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Title: Selection of the optimal nebulizer for further clinical development of inhaled nebulized nitrite (AIR001) in pulmonary arterial hypertension patients

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Body: Introduction: Clinical trials utilizing nebulized inhaled Nitrite (AIR001), in patients with Pulmonary Arterial Hypertension (PAH) require a portable, highly efficient nebulizer capable of monitoring adherence and compliance. Objectives: To evaluate the pharmacokinetics (PK), safety, and tolerability of AIR001 comparing the Philips I-neb AAD System (Philips Respironics, USA) with the Solo-Idehaler (nebulization head, Aeroneb® Solo (Aerogen, IR), aerosol-reservoir attachment, Idehaler™ (Diffusion Technique Francais, FR). Methods: Utilizing a randomized, crossover, open-label design, 6 subjects received equivalent doses of AIR001 (based on standard in vitro characterization with AIR001 and the resulting % efficiency of each nebulizer to deliver drug). PK parameters for plasma nitrite and nitrate were determined. Supine and orthostatic hemodynamics were evaluated. Adverse events were monitored as was clinical chemistry, hematology, venous and percutaneous methemoglobin, and SaO_2. Results: Nitrite PK differences were not statistically significant ($p < 0.05$) between devices.

Efficiency was greater for the I-neb AAD System with no differences in safety or tolerability between devices. Conclusions: Because of precise dosing, adaptive capacity, and its ability to monitor adherence and compliance, the I-neb AAD is optimal for further study of AIR001 in patients with PAH.