, but views are influenced by clinical trial experiences.

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient?
There are differences in opinion about the criteria for initiation and ceasing of treatment as well as the exact protocol and drugs used as it is a constantly evolving field as more drugs become available and more information becomes available about the long-term outcomes of treatment. There are different subgroups according to the HBeAg and AntiHBe status and patients are treated differently. There is also a need for a consensus about treatment in different age groups, particularly children where different outcomes should be considered.

Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?
There are different subgroups according to the HBeAg and AntiHBe status and patients are treated differently. There is also a need for a consensus about treatment in different age groups, particularly children where different outcomes should be considered.

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics?
At the moment the treatment and follow-up is done in specialist centres, which is appropriate at this stage

Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?
There would be a need for additional training in understanding the mode of action and adverse event profile of the new agent and for the follow up of all patients to ensure drug activity and monitor for emergence of resistant virus.

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?
I have no direct knowledge of these practices, but I would imagine that in some clinical situations, antiviral drugs are used in settings outside of those for which they are licensed.(e.g. in acute hepatitis B)

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.
I have no direct knowledge of clinical guidelines used in specialist centres.

**The advantages and disadvantages of the technology**

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK.

Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?
There is currently very little choice in the range of drugs for the treatment of hepatitis B, with a limited range of drugs, the issue of drug resistance is a problem and with a wider range of antiviral drugs, patients can be more effectively managed. When resistance one drug arises, drugs with different targets can be used as an alternative or in addition.

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.
I have no direct knowledge of such rules, however on mono-treatment the emergence of virus resistant to treatment has been a problem for all antiviral drugs. Patients with resistance to Lamivudine have virus, which is susceptible to Tenofovir and patients with resistance to Adefovir can also respond to treatment with Tenofovir, though not as well a treatment naive patients. The establishment of the nature of the resistant virus and the follow up of patients who fail on therapy is an important factor, which requires laboratory testing and the development of expertise in assessing the nature of the mutations and formulating the advice regarding alternative treatment options. In the future more regular laboratory testing to establish HBV DNA levels to ensure continued viral suppression will be required. The costs of the additional laboratory testing should be recognised within the appraisal. The management of patients whose therapy is to be discontinued for any reason is also complex as the rapid withdrawal of a suppressive drug may have an adverse effect on the patient.
The resistance profile for this drug suggests that resistant virus emerges with a lower frequency than current antiviral agents, in one study no resistant virus emerged during a 72-week treatment.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed

in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting?
I am not familiar with all of the clinical trial work, but Tenofovir has been successfully used for the suppression of virus replication of hepatitis B in both HBeAg positive and HBeAg negative persistent infections. It has been successfully used in treatment naïve patients and those who have failed on Lamivudine and who are failing on Adefovir. The patient groups in these studies are typical of UK patients in terms of pre-treatment HBV DNA and ALT levels and the results are likely to be replicated in UK patients and in UK practice, more information may be required about the response of patients in all genotypes, particularly those common in UK patients.

What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?
The most important outcomes of treatment for hepatitis B are suppression of inflammation in the liver and consequent improvement for long-term clinical outcomes. However, suppression of viral replication is taken as a surrogate marker, which can be easily measured and monitored by quantitative laboratory assays for hepatitis B DNA. Improvement in liver function as measured by reduction in the ALT level is also taken as an indicator of reduced inflammation and can be easily measured by quantitative laboratory assays. Such improvements have been observed in patients with and without pre-existing cirrhosis as ascertained by liver biopsy. The seroconversion from HBeAg to AntiHBe is usually associated with a reduction in virus replication, but is less readily achieved by antiviral treatment (only 5% after 64 weeks treatment) The loss of HBeAg and the seroconversion to AntiHBe is the a preferred outcome for children, where potentially life long antiviral treatment would be difficult to manage.

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?
Many of the antiviral drugs used in hepatitis B have already been used in the treatment of HIV where adverse events in clinical practice would have been observed. Renal dysfunction is an issue which must be followed-up biochemically. I am not aware of any developments that have arisen through clinical practice

**Any additional sources of evidence**

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.
I do not have access to information other than abstracts from scientific meetings..

**Implementation issues**

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition?
Approval of Tenofovir as additional antiviral agent against hepatitis B would open up a wider range of drugs for use in the suppression of hepatitis B replication and so reduce the rate and extent of progression of liver damage and improve health outcomes for the patient. As some of the drugs already in use have had problems of virus resistance, an agent such as tenofovir with a low resistance profile will be an acceptable agent for use in those who have already developed resistance and in new patients.

Would NHS staff need extra education and training?
NHS staff would require education and training. As well as clinical staff and facilities the NHS would also need to support laboratory investigations to monitor response to treatment and where treatment failures occurred would need to provide information on the nature of any resistant organisms by amplification and sequencing of the patients' hepatitis B DNA. A body of knowledge would have to be developed to recognise antiviral drugs with similar mutation patterns – so that appropriate alternative drugs could be recommended (as is the case with HIV presently).
.

There would be a need for additional training in understanding the mode of action and adverse event profile of the new agent and for the follow up of all patients to ensure drug activity and monitor for emergence of resistant virus.

Would any additional resources be required (for example, facilities or equipment)?
There would be a need for additional resources for laboratory testing to diagnose the condition and assess suitability for treatment, and then for monitoring the response and performing complex assays to establish the exact nature of the resistant virus, which would then enable decisions to be made on alternative drugs with different genotypic variations in drug resistance. . A body of knowledge would have to be developed to recognise antiviral drugs with similar mutation patterns – so that appropriate alternative drugs could be recommended (as is the case with HIV presently).The resources for funding such laboratory investigations must be included when considering the overall costs of using such antiviral agents