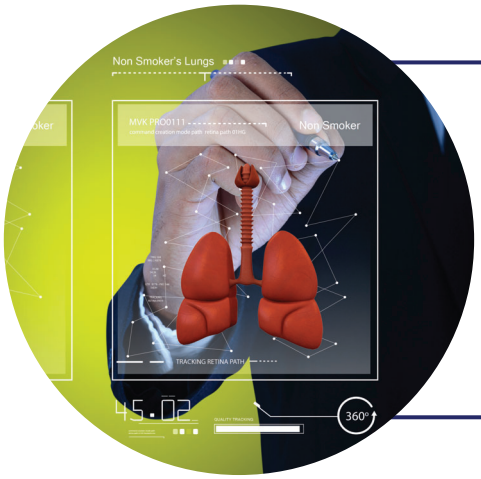
Objective Airway Challenge Testing in Clinical Research

The need to properly identify specific study populations has increased in recent years with the influx of specialized pharmacologic treatments for respiratory conditions. Direct and/or indirect airway challenge testing can offer insight into investigational drugs as objective measures to aid in phenotyping patient populations, assess response to therapies and evaluate bioequivalence.

Utilization of airway challenge testing in respiratory research is applicable beyond asthma studies. Additional disease states such as Allergic Rhinitis, Chronic Cough, and Idiopathic Pulmonary Fibrosis may potentially benefit from objective assessment of airway hyperresponsiveness and inflammation.[1-4,14]



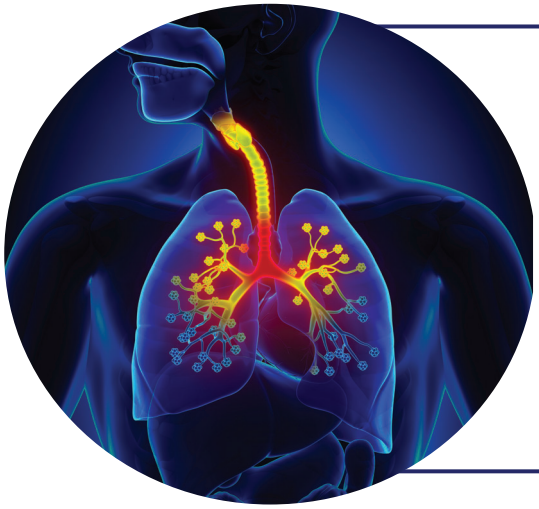
Inclusion / Exclusion Study Criteria

Correctly identifying patient populations in all phases of clinical trials is paramount to achieving successful study endpoints as well as reducing study costs associated with erroneous data. As established in the 2007 Expert Panel Report (EPR)[5], airway hyperresponsiveness and inflammation are two of the key characteristics of clinical asthma.

Since 1986 Methacholine Challenge Testing (MCT) has been utilized to directly assess airway hyperresponsiveness in clinical research studies to identify the target patient population. Indirect challenges additionally inform on both the pathogenesis of asthma and the role of anti-inflammatory agents in its treatment.[16]

Study of Pharmacodynamics / Bioequivalence

MCT has been an established marker for the assessment of study medications in compliance with FDA approval criteria. Current FDA draft guidance for generic albuterol products lists MCT as one of the methods to prove bioequivalence as a marker for the relative amount of beta agonist delivered to the airways.[8,9,13] Clinical pharmacologic dose-ranging studies can be assessed with MCT prior to and then following the test drug for bronchoprotective properties.[10, 11,12]



Development of Respiratory Treatments

In recent years, significant research has been realized in the identification of valid biomarkers for asthma.[6]

The term “precision medicine” has been proposed to define treatments targeted to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentations. Inherent in this definition is the goal of improving clinical outcomes for individual patients and minimizing unnecessary side effects for those less likely to have a response to a particular treatment.[7,15]

Airway challenge tests allow monitoring of disease activity and effectiveness of treatments and can provide a robust disease model in early phase clinical trials.[17-20]

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methapharm Respiratory

Provocholine®
[methacholine chloride]

INDICATION: Provocholine is indicated for the diagnosis of bronchial airway hyperreactivity in adults and pediatric patients 5 years of age and older who do not have clinically apparent asthma.

WARNING: Severe bronchoconstriction can result from Provocholine administration (including the lowest dose). The use of Provocholine is contraindicated in pediatric and adult patients with baseline FEV_1 < 60% predicted or adults with FEV_1 < 1.5 L. Because of the potential for severe bronchoconstriction, the use of Provocholine in patients with clinically apparent asthma or wheezing is not recommended [see Warnings and Precautions – Section 5.1 of the Prescribing Information].

Emergency equipment and medication should be immediately available to treat acute respiratory distress. If severe bronchoconstriction occurs, reverse immediately with a rapid-acting inhaled bronchodilator agent (-agonist) *[see Warnings and Precautions – Section 5.1 of the Prescribing Information].*

If baseline spirometry is not performed or is measured inaccurately, the initial FEV_1 may be underestimated. In this situation, decreases in FEV_1 may not be detected after administration of escalating Provocholine doses, which may result in administration of unnecessary higher doses and an increased risk for excessive bronchoconstriction *[see Warnings and Precautions – Section 5.1 of the Prescribing Information].*

aridol®

(mannitol inhalation powder)

INDICATION: ARIDOL is a sugar alcohol indicated for the assessment of bronchial hyperresponsiveness in adult and pediatric patients 6 years of age or older who do not have clinically apparent asthma.

WARNING: Mannitol, the active ingredient in ARIDOL, acts as a bronchoconstrictor and may cause severe bronchospasm. Bronchial challenge testing with ARIDOL is for diagnostic purposes only. Bronchial challenge testing with ARIDOL should only be conducted by trained professionals under the supervision of a physician familiar with all aspects of the bronchial challenge test and the management of acute bronchospasm. Medications (such as short-acting inhaled beta-agonist) and equipment to treat severe bronchospasm must be present in the testing area. If severe bronchospasm occurs it should be treated immediately by administration of a shortacting inhaled beta-agonist. Because of the potential for severe bronchoconstriction, the bronchial challenge testing with ARIDOL should not be performed in any patient with clinically apparent asthma or very low baseline pulmonary function tests (e.g., FEV_1 <1-1.5 liters or <70% of the predicted values) *[see Warnings and Precautions (5.1) of the Prescribing Information]*.

For complete prescribing information, please consult the Package Insert which is available for download at www.provocholine.com or www.aridolchallenge.com or on request by calling Methapharm Medical Information at 1-866-701-4636.

References

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