Aurora Rulebook

0. Scope & Canonical References

Jurisdiction for v1: India (global-ready later, but India is source of truth).

The system **must align with and map to** (no guessing):

- **ICMR National Ethical Guidelines for Biomedical & Health Research Involving Human Participants, 2017 + 2024 Addendum**.
- **ICMR Ethical Guidelines for Application of AI in Biomedical Research & Healthcare, 2023** (for how *our* AI behaves).
- **CTRI Dataset & Description (1 Aug 2021)** for field definitions and registration mapping.
- **ICH E6(R3) Final Guideline 2025** + supporting materials for GCP, electronic systems, audit trails.
- **Indian GCP / NDCT 2019 framework** concepts (safety reporting, consent, responsibilities), consistent with above.

Where there is conflict, **local regulation + ICMR + CTRI** take precedence for Indian deployments.

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1. Core Principles

1. **Purpose:**
   Turn a clinician's idea into a coherent, standards-aligned **baseline draft package + live study workspace**, not a final legal or regulatory approval.
2. **Clinician-first:**
   Start in natural clinical language; no stats jargon required to begin.
3. **Baseline, not black-box:**
   System outputs strong drafts; PI & IEC remain fully responsible.
4. **Constrained, not anything-goes:**
   Only approved study patterns and formulae. Anything else is explicitly "out of scope" or "needs expert review".
5. **Transparent & auditable:**
   Every decision traceable: who/what/when/why.
6. **Ethics & safety baked-in:**
   Enforce presence of core ethical elements. Block or flag unsafe designs.
7. **Humans in the loop:**
   Smooth handoff to statisticians, IECs, research offices — we assist, not replace.

2. Supported Study Designs (Design Rulebook)

v1 Allowed Designs (whitelist)

AI may only default to these, unless user explicitly chooses “advanced”:

1. **Prospective Cohort**
2. **Retrospective Cohort**
3. **Cross-sectional Study**
4. **Case-control Study**
5. **Simple Registry / Disease or Quality Registry**
6. **Simple 2-arm Parallel-group RCT** (superiority/equivalence/non-inferiority with clear constraints)
7. **Single-arm Trial**
8. **Diagnostic Accuracy Study**

Advanced modes (behind explicit toggle & extra checks):

- Cluster RCT
- Non-inferiority / equivalence RCT
- Pre–post / quasi-experimental
- Adaptive designs

If the AI cannot map an idea to a valid template, it must:

- Clearly say: **“Not supported by current templates.”**
- Suggest nearest valid design or recommend human expert input.
- Not force-fit or hallucinate.

For each design, the system must hold a template definition including:

- PICO
- Typical objectives
- Allowed primary outcomes
- Required schedule & follow-up (if applicable)
- Minimal core variables

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3. Product Outputs (What the System Must Produce)

For a supported design, v1 must be able to generate, in a single flow:

1. **Structured Study Spec (JSON)**

2. **Draft Protocol** (ICMR-style headings)
3. **Sample Size Justification** (deterministic, formula-based)
4. **Draft Statistical Analysis Plan (SAP)**
5. **CRF / eCRF Schemas & printable CRFs**
6. **Draft Participant Information Sheet (PIS) + Informed Consent Form (ICF)**
7. **IEC Cover Letter / Summary Note**
8. **Ethics & Regulatory Checklist** (ICMR & Indian GCP aligned)
9. **CTRI Mapping Sheet** (aligned to CTRI Dataset fields)
10. **Live Study Workspace**
    - Configured eCRFs
    - Role-based access
    - Full audit trail

All docs must be clearly watermarked:

> "AI-generated draft based on user inputs. Requires review and approval by Principal Investigator and Ethics Committee. Not a legal or regulatory approval."

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4. Tech & Architecture Rulebook

1. **Architecture:** Modular, API-first, multi-tenant.
2. **Core services:**
    - `auth-service` – users, orgs, roles.
    - `study-service` – study specs & versions.
    - `template-service` – designs, CRFs, text blocks.
    - `orchestrator-service` – all LLM/stat pipeline calls.
    - `doc-service` – DOCX/PDF generation.
    - `crf-service` – schema + runtime for eCRFs.
    - `audit-service` – append-only logs.
3. **Data:**
    - Postgres (or equivalent) for entities.
    - S3-compatible storage for generated docs.
    - Redis/queue for async tasks.
4. **LLM use:**
    - Frontend never calls LLM directly.
    - All calls go via `orchestrator-service`.
    - Responses must conform to strict JSON schemas.
    - If invalid / ambiguous → retry or escalate; never silently fudge.
5. **Auditability (E6(R3)-style):**

- Every important action = `AuditEvent`:
  - who, when, what changed, previous value, reason (for data edits).
- Secure, computer-generated, timestamped, immutable.

