UNIT 3

COURSE NAME: QCSH

TOPIC: ICH GUIDELINES

Case Study 1: Ginkgo biloba Dry Extract - Application of ICH Q3C for Residual Solvents and PDE Calculation

Overview: This case study focuses on the toxicological evaluation of Ginkgo biloba L. dry extract for oral use, determining the Permitted Daily Exposure (PDE) to assess cross-contamination risks in multi-purpose manufacturing lines. The extract is commonly used in herbal medicines for cognitive enhancement and circulatory support.

Compliance with ICH Guidelines:

- **Quality Control Aspects**: Following ICH Q3C (R8) for impurities (residual solvents), the PDE was calculated using preclinical data from acute (OECD 423) and repeated-dose (OECD 407) toxicity studies in mice. NOAEL was established at 120 mg/kg/day, resulting in a PDE of 0.1 mg/day after applying safety factors (F1=12 for interspecies, F2=10 for variability, F3=10 for study duration, F4=5 for potential fetal toxicity, F5=1).
- **Challenges and Implementation**: Studies showed low toxicity with minor effects like altered weight gain and hematological changes at higher doses. The PDE was integrated into cleaning validation, yielding a maximum residual concentration (MRC) of 250 µg/mL, exceeding the 10 ppm limit, confirming safe manufacturing without process adjustments.
- **Outcome**: This application ensures quality control by minimizing residual risks, aligning with ANVISA RDC 658/2022 for herbal safety. No adverse effects were noted below PDE, supporting its use in pharmaceuticals.

Case Study 2: St. John's Wort Extract and Capsules - ICH Q1 Stability Testing

Overview: St. John's wort (Hypericum perforatum L.) is a popular herbal remedy for mild depression. This study evaluated the stability of a commercial dried extract and its capsule formulations under ICH-recommended conditions to ensure product quality over time.

Compliance with ICH Guidelines:

- **Quality Control Aspects**: Thermal and photostability were tested per ICH Q1A (R2), focusing on key markers (flavonols, hyperforins, hypericins). Photostability revealed high photosensitivity, partially mitigated by capsule pigments and amber packaging. Thermal testing showed t90 <4 months for hyperforins and hypericins, even with stabilizers like ascorbic acid.
- **Challenges and Implementation**: Direct ICH application highlighted inadequacies for herbals due to rapid degradation; adapted storage (e.g., light-protected, cool conditions) was recommended. Constituents degraded variably based on formulation.
- **Outcome**: The study underscored the need for herbal-specific adaptations to ICH Q1, improving quality control by specifying protective measures. This led to better shelf-life predictions and reduced post-market degradation issues.

Case Study 3: Valerian Root - ICH Q2 Analytical Method Validation for Valerenic Acids

Overview: Valerian root (Valeriana officinalis) is used for sleep and anxiety relief. This case examines the development and validation of a micellar liquid chromatography (MLC) method for separating sesquiterpenic acids (valerenic, hydroxyvalerenic, acetoxyvalerenic) in extracts.

Compliance with ICH Guidelines:

- **Quality Control Aspects**: The method was validated per ICH Q2 (R1) for specificity, linearity, precision, accuracy, LOD/LOQ, and robustness. Selectivity separated isomers; linearity ranged 0.5–50 µg/mL (r^2 >0.999); precision RSD <2%; accuracy 98–102%; LOD 0.1–0.3 µg/mL.
- **Challenges and Implementation**: Herbal matrix complexity required micellar mobile phases (SDS-based) for eco-friendly separation without organic solvents. Robustness tested pH, surfactant concentration, and flow rate variations.

- **Outcome**: Validated method enabled consistent quantification, enhancing quality control for valerian products. It supported batch release and stability monitoring, reducing variability in commercial formulations.

Case Study 4: Echinacea Species - ICH Q2-Inspired HPLC Validation for Phenolic Compounds

Overview: Echinacea purpurea and related species are immune-boosting herbals. This study extended an HPLC-UV method validation for quantifying phenolics (caftaric acid, chlorogenic acid, cynarin, echinacoside, cichoric acid) in raw materials, extracts, and tinctures.

Compliance with ICH Guidelines:

- **Quality Control Aspects**: Aligned with ICH Q2 principles (though AOAC-referenced), validation covered selectivity (Rs >1.5), linearity (r^2 ≥99.5%), precision (RSD 1.04–5.65%), accuracy (90–114% recovery), and stability (no degradation over 6 days). MDL 0.015–0.070 µg/mL; LOQ 10x MDL.
- **Challenges and Implementation**: Addressed interferents (e.g., goldenseal, vitamins) with no peak overlap. Stability confirmed during extraction and analysis, preventing cichoric acid loss.
- **Outcome**: The method ensured reliable quality control across matrices, facilitating consistent potency in supplements. It minimized errors in labeling and supported regulatory compliance for herbal efficacy claims.

Case Study 5: Ginseng Extracts - ICH Q3C for Residual Solvents Control

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Overview: Korean red ginseng (Panax ginseng) extracts are used for energy and vitality. This study analyzed residual solvents under varying extraction conditions to ensure safety and quality.

Compliance with ICH Guidelines:

- **Quality Control Aspects**: Residual solvents (e.g., ethanol, acetone) were quantified per ICH Q3C (R8) limits (Class 2/3). Extractions at different temperatures/pressures showed ethanol <5000 ppm, acetone <50 ppm in optimized conditions. Mineral contents (e.g., As <0.1 ppm) were also monitored.
- **Challenges and Implementation**: High-temperature extractions increased solvent residues; optimized parameters (e.g., 70% ethanol, 80°C) minimized them below PDE thresholds. GC-headspace analysis validated for accuracy.
- **Outcome**: Compliance reduced health risks from volatiles, improving ginseng product safety. This approach standardized manufacturing, preventing recalls and enhancing global market access for herbal supplements.