# Step 12 — Complete Case Study: Documentation Requirements in Dissolution Method Development

This case study provides a comprehensive example of documentation required during dissolution method development and validation. The study is based on a real-world pharmaceutical product and is structured to reflect regulatory expectations from ICH, FDA, EMA, and USP.

## Case Study: Immediate-Release Paracetamol 500 mg Tablets

\*\*Product Name:\*\* Paracetamol (Acetaminophen) 500 mg tablets

\*\*Therapeutic Category:\*\* Analgesic and Antipyretic

\*\*Objective:\*\* To develop and validate a robust dissolution method for quality control and stability testing.

## Method Parameters

• \*\*Apparatus:\*\* USP Apparatus II (Paddle)

• \*\*Medium:\*\* 900 mL of 0.1 N HCl (pH 1.2) to simulate gastric fluid without enzymes.

• \*\*Temperature:\*\* 37 ± 0.5 °C

• \*\*Agitation Speed:\*\* 50 rpm

• \*\*Sampling Times:\*\* 5, 10, 15, 30, and 45 minutes

• \*\*Detection Method:\*\* UV-Vis spectrophotometry at 243 nm

## Development Phase Documentation

1. \*\*Justification of Medium Selection:\*\* Paracetamol exhibits good solubility in acidic medium. 0.1 N HCl ensures sink conditions are achieved throughout the test (at least 3x the highest dose solubility).

2. \*\*Rationale for Apparatus Selection:\*\* USP Apparatus II (paddle) is standard for immediate-release oral solid dosage forms and provides reproducible hydrodynamics.

3. \*\*Optimization Trials:\*\* Initial trials with different agitation speeds (50, 75, 100 rpm) showed that 50 rpm provided discriminative yet consistent dissolution profiles. Higher speeds caused rapid tablet disintegration, masking formulation differences.

4. \*\*Risk Assessment (QbD):\*\* Identified critical variables included agitation speed, medium composition, and deaeration of the medium. Control strategies were defined accordingly.

## Validation Phase Documentation

\*\*1. Accuracy:\*\* Recovery studies were conducted by spiking paracetamol standard into dissolution medium. Recoveries were between 98.5% and 101.2%, meeting the acceptance criteria (95–105%).

\*\*2. Precision:\*\* Repeatability (%RSD of 6 tablets) was 1.1%, and intermediate precision (%RSD across two analysts and instruments) was 1.8%.

\*\*3. Specificity:\*\* Placebo tablets without API were tested and showed no interference at 243 nm.

\*\*4. Robustness:\*\* Small variations in rpm (±2) and temperature (±0.5 °C) showed no significant impact on dissolution profiles (%RSD < 2%).

\*\*5. Stability of Sample Solution:\*\* Drug in dissolution medium was stable for 24 hours at room temperature (deviation < 2%).

## Dissolution Profile Results

Average % Drug Release (n=6 tablets):

• 5 min: 45%
• 10 min: 72%
• 15 min: 88%
• 30 min: 98%
• 45 min: 100%

Acceptance Criteria: Not less than (NLT) 80% of label claim dissolved within 30 minutes. The developed method meets this requirement.

## Reporting and Documentation

The final report included the following sections:

• Raw data including UV absorbance readings at each sampling point.

• Tabulated dissolution results with calculated % drug release.

• Graphical dissolution profiles (% release vs. time).

• Statistical treatment including mean, SD, %RSD, and f2 similarity factor if comparative studies are performed.

• Justification of method parameters with supporting scientific rationale.

• Validation summary with results for accuracy, precision, specificity, robustness, and stability.

• Approval signatures from Analyst, Reviewer, and QA as per GMP documentation requirements.