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5. Backend & Data Model Rules

Required entities:

- `User`, `Organization`
- `Study`
- `StudyVersion`
- `Template` (designs, SAP snippets, PIS/ICF blocks, CRFs)
- `Document` (type, version, link)
- `CRFSchema`
- `ParticipantRecord`
- `AuditEvent`

Versioning:

- Any major change creates a new `StudyVersion`.
- Each `StudyVersion` ties together:
  - Design
  - Sample size assumptions
  - SAP
  - CRFs
  - Generated docs
  - Checklists

No hard delete for study definitions or documents, only supersede.

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6. Frontend / UX Rulebook

6.1 Flow

Top-level wizard (fixed):

1. **Idea**
2. **Design**
3. **Sample Size**
4. **Documents**

5. **Review & Compliance**
6. **Launch Workspace**

6.2 Clinician Comfort Zone

- Start with natural prompts:
  - “What do you want to study?”
  - “In whom?”
  - “What outcome matters?”
  - “Over what time frame?”
  - “What’s realistically feasible (N, follow-up)?”
- Show “Study Story”:
  - Plain-language summary of PICO & design.
  - User confirms/edits before moving on.

No one is forced to write “Methods” from scratch.

6.3 Safety UX

- Red / amber flags for:
  - Unsupported design
  - Missing critical elements
  - Ethical/safety concerns
- **Launch** button disabled until critical checklist items are resolved/acknowledged.

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7. Templates Rulebook

7.1 Protocol Template (ICMR / GCP-aligned)

Mandatory top-level headings (not deletable):

1. Title, identifiers
2. Background & rationale
3. Objectives (primary, secondary)
4. Study design (explicit classification)
5. Study setting & population
6. Inclusion / exclusion criteria
7. Intervention / exposure (if applicable)
8. Outcome measures (definitions + timepoints)
9. Sample size & justification
10. Study procedures & schedule of visits

11. Data collection & management
12. Statistical analysis plan (summary)
13. Safety reporting
14. Confidentiality & data protection
15. Ethical considerations
16. Compensation & injury management (PI to fill specifics per policy)
17. Dissemination plan

AI fills with structured content + template text; human edits allowed.

7.2 SAP Template

Must include:

- Study overview
- Endpoint list + definitions
- Analysis populations (e.g. ITT, PP, safety)
- Primary endpoint analysis:
  - test/model, covariates if any
- Secondary endpoints:
  - descriptive / exploratory
- Handling of:
  - missing data (default: complete case + sensitivity text)
  - protocol deviations (pre-spec categories)
- Interim analysis (if any; default none)
- Software statement

Linked directly to protocol and sample size parameters.

7.3 eCRF Templates

For each study, AI derives eCRFs from spec:

- Screening & eligibility (incl. consent)
- Baseline demographics & clinical data
- Intervention/exposure log
- Visit forms → auto-built from schedule
- Outcome forms aligned exactly to endpoints
- Adverse event / SAE forms:
  - fields per Indian GCP & ICH (onset, severity, causality, outcome)
- Protocol deviations
- Study completion / withdrawal

All edits create audit trail entries.

7.4 PIS/ICF Templates (ICMR-based)

Must (at minimum) include elements drawn from ICMR guidelines:

- Statement that this is research
- Purpose & procedures in simple language
- Duration & number of contacts
- Risks/discomforts
- Expected benefits or explicit “no direct benefit”
- Alternatives (where applicable)
- Confidentiality + data storage & usage
- Voluntariness & right to withdraw without penalty
- Compensation & free medical care for study-related injury (text left configurable)
- Contacts for PI & EC
- Future use of samples/data (yes/no options)
- Signature/Thumb impression blocks; witness/LAR/assent as applicable

AI may localize wording but must not omit any required element.

7.5 IEC Submission Pack

Auto-compiled:

- Protocol
- SAP
- PIS/ICF (all relevant languages/versions)
- CRF examples
- Cover letter (study overview)
- Risk-benefit summary
- Ethics & compliance checklist

Marked as “Draft for IEC review”.

