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In Vitro and *In Vivo* Development of Drug Resistance by Rhinoviruses W. Al-Nakib[1,2]; S. Yasin[2] and C.J. Dearden[2]; Department of Microbiology, Faculty of Medicine, University of Kuwait[1] and MRC Common Cold Unit, Salisbury, England[2]

This study describes the development of drug resistance by rhinoviruses both *in vitro*, in two different cell-lines, and also *in vivo* in man following treatment with an anti-rhinovirus compound. *In vitro* studies suggested that drug resistance can develop with a high frequency and to a high concentration of the drugs. This paper describes the characterisation of these drug resistant mutants in relation to the parent virus as well as a drug sensitive strain which has been passaged at the same level as the mutant but without drug. The development of drug resistance *in vivo*, in man is also being investigated. Thus, serial nasal washings from volunteers challenged with HRV-9 and treated with an anti-rhinovirus drug (20 volunteers) or placebo (20 volunteers) are being examined for the presence of a virus that can grow at drug concentrations that are normally inhibitory for HRV-9. These experiments are nearing completion and results will be presented at this meeting.

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Biological Properties of Amantadine-Resistant Influenza Virus Mutants
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The appearance of amantadine-resistant influenza virus mutants has been documented in the laboratory and in virus isolates from the field. It can be expected that these mutants will be generated if amantadine is used on a large scale; however, the biological potential of such mutants is not known. To be a severe threat to the control of an influenza virus epidemic with the drug, the resistant mutants would have to be genetically stable, transmissible, and cause disease with a severity similar to that of the parental virus. This study examined these biological properties using amantadine-resistant mutants generated in an avian influenza virus model. The drug-resistant virus generated in this study was found to be virulent, genetically stable, and showed no measurable selective disadvantage when competing for passage in uninfected hosts with the wild-type virus. The mutations responsible for amantadine-resistance in this model system are in the M2 polypeptide and are identical to those found in amantadine-resistant human influenza virus strains. The data suggest that amantadine-resistant virus does have the biological potential to interfere with the large-scale use of the drug during a severe influenza virus outbreak. Some precautions to prevent the transmission of amantadine-resistant virus, such as isolation or vaccination, may be appropriate.