**Mock Document #3: Statistical Analysis Plan (SAP)**

**Title:** *Statistical Analysis Plan for Study HF-203: Dapagliflozin in HFrEF*  
**Protocol Number:** HF-203  
**Version:** 1.1  
**Prepared by:** Global Biostatistics  
**Date:** [Fictional] December 2023

**1. Study Overview**

* **Design:** Randomized, double-blind, placebo-controlled, parallel-group, event-driven
* **Objective:** To assess the effect of dapagliflozin vs. placebo on cardiovascular outcomes in patients with HFrEF
* **Sample Size:** ~4,500 participants
* **Follow-up Period:** Minimum 12 months or until event target reached

**2. Analysis Populations**

| **Population** | **Definition** | **Purpose** |
| --- | --- | --- |
| **Intent-to-Treat (ITT)** | All randomized participants | Primary efficacy analysis |
| **Per-Protocol (PP)** | ITT population minus major protocol violators | Sensitivity analyses |
| **Safety Population** | All who received ≥1 dose | Safety endpoints |

**3. Primary Endpoint**

* **Endpoint:** Time to first occurrence of CV death or hospitalization for heart failure
* **Analysis Method:** Cox proportional hazards model
* **Covariates:** Baseline eGFR, diabetes status, region
* **Alpha Level:** 0.05 (2-sided)
* **Interim Analysis:** Group sequential design with O'Brien-Fleming boundaries

**4. Secondary Endpoints**

* Change from baseline in:
  + **NT-proBNP** at Week 12
  + **KCCQ clinical summary score**
  + **eGFR slope**
* **Statistical Tests:** ANCOVA, MMRM
* **Adjustment:** Hierarchical testing to control type I error

**5. Missing Data Handling**

* For time-to-event: Participants lost to follow-up will be censored at last known alive
* For continuous variables: Multiple imputation under MAR (missing at random) assumption
* Sensitivity analyses using tipping point and pattern mixture models

**6. Subgroup Analyses**

Prespecified subgroups include:

* Diabetes vs. non-diabetes
* Baseline eGFR <60 vs. ≥60
* Sex, region, age (<65, ≥65)  
  Interaction terms will be explored; results considered exploratory

**7. Software and Validation**

* **Software Used:** SAS 9.4 and R 4.2
* Validation will follow internal SOPs including double programming and blinded review

**8. Tables, Listings, Figures (TLFs)**

Templates will be finalized prior to database lock and include:

* Kaplan-Meier survival curves
* Forest plots for subgroups
* Longitudinal plots for biomarkers

**9. References**

* ICH E9: Statistical Principles for Clinical Trials
* DAPA-HF Trial SAP Template
* Internal SOP-BIO-101, SOP-BIO-210

**Supports CSP Prompts Like:**

* #HC\_AI\_Statistical\_Methods#
* #HC\_AI\_Analysis\_Population#
* #HC\_AI\_Research\_Hypothesis#