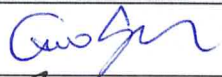

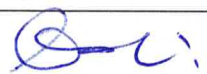

	<p>STANDARD OPERATING PROCEDURE</p> <p>Pipette Use, Maintenance and Calibration</p>	<p>Document: PRD004-1 Effective Date:20Mar2025 Status: Effective Page 1 of 5</p>
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Document Authorization:

	Name	Date	Signature
Owner	Sijin Guo	20Mar2025	
Operation Management	Baozhong Zhao	20Mar2025	
Quality Assurance	Xibo Li	20Mar2025	

Changes from previous version:

Section	Summary of Changes	Change Control Number
ALL	1. New document	


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	<p style="text-align: center;">STANDARD OPERATING PROCEDURE</p> <p style="text-align: center;">Pipette Use, Maintenance and Calibration</p>	<p>Document: PRD004-1 Effective Date: 20Mar2025 Status: Effective Page 2 of 5</p>
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1. PURPOSE

The purpose of this document is to describe the procedures for management of pipettes and apply to all staff using.

2. SCOPE

This document covers all aspects of pipette use including accuracy and precision measurements, maintenance and calibration.

3. INTERNAL REFERENCES

Document ID	Title

4. EXTERNAL REFERENCES

Document ID	Title
ICH Q7 (API)	Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients
ICH Q9	Quality Risk Management
ICH Q10	Pharmaceutical Quality System

5. RESPONSIBILITIES

Job Function and/or Department	Responsibility
Operational Employees	Employees who are trained in the use of pipettes are responsible for adhering to this procedure.
Operational Management	Responsible for ensuring pipette procedure is followed and collaborating with Quality Assurance to ensure the appropriate calibration schedule is adhered to.

6. DEFINITION

Term	Definition
Electronic Pipette	Battery or AC power supplied pipettes with volume programming capabilities for the transfer of liquids within an indicated volume range.
Manual Pipette	Dial, knob, or bulb-based volume adjustment for the transfer of liquids within an indicated volume range.
Multi-Channel Pipette	Electronic or manual pipettes with 8 – 16 fixed or expandable channels for the transfer of liquids within an indicated volume range
Pipette Aid	Electronic or manual aid for transfer of liquids with NO indicated volume range.
Pipette	Device used for the transfer of either variable (non-indicated volume ranges) or precise (indicated volume ranges) volume transfer of liquids.

7. PROCEDURE

7.1. General Instructions

- 7.1.1. Operators should ensure all pipettes with indicated volume ranges have an equipment asset ID label and current calibration label.
 - 7.1.1.1. Pipettes out of calibration or lacking the appropriate labeling shall be removed from service and brought to the attention of operational management.
 - 7.1.1.2. A pipette should never be used to measure a volume outside the range within which the pipette was calibrated. Even within the pipette's calibrated range, thought should be given to any potential inaccuracy of low volume pipetting, especially if the liquid has an increased viscosity, such as high-concentration or PEG/cholesterol containing oligonucleotides.

7.2. Operation

- 7.2.1. Pipette Selection. Some important factors to consider are:
 - 7.2.1.1. **The Volume of Liquid Required.** This may vary from microliters (µL) to liters. Choose a pipette that is accurate and precise at the volume to be measured. It is inappropriate to use a 1mL variable pipette to measure 10mL by repeat pipetting, for example, where a 10mL pipette is available.

