**Mock Document #6: Regulatory Briefing Book**

**Title:** *FDA Pre-IND Briefing Package – Dapagliflozin for Heart Failure with Reduced Ejection Fraction (HFrEF)*  
**Submission Type:** Pre-IND Meeting Package  
**Sponsor:** [Fictional Pharma Inc.]  
**Date Submitted:** [Fictional] June 2023  
**Meeting Date:** July 2023  
**Region:** FDA – Division of Cardiology and Nephrology

**1. Cover Letter Summary**

This briefing document supports a pre-IND interaction to align on the clinical development strategy for dapagliflozin in HFrEF. The sponsor seeks FDA feedback on trial design, population, endpoint selection, and safety monitoring prior to Phase 3 initiation.

**2. Table of Contents**

1. Product Background
2. Clinical Development Plan Summary
3. Phase 3 Protocol Synopsis
4. Benefit-Risk Rationale
5. Proposed Statistical Methods
6. Regulatory Strategy and Milestones
7. Specific FDA Questions

**3. Product Background**

Dapagliflozin is a selective SGLT2 inhibitor with a well-characterized safety profile in over 15,000 patients across diabetes and renal studies. Its emerging role in heart failure is supported by DAPA-HF and DECLARE-TIMI data.

**4. Clinical Development Summary**

* **Target Indication:** Reduce HF hospitalization and CV mortality in HFrEF
* **Phase 3 Plan:** Global event-driven RCT, n=4500, ITT primary analysis
* **Population:** NYHA Class II–IV, LVEF ≤40%, eGFR ≥30, both diabetic and non-diabetic

**5. Key Protocol Elements**

* **Primary Endpoint:** Time to first CV death or HF hospitalization
* **Secondary:** NT-proBNP change, QoL (KCCQ), renal function
* **Randomization:** 1:1, stratified by diabetes status and region
* **Duration:** Event-driven; expected 24-month accrual + follow-up

**6. Benefit-Risk Assessment**

* **Expected Benefit:** Reduce morbidity in residual risk HF population
* **Known Risks:** Genitourinary infections, hypotension, DKA
* **Mitigation:** Routine labs, stopping rules, DSMB oversight

**7. Proposed Statistical Plan**

* Cox model with pre-specified covariates
* Hierarchical testing for secondary endpoints
* Interim analysis after 50% of events with non-binding futility boundary

**8. Regulatory Questions Submitted**

| **Question** | **Topic** |
| --- | --- |
| 1 | Is the proposed primary endpoint acceptable for label claim? |
| 2 | Does the agency agree with enrolling both diabetic and non-diabetic populations? |
| 3 | Are exclusion criteria and monitoring plans adequate for renal safety? |
| 4 | Is the proposed group sequential design acceptable? |

**9. Appendices**

* Protocol synopsis v0.3
* IB summary table
* FDA meeting request letter
* Draft eCRF templates

**Supports CSP Prompts Like:**

* #HC\_AI\_Benefit\_Risk\_Assessment#
* #HC\_AI\_Study\_Rationale#
* #HC\_AI\_Statistical\_Methods#
* #HC\_AI\_Endpoints#
* #HC\_AI\_Regulatory\_Justification# *(if added)*