《化学药品吸入液体制剂药学研究技术要求（征求意见稿）》反馈意见表

"Technical Requirements for Pharmaceutical Research on Chemical Inhalation Liquid Preparations (Draft for Solicitation of Comments)" Feedback Form

反馈单位/企业名称	International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS)
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反馈意见和建议 **(Feedback and Suggestions)**

序号	修订的位置（页码和行号） Page and Line Number (these refer to those in the original Chinese	原文描述 Original Text	修改建议 Proposed Changes	修改理由或依据 Rational for Proposed Change
1	General Comment			We welcome the development of the guidance and the references to utilisation of existing technical guidelines globally. The inclusion of references to ICH guidelines throughout the guidance aligns with global practices, as do the references to domestic and foreign pharmacopoeias.
2	General Comment			The guideline is well written and comprehensive. The requirements stipulated in the guideline are consistent with those of similar guidelines by the US FDA.
3	Pages 5-6, Section 4.2 Nebulization Performance Research		Please add text that considers nebulization performance across the nebulization time.	During development, it is important to characterize the consistency of the nebulization performance across the nebulization time.
4	Page 6, Line 114		Consider adding: "For mesh nebulisers perform a user study including regular use and cleaning over time to qualify the cleaning procedure and establish a recommended mesh replacement frequency"	The mesh in a mesh nebuliser may be clogged over time and may need to be replaced with a certain frequency, which depends on the drug formulation, use frequency and patient cleaning procedure. If clogged, delivery time and droplet size distribution may be impacted.
5	Page 7, Lines 125-130 and Page 10, Lines 200-202	制剂生产商需结合原料药生产工艺，根据相关指导原则、国内外药典标准，对原料药的质量进行充分研究与评估,关注溶液的澄清度和颜色、有关物质、残留溶剂、微生物限度等检查，以满足制剂工艺和质量的控制要求；同时需关注对致突变杂质和元素杂质的研究和评估。原料药内控标准原则上应不低于国内外现行版药典标准。 Preparation manufacturers should consider the production process of drug substance, perform comprehensive evaluation and study on the quality of the drug substance in accordance with relevant guidelines and domestic and foreign pharmacopoeia standards, and focus on the test of clarity and color of the solutions, related substances, residual solvents, and microbial limits, so as to meet the requirements for preparation process and quality control. At the same time, attention should also be paid to the research and evaluation of mutagenic impurities and elemental impurities. In principle, the internal control standards for drug substance should not be lower than the existing domestic and foreign pharmacopoeia standards	Please clarify about 'domestic and foreign pharmacopoeia; standards' mentioned in the guideline. For example, which regional pharmacopoeia is qualified as the 'foreign pharmacopoeia', JP, EP or USP? It would be helpful if this is clearly stated in the guideline. Further, which standards should be followed if there are inconsistencies between domestic and foreign pharmacopoeia or between (qualified) foreign pharmacopeia?	Clarification regarding the "foreign pharmacopoiea" will assist industry in meeting CDE/NMPA expectations
6	Page 8, Section 6.1 Quality Research 质量研究			We welcome the recommendation to follow QbD for development and control (CQA and QTPP) in this guidance. We strongly support that approach that the applicant will define and justify the CQAs of the formulation/product they have developed rather than use a required or pre-determined list of CQAs.
7	Page 8, Lines 169-171	应明确检测环境的温度和湿度要求。递送特性检查采用的雾化时间和气流速度对测定结果存在较大影响，注意进行相关考察。 The temperature and humidity requirements of the testing environment should be clearly defined. The nebulization time and air velocity adopted in the delivery characteristics test have a greater impact on the measurement results, so pay attention to relevant investigations.	Consider adding a reference to pharmacopoieal test requirements. For example, 15 liters per minute and the use of a cold impactor for any droplet size determination, as well as standard breathing patterns for delivered dose testing.	There is potential here to align with global standards regarding nebulisation testing. It is unclear what "pay attention to relevant investigations," means, and referencing existing pharmacopoeial tests could help clarify. Jet nebuliser flow rate is an important parameter and is different from the dose testing equipment flow rate. This difference could be mentioned as well.
8	Page 10, Section 6.2 Quality Standards		Please add, "dose content uniformity for the amount of drug dispensed from the ampoule" (tested at release and in stability studies)	This test result describes the actual patient dose after opening, potential shaking, and squeezing, and may reveal any drug loss in the ampoule -- for example, due to wall adsorption (in particular for aged samples). This test is a critical attribute, and describing it clearly in this guideline will provide further clarity to the industry.
9	Page 10, Lines 207-209, Quality standards	此外，基于品种特性、历史批次研究数据等的风险评估，吸入混悬液必要时应将递送速率和递送总量、微细粒子剂量检查订入制剂放行标准。 In addition, based on the risk assessment of product characteristics and research data of previous batches, the inspection on the delivery rate, total delivery amount, and fine particle dose of the inhalation suspension should be included into the preparation release standard when necessary	Please consider deleting this paragraph.	There is no scientific rationale to include delivery rate, total delivery amount and fine particle dose in release testing/QC specifications for a nebulisation product (liquid preparation). These performance attributes are mainly determined and affected by the nebulization device used, which should be controlled by other means.
10	Pages 10-11, Lines 217-219, Stability Study	...递送速率和递送总量，空气动力学粒径分布空气动力学粒径分布(APSD)/微细粒子剂量,... ...delivery rate and total delivery amount, aerodynamic particle size distribution (APSD)/fine particle dose…	Please consider deleting tests for delivery rate and total delivery amount, aerodynamic particle size distribution/fine particle dose from the stability study recommendations.	There is no rationale for including these items in a stability study, as they are not regarded as stability indicating test items.
11	Page 11, Lines 236-237	除药品有效期外，建议根据研究结果在说明书中规定药品开启后（例如去除外包装）的使用有效期。 In addition to the shelf life of the drug, it is recommended to specify the validity period of the drug after it is opened (for example, the outer package is removed) based on the study results.	Consider revising to read, "...specify the validity period of the drug after it is opened (for example, the outer package is **opened or** removed)…"	An outer pouch or packaging may contain multiple dosage units and it is recommended to maintain as outer pack after opening to, for example, protect drug from light.