- 7.2.1.2. **Accuracy Required.** This will also influence the choice of pipettes. Various operations may require different degrees of accuracy. For example, when working quantitatively it is especially important to be as accurate as possible. Alternatively, there are occasions when a measuring cylinder will be accurate enough. The potential consequences of any inaccuracies should always be considered when preparing solutions.
- 7.2.1.3. **The Number of Transfers.** If performing multiple transfers of the same volume, a multi-dispense pipette may be used. The multi-dispensing pipettes have various tip sizes available. The minimum volume recommended to be dispensed is 10% of the max tip volume. For example: 1250µL tip range: 12.5µL - 1250µL & 50mL tip volume range: 5mL to 50mL. They can be used at 1% of the maximum tip volume; however, the accuracy of the pipette will be affected.
- 7.2.1.4. **The Nature of the Liquid to be Measured.** It is not possible to handle all liquids in the same way and consideration must be given to such factors as safety and viscosity BEFORE pipetting solutions. Corrosive liquids such as acids, for example, are pipetted better with a positive displacement pipette method to avoid potential pipette damage. A positive displacement pipette method would also be better suited for any liquid which poses a contamination risk, although an alternative in this case would be the use of filtered tips. Additionally, some organic solvents are volatile and would be better suited for measurement using a positive displacement pipette method, as would liquids with increased viscosity, where the liquid can 'cling' to the tip wall and respond slowly during aspiration and dispensing. An alternative technique such as gravimetric measurement would be better suited where critical measurements are required for highly viscous liquids.

7.2.2. Setting Volume

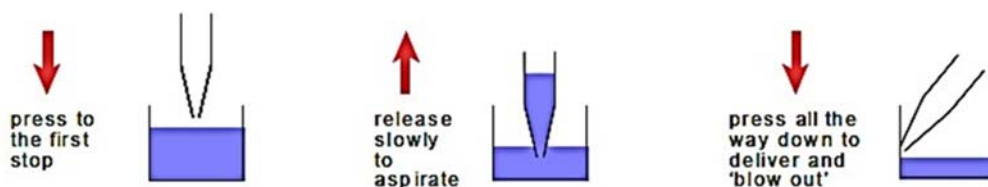
- 7.2.2.1. If the pipette is equipped with a locking mechanism, release the lock before adjusting the volume setting.
- 7.2.2.2. Turn the dial slowly when adjusting to a lower volume setting, making sure not to overshoot the mark.
- 7.2.2.3. When adjusting to a higher volume setting, pass the required value by approximately 1/3 of a turn and then slowly decrease the volume (rack down) until it reaches the set point. Make sure not to overshoot the mark.

7.2.3. Pipetting Modes

- 7.2.3.1. Air Displacement (Forward Pipetting; refer to Figure 1): The most common method of pipetting aqueous liquids.

- 7.2.3.1.1. Press to the first stop.
- 7.2.3.1.2. Release slowly to aspirate.
- 7.2.3.1.3. Press all the way down to the second stop to deliver liquid and "blow out."

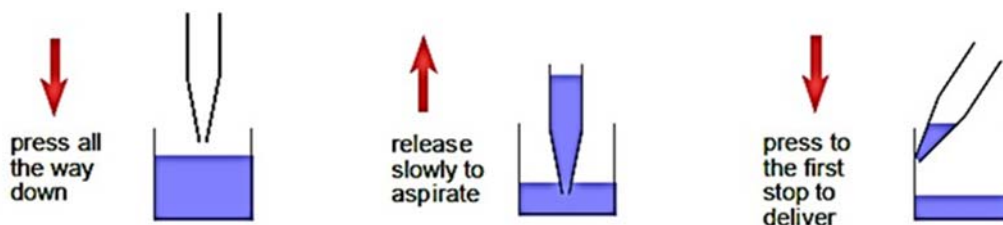
FIGURE 1: AIR DISPLACEMENT – FORWARD PIPETTING



- 7.2.3.2. Air Displacement (Reverse Pipetting; refer to Figure 2): Useful for biological or foaming liquids or when repeat dispensing the same liquid.

- 7.2.3.2.1. Press all the way down to the second stop.
- 7.2.3.2.2. Release slowly to aspirate.
- 7.2.3.2.3. Press to the first stop to deliver.

