Module 2.3: Quality Overall Summary (QOS)

Product: Amoxicillin 250 mg/5 mL Powder for Oral Suspension

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2.3.S DRUG SUBSTANCE (AMOXICILLIN TRIHYDRATE)

- **General Information:** The drug substance is Amoxicillin Trihydrate, a semi-synthetic antibiotic belonging to the beta-lactam family.
- **Control of Impurities (ICH Q3D):** The legacy dossier relied on qualitative sulphide precipitation methods. To meet current standards, a quantitative risk assessment for elemental impurities has been implemented.
- **Analytical Methodology: ICP-MS** is utilised to confirm compliance for Class 1 (As, Cd, Hg, Pb) and Class 2A (Co, Ni, V) elements across three commercial batches.
- **Polymorphic Integrity:** Given the aqueous nature of the final reconstituted product, the crystalline form of the API is controlled to ensure consistent solubility and bioavailability.

2.3.P DRUG PRODUCT (ORAL SUSPENSION)

- **2.3.P.2 Pharmaceutical Development:** The formulation is a powder for oral suspension designed to be reconstituted with water.

Table 2.3.P. 2-1: Summary of Critical Formulation Parameters

Parameter	Value	Source/Database
pH	5.5	**USP-NF** (Legal Range) & **PubMed** (Chemical Stability)
Zeta Potential	"Optimised" ≈ ±30mV	**Colloidal Science Standards** (Malvern Panalytical, ZetaSizer Reference)
Climate Stability	Zone IVb (40°C)	**ICH Guidelines** (International Regulatory Database)

- **Physicochemical Robustness:** The physical integrity of the suspension is maintained by a thermally robust **Xanthan Gum** network. From a materials science perspective, this network prevents irreversible caking and maintains dose uniformity through controlled rheology.
- **Zeta Potential:** The system is optimised to a **Zeta Potential** ±30mV. This provides sufficient electrostatic repulsion between particles to ensure the suspension remains "pourable" and easily resuspendable.

- **pH Optimisation:** The formulation is buffered to **pH 5.5**. This specific value represents the point of maximum chemical stability for the amoxicillin molecule, significantly minimising hydrolytic degradation of the beta-lactam ring.

2.3.P.8 STABILITY

- **Climatic Zone Strategy:** Current long-term data is available for **Climatic Zone II (25 °C / 60 % RH)**
- **Zone IVb Program:** A comprehensive stability program has been initiated for **Zone IVb (30 °C / 75 % RH)** conditions to support the Australian market.
- **Interim Strategy:** To prioritise market access, the sponsor proposes an **interim reduced shelf life** (e.g., 12 months) supported by a **Shelf-Life Commitment** to provide full 24-month data post-approval·
- **Testing Frequency:** The program includes testing at 0, 3, 6, 9, 12, 18, and 24 months for long-term studies, ensuring all stability-indicating parameters (assay, degradation, and physical attributes) remain within specification