EMA preclinical overview

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Introduction

- A revision of EMA/CHMP guidance on HCV drug development is ongoing
- According to plan, draft guidance will be posted on the EMA website January 2011 for consultation
- *Note that the statements on these slides are preliminary and may be subject to change*

Preclinical virology

- An initial application dossier should contain an extensive evaluation of the *in vitro* activity of a new DAA or HTA, an exploration of its mechanism of action, its activity against viruses other than HCV (HIV, HBV), the risk of selection for drug-resistant variants, and the potential for cross-resistance with other agents. HCV genotype- and subtype specific activity should be investigated.
- The *in vitro* antiviral activity of a new agent should be investigated in combination with interferon, ribavirin and other potential agents for use in combination.

Preclinical virology

- Cell-free functional assays (such as polymerase or protease assays) and cell-based assays such as the subgenomic HCV-replicon system are often used in the study of anti-HCV activity *in vitro*, including the assessment of phenotypic resistance. Modifications of these systems are used by different developers and academic centres, and there are presently no standardised methodologies for these investigations.
- *It is expected that applicants will provide a full justification for the range of studies performed, and the methods used.*

Preclinical toxicology studies

- General guidelines for preclinical toxicology studies should be followed.
- It is anticipated that combination drug regimens will be pursued. Combination toxicology studies will not be required unless data on the single agents give rise to specific concerns about additive or synergistic toxicity.
- However, in case of unexpected drug toxicities within clinical trials, further preclinical studies may be warranted.