FIGURE 2: AIR DISPLACEMENT – REVERSE PIPETTING



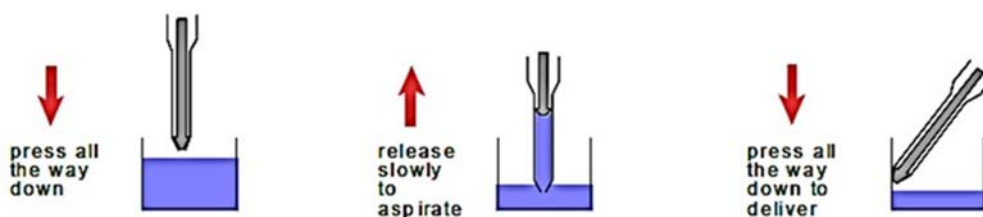
7.2.3.3. Positive Displacement (refer to Figure 3): Useful for small volumes of liquid, particularly organic solvents or high viscosity, biological or foaming liquids.

7.2.3.3.1. Press all the way down.

7.2.3.3.2. Release slowly to aspirate.

7.2.3.3.3. Press all the way down to deliver.

FIGURE 3: POSITIVE DISPLACEMENT



7.2.4. Pipetting Execution

7.2.4.1. Attach the correct tip to the pipette, ensuring an airtight seal.

7.2.4.2. Condition the tip with sample three times by slowly aspirating and dispensing.

7.2.4.3. Slowly aspirate sample liquid while holding the pipette in a near vertical position. Avoid inserting the tip deeply into the sample liquid as it can impact the amount of material that is transferred.



When aspirating liquid, take care not to aspirate air into the tip as it can significantly impact results. If necessary, dispose of the soiled tip and use a fresh tip.

7.2.4.4. Wipe the pipette tip against the inside of the vessel to remove any excess liquid.

7.2.4.5. Place the pipette tip at an angle (10 to 45 degree) against the inside surface of the receiving vessel and dispense sample liquid.

7.2.4.6. Keeping the plunger pressed, remove the pipette by drawing the tip along the inside surface of the receiving vessel.

7.2.4.7. Eject the tip into an appropriate waste container.



Always change the pipette tip before aspirating a different sample liquid, after changing the volume setting, or if pipetting from a primary container.

7.2.4.8. Dispensing with a Multichannel Pipette

7.2.4.9. It may be appropriate to use a multichannel pipette for some laboratory operations, such as to dispense a liquid into several wells simultaneously. Using a multichannel saves time and provides efficiency, which are important factors when processing large numbers of samples.

7.2.4.10. Always check that all tips are properly seated before pipetting using a multichannel pipette.

7.2.4.11. After aspirating, visually check that each tip contains the same relative amount of liquid and that no bubbles are present. If either scenario exists, dispense the liquid back into the original solution and perform a fresh aspiration.

7.3. Care

- 7.3.1. Do not leave the pipette on its side with any trace of liquid in the tip (i.e., used) as the liquid may seep back into the pipette body.
- 7.3.2. Store pipettes on a pipette stand when not in use. Do not leave a pipette on the work surface when it is not in use. The pipette may come into contact with biological liquids, organic solvents, or corrosive liquids that may damage/contaminate a pipette.
- 7.3.3. When pipetting from deep containers (such as tall, narrow sample tubes), it is possible for reagent or matrix to come in contact with the outside of the pipette barrel. If this happens, the outside of the pipette barrel must be cleaned immediately to avoid cross contamination (IPA wipes or a similar solution is sufficient).
- 7.3.4. If a pipette has been dropped, it is not dispensing the correct volume or not dispensing at all or has been contaminated (especially if the pipette has no filter), remove the pipette from use until it can be cleaned, repaired, and calibrated. Document the request on FM-208964 Pipette Repair Request form.
- 7.3.5. Decontaminate the exterior surface with a 70% IPA pre-moistened wipe as needed and prior to being sent for repair and/or calibration.

7.4. Maintenance and Calibration

- 7.4.1. Calibration may be performed in house or mailed to an external vendor.