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## **ACCEPTED MANUSCRIPT**

## Determination of pore size distributions of virus filtration membranes using gold nanoparticles and their correlation with virus retention

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Virus filtration membranes contribute substantially to the virus safety of biopharmaceutical drugs due to their capability to retain viral particles mainly based by the size-exclusion mechanisms. In this work, virus filtration membranes were challenged with gold nanoparticles (GNPs) in order to determine pore size distributions (PSDs) for a wide range of different commercial and non-commercial parvovirus retentive membranes differing in structure, material and surface chemistry. The retention mechanism of GNPs was investigated and effectively shifted towards size-exclusion by using an anionic surfactant to suppress particle adsorption to the membrane surface. This allowed insights into the relevance of particle retention based on size-exclusion mechanisms of the respective membranes. Membrane PSDs investigated through GNP challenges were for some membranes compared with PSDs investigated by liquid-liquid displacement porometry (LLDP). In addition, virus retention performance using Pseudomonas aeruginosa bacteriophage PP7 as accepted model virus was determined for the entire set of membranes and correlated with the cut-off pore size obtained from experiments using GNPs. Exemplarily, retention was examined for one membrane type using a set of different sized viruses (PCV-2, PP7, MVM, HAV) ranging from 18-28 nm and compared to GNP retention.

Keywords: Gold nanoparticles, Membrane structure, Particle retention, Pore size distribution, Virus filtration, Virus retention

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