

Pulmonary Sampling Techniques & Sample Analysis



Bronchoalveolar lavage (BAL) and sputum sampling are two internationally accepted techniques often applied in pulmonary research to obtain airway samples for biomarker assessments and immunophenotyping.

- ▶ **Bronchoalveolar Lavage (BAL):** Extracts non-adherent cells and lung lining fluid from the mucosal surface in bronchoalveolar spaces, including lower respiratory tract
- ▶ **Sputum:** Mix of mucus and saliva discharge expectorated from the upper or lower respiratory system

BAL and sputum samples contain cellular and biochemical markers that can be helpful to monitor safety and early signals of efficacy for (inhaled) drug development. In addition, both techniques can provide insight into drug delivery to the lung. However, there are some key advantages and procedural limitations associated with each technique.

Sample Type	Advantages	Limitations
BAL	<ul style="list-style-type: none"> ✓ Provides a snapshot of cellular and humoral immune responses in the lung ✓ Drug PK assessment ✓ Assessment of biomarker expression ✓ Distal airway microbiological analysis ✓ Can be combined with biopsy to sample mucosal and submucosal tissues ✓ Can be combined with brushings to obtain samples of epithelial cells to <i>ex vivo</i> analysis 	<ul style="list-style-type: none"> ✗ Relatively invasive endoscopy procedure ✗ Resource intensive ✗ Specialist medical personnel required ✗ Max 2-3 samples per period per subject ✗ COPD patients could have low sample volume recovery as well as adverse events of coughing, bronchospasm, wheezing, and fever
Sputum	<ul style="list-style-type: none"> ✓ Noninvasive sample collection ✓ Relatively frequent sampling feasible ✓ Cellular composition assessment ✓ Fluid phase biomarker detection 	<ul style="list-style-type: none"> ✗ Sample integrity affected by viscosity and protease / ureases degradation ✗ Sample processing procedure critical

An Overview of the BAL Collection Procedure

- Performed by a Qualified Clinical Bronchoscopist
- Flexible bronchoscope guided into the targeted subsegment of the lung
- Room temperature sterile saline is instilled and gradually withdrawn 3-5 times
- Suction is applied to collect instillation fluid
- Collected BAL fluid can then be processed, stored and analyzed (e.g. for biomarkers, cell count or microbiome)
- Potential adverse events associated with the procedure include fever and hypoxemia, which can be managed with acetaminophen and oxygen administration as needed

Sputum Sample Collection at a Glance

- Fasted participants first rinse their mouth with water for 10-15 seconds to remove debris from the oral cavity to avoid food or beverage contamination
- Participants are instructed to breathe deeply, then expectorate the sputum sample for collection into a sterile container
- To obtain lower respiratory samples, a hypertonic sterile saline solution is inhaled via a nebulizer for approximately 5 minutes prior to expectoration of the sample
- Typically, a 1-2 mL sample is collected and immediately processed

Celerion's Pulmonary Sampling Experience & Expertise

Celerion's clinical pharmacology unit (CPU) in Belfast, UK, has extensive experience with bronchoscopies and BAL sampling as well as sputum collection. Clinical expertise is key for bronchoscopy and associated sample collections as well as for the adequate collection and processing of sputum samples.

- Dedicated bronchoalveolar procedure room ("bronchoscopy suite")
- Qualified Clinical Bronchoscopists with >10 years of experience
- Capacity to conduct BAL collections from multiple subjects on a single day expectoration of the sample
- On-site respiratory suite offering a full complement of respiratory assessments including lung clearance index (LCI), spirometry, whole body plethysmography and fractional exhaled nitric oxide (FeNO)
- Experience with challenge tests (LPS, methacholine, adenosine, tussigenic agents etc.)

Why Choose Celerion Belfast, UK?

At Celerion, we believe in working together to create a healthier world. From study start up to closeout, we are with you every step of the way. Our clinical research services are all-inclusive and on-site, so you can be sure that our signature speed, expertise, and strategic insights are applied at every stage of your study.

- ▶ **Clinical Facilities:** MHRA-accredited clinical facility includes 78 beds across 4 wards
- ▶ **Personalized Study Design:** tailored study designs and protocols to optimize clinical trials
- ▶ **Participant Recruitment:** vast database of healthy volunteers and access to exploratory patient cohorts within 4 respiratory disease areas: asthma, chronic cough, COPD and cystic fibrosis
- ▶ **Clinical Laboratory Testing:** on-site, fully dedicated MHRA-accredited Clinical Laboratory
- ▶ **Quality Management:** highly experienced team will help ensure your study is conducted ethically, reliably and in compliance with regulatory standards avoiding unnecessary delays
- ▶ **Data Management and Biometrics:** bridging the gap between medical practice and laboratory science to support informed go/no-go decisions earlier
- ▶ **Client Data Portal:** real-time data access via Celerion's proprietary client portal, Celexus®

Bioanalytical Assessments

BAL and sputum samples can be processed to investigate several aspects of lung health and impact of stimuli:

- Flow cytometry analysis of immune cell populations and activation within the lumen of the lung
- Transcriptomic analysis by next generation RNA-sequencing by batch/single cell RNAseq
- Biomarker assessments, for example chemokines (CXCL2, CCL2) and cytokines (IL-6, IFN γ , IL-10, TNF α)
- Cytospin preparations allow cell morphology assessment
- Pharmacokinetics (PK) and pharmacodynamic (PD) assessments
- Lung microbiome delineation
- Brushings can be utilized to derive primary cells for *ex vivo/in vitro* experimental models

RESOURCES:

[Respiratory Disease Expertise](#)

[Belfast Clinical Pharmacology Unit](#)

[Sputum Biomarker Bioanalysis](#)

[Supporting Inhaled Drug Development](#)