1. Executive Summary

Background
Hepatitis C (HCV) infection is believed to affect between 0.1% and 1.0% of the population in England and Wales. A chronic disease with slow progression, hepatitis C can cause severe liver damage and eventually death if the viral infection is not cleared. Although some patients clear the virus spontaneously, many patients remain infected and go on to develop chronic hepatitis C. Pegylated inferferon α in combination with ribavirin is the best treatment currently available for the infection. Patients receiving the drug regimen may attain a sustained virologic response (SVR) to treatment, defined as having undetectable viral RNA in the blood both at treatment end, as well as 24 weeks after that. Patients infected with certain HCV genotypes, namely genotypes 1 or 4, are less likely to attain SVR than patients infected with genotypes 2 or 3.

NICE technology appraisals TA75 and TA106, recommend the use of pegylated interferons in combination with ribavirin for the treatment of chronic hepatitis C. Since the publication of the guidance, use of these drugs in the NHS has increased, however, new licenses have now been granted in further sub-populations and the Institute has recognised this in its commissioning of a new HTA. This HTA focuses specifically on the new indications for pegylated interferons, namely:

- Retreatment in patients who failed to attain SVR on their previous course of interferon-based (with or without ribavirin) therapy
- Treatment of patients co-infected with HIV and HCV.
- Rapid treatment in eligible subpopulations over and beyond existing rapid treatment rules (Roche Products Ltd. License extension only, not Schering-Plough)

This submission presents information from pivotal trials in the retreatment and co-infection license extensions, as well as from two newer trials conducted since the license was awarded. This evidence base also informs an economic evaluation comparing the costs and benefits of the therapy compared to standard care (i.e. no pegylated interferon-based treatment).

Efficacy
In retreatment trials, up to 23% of patients attained an SVR despite having previously failed therapy. This SVR rate varied substantially by viral genotype, liver fibrosis state and by the patient's previous reason for not attaining SVR. Prior non-responders, whose viral RNA burden was never remarkably reduced by the prior therapy, were least likely to clear the virus on retreatment with SVR rates between 15 and 18 percent. In contrast, better SVR rates (up to 41%) were seen in patients whose previous treatment was not successful due to an apparent initial response but subsequent relapse after end of treatment. Similarly, patients with difficult-to-treat HCV genotype 1 had a lower SVR (16%) compared to patients with easier-to-treat genotypes 2 and 3 (about 58%).

Trials of HIV/HCV co-infected patients found that between 27 and 42 percent of the treated population could attain SVR. In a similar pattern to the retreatment indication, attainment of SVR was strongly predicted by HCV genotype as well as HIV disease burden.

Safety
The safety profile of the treatment is well-documented in the studies we identified. The rates and types of SAEs observed under retreatment or HIV/HCV co-infection scenarios do not differ substantially from what is observed in standard, first-time therapy as described in previous technology appraisals.

Cost-effectiveness
The economic assessment model was based on previous work carried out in NICE technology appraisal TA106. The model used efficacy data from the most relevant trials in retreatment and HIV/HCV co-

infection settings. Disease outcomes as well as costs were estimated, and cost-effectiveness was assessed in comparison with 'standard care' i.e. no treatment with interferon or pegylated interferon. The base-case results for the retreatment and HIV/HCV co-infection scenarios gave incremental cost-effectiveness ratios (ICERs) of £4,387/QALY and £1,077/QALY respectively.

Genotype played a strong role in cost-effectiveness due to its influence on efficacy. Patients with genotype 1 or 4 HCV were invariably less cost-effective to treat with ICERs of £7,177/QALY and £1,637/QALY in retreatment and HIV/HCV co-infection scenarios respectively. In comparison, patients with HCV genotypes 2 or 3, had ICERs of £783/QALY and £403/QALY in retreatment and HIV/HCV scenarios.

ICERs for the retreatment scenario were higher in difficult-to-treat subgroups. For 'prior non-responders to therapy' the ICER was £7,581/QALY. By contrast, subgroups who were prior 'relapsers', or whose prior treatment failed for other reasons respectively had ICERS of £2,048/QALY and £3,013/QALY.

Despite the differences observed, all cost-effectiveness estimates placed the ICER well below a threshold of £20,000. Furthermore, probabilistic analysis of uncertainty around the data going into the economic model shows that the findings are extremely robust. In all scenarios there was a greater than 90% chance that the treatment would be cost-effective at £20,000/QALY. The results demonstrate that pegylated interferon α-2b and ribavirin represent cost-effective treatment options in both retreatment and HIV/HCV co-infection scenarios within the NHS of England and Wales. Difficult-to-treat populations should be carefully considered especially in retreatment scenarios, where the patient's prior treatment response history is a key predictor of future success.

Budget impact

Using recently published figures from NICE regarding the use of drugs to treat hepatitis C, we estimate that over 20,000 people in England and Wales may be considered for retreatment. Assuming a 2% uptake of pegylated interferon α-2b and ribavirin therapy in 2011, increasing by 1% each year thereafter, the annual budget impact to the NHS including drug costs, assessments and monitoring would be £2.5m in 2011, rising to £6.6m in 2015.

The HIV/HCV population is substantially smaller than the retreatment population, numbering 2,050 by our estimates and increasing by around 80 patients per year. Assuming an initially uptake of 5% in this population in 2011 increasing by 1% each year thereafter, the estimated annual budget impact is £0.6m in 2011 rising to £1.0m in 2015.