Analytical Technique Limitation Document

Document No.	ATL-2024-001
Date	2024-06-18
Prepared by	Analytical Development Team
Technique	High-Performance Liquid Chromatography (HPLC)

1. Objective

To document and communicate the limitations of the HPLC analytical technique as currently implemented in the laboratory to support method selection, troubleshooting, and interpretation of results.

2. Scope

This document applies to the use of HPLC for the determination of active pharmaceutical ingredients and their related substances in tablet formulations within the Analytical Chemistry Department.

3. Identified Limitations

1. **Detection Sensitivity:** Low UV-absorbing compounds may not be detected efficiently at standard wavelengths.
2. **Matrix Effects:** Co-eluting excipients can interfere with analyte quantification.
3. **Limited Volatility:** Non-volatile or thermally unstable compounds may not be suitable for the selected mobile phase.
4. **Solubility Constraints:** Poorly soluble analytes may require sample pre-treatment or alternative methods.
5. **Calibration Range:** The method's linearity is validated between 0.5â€“100 Âµg/mL only.

4. Potential Impact

- False negatives or inaccurate quantification if analytes are below the detection limit.
- Increased risk of out-of-specification results due to matrix interference.
- Restrictions in sample types that can be analyzed without additional processing.

5. Recommendations

- Consider alternative detection modes (e.g., MS or fluorescence) for low UV-absorbing compounds.
- Use matrix-matched calibration or sample clean-up for complex samples.
- Consult with analytical chemists to evaluate the suitability of method for new sample types.

Important Notes

- This document should be reviewed periodically and updated when changes in method or technique occur.
- The limitations noted here do not encompass all possible constraints; refer to method-specific documents when available.
- Disseminate this document to all personnel involved in analysis and data interpretation.
- Consult the relevant regulatory and validation guidelines for critical decision-making.