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## Opportunities, challenges and solutions for pulmonary antibiotic delivery

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Many infectious diseases emerge in the lungs or enter the human body through the lungs. Therefore, the lungs are an excellent port of entry for antibiotic drugs. A major advantage of pulmonary administration of antibiotics against lung diseases is deposition directly at the site of infection. This may enable to lower the dose compared to oral or parenteral administration, which reduces their adverse systemic side effects. On the other hand with higher drug concentrations from the same dose as given parenterally, it may become possible to eradicate drug resistant organisms as resistance often depends on the drug concentration achieved. Inhalation is also a non-invasive way of administration compared to injection. Dry powder inhalation offers additional advantages as the drug can be delivered in the dry state. This increases the stability and shelf life of the drug and eliminates the need for reconstitution of freeze dried powders for injection. It may even eliminate the need for a cold chain which could be relevant in rural areas of developing countries. Safe reconstitution and injection are furthermore often impossible in such areas due to a lack of sterile water and clean needles. Compared to nebulisation, dry powder inhalation saves considerable time whereas the efficacy of delivery may be much higher. The high doses and often unfavorable physicochemical properties for inhalation set high standards for dry powder inhaler formulations and devices however. Solutions are often found in particle engineering and powder processing while neglecting the opportunities for improved inhaler design. The incorporation of excipients increases the amount of powder to be inhaled and introduces yet unknown safety risks for the long term. The presentation will deal with the opportunities and challenges for dry powder antibiotic inhalation but also possible solutions and some very promising data will be presented.

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## Fate and effect of antibiotics from anthropogenic wastes and resistance risk assessment

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The anthropogenic sources wastes, including domestic sewage and husbandry wastewater, to and sludge to garbage and municipal solid waste are regarded as main contributors to the elevated level of antibiotics in the environment. This paper introduces recent studies on the occurrence and dynamic models of antibiotics in anthropogenic wastes, their effects on wastes bio-processing and the corresponding risk assessment methodology. Our results show that removal of antibiotics is more dependent on their sorption potential than on their biodegradability within a treatment system. Furthermore, the presence of antibiotics at trace levels is reportedly inhibitory to bio-treatment systems particularly to nitrification. However, after prolonged acclimatization microorganisms may come to the fore that can subsist on antibiotics, while these inhibitory effects can also be alleviated as a consequence of the evolution of Antibiotic Resistance Genes (ARG) and/or succession of a microbial community that is gradually dominated by antibiotic insensitive microorganisms. The spread of ARGs and their recruitment by clinically important bacteria have not been studied in enough detail to allow assessment of the related risks. Defining risk determinants and proposing validated risk quantification models are imperative as necessary steps towards a comprehensive risk assessment framework for the presence of antibiotics and antibiotic resistance in anthropogenic wastes.

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