7.6 CTRI Mapping Template

Built to mirror CTRI Dataset fields:

Includes:

- Titles (public/scientific)
- Study type, design, phase
- Health condition(s)
- Interventions (generic names)

- Inclusion/exclusion criteria
- Outcomes (names + metrics + timepoints)
- Sample size (per arm & total)
- Randomization, allocation concealment, blinding
- Sites & investigators (to be filled)
- Ethics committee details & approval status (to be filled)
- DCGI / other regulatory approvals (to be confirmed by user)

System fills what it can from spec; everything else flagged clearly as **"PI to complete; AI cannot infer."**

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8. Stats & SAP Formula Rulebook

All calculations are deterministic in code; LLMs cannot alter numeric results.

Supported v1 formulas (examples, not exhaustive):

1. **Two proportions (parallel groups)**
   Standard normal approximation or exact methods, using:
   - α (default 0.05), power (default 80–90%), p1, p2, allocation ratio.
2. **Two means (parallel groups)**
   Using SD (or pooled), Δ (difference), α, power.
3. **Single proportion (precision)**
   $n = Z^2 \times p(1-p) / d^2$.
4. **Time-to-event (log-rank)**
   Based on expected event rates, HR, accrual/follow-up assumptions.
5. **Diagnostic accuracy**
   - Sensitivity or specificity: $n = Z^2 \times Se(1-Se)/d^2$, similarly for Sp.
6. **Cluster adjustment (if cluster design chosen)**
   - Design effect: $DE = 1 + (m-1)*ICC$.
7. **Dropout adjustment**
   - $n_{adj} = n / (1 - dropout\_rate)$.

Rules:

- Always display:
  - Chosen formula
  - Parameters (α, power, assumed rates/effects)
- Provide:
  - Scenario table (e.g. low/median/high event rates)
- For primary endpoint only by default.

- Multiplicity for co-primaries: simple Bonferroni or gatekeeping only when explicitly requested.

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9. AI Autonomy Rulebook

AI MAY:

- Parse free-text ideas into structured PICO.
- Suggest a design from allowed list.
- Generate:
  - Draft protocol text
  - Draft SAP text (based on chosen methods)
  - CRF schemas
  - PIS/ICF drafts with required elements
  - IEC checklist
  - CTRI mapping (partial)
- Enforce cross-document consistency:
  - Same primary outcome everywhere
  - Same N everywhere
  - Same design labels everywhere

AI MAY NOT:

- Claim or imply:
  - IEC approval
  - CTRI registration
  - DCGI / regulatory clearance
- Invent:
  - Ethics approval numbers
  - Sponsor / funder
  - Insurance terms
- Introduce:
  - Study designs outside whitelist without explicit user action
  - Stats methods not in the approved catalog
- Remove:
  - Mandatory ethics / consent / safety sections.

When in doubt:

- AI must **stop and surface a clear question or warning**, not guess.

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10. Guardrails & Safety

1. **Unsupported / weird designs**
   - If no template match → “Not supported in v1”; export idea summary for expert.
2. **Ethically risky content**
   - High-risk interventions, vulnerable groups, no consent, data misuse:
     - Show blocking alert:

       > “Proposed design conflicts with ethics/GCP guidance. Please revise or consult your IEC.”

   - Provide links / references (not legal advice).
3. **Scientific nonsense**
   - Eg: RCT with one arm; primary outcome absent from CRF; N=10 for 8 endpoints:
     - Flag as **Critical** in checklist.
     - Block “Lock & Launch” unless explicitly overridden with justification.
4. **AI Ethics (ICMR AI Guidelines)**
   - Clearly indicate AI-generated sections.
   - Provide explainability: why a design/method was suggested.
   - Ensure privacy: no training on identifiable user/participant data.

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11. Checklists Rulebook

11.1 Pre-Lock Study Checklist (must run before Launch)

Critical items (must be green or explicitly acknowledged):

1. Study design = supported / intentionally advanced.
2. Primary objective & outcome:
   - clearly defined
   - mapped to CRF & SAP.
3. Sample size:
   - formula documented
   - assumptions set.
4. Protocol:
   - all mandatory sections non-empty.
5. PIS/ICF:
   - includes all essential elements (ICMR).
6. SAP:
   - consistent with protocol & outcomes.

7. CRFs:
    - include fields for primary/secondary endpoints.
8. Ethics:
    - obvious conflicts flagged; user responded.
9. CTRI mapping:
    - key fields populated or flagged “PI to fill”.

If unresolved criticals → **no Lock & Launch.**

11.2 Workspace Checklist

- Confirm:
    - CRFs bound to correct StudyVersion.
    - Roles set correctly.
    - Audit logging functioning.

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12. Extensibility & Versioning Rules

- All templates and regulations are **versioned**:
    - e.g. `ICMR_2017_v1`, `ICMR_Addendum_2024_v1`, `CTRI_2021_v1`, `ICH_E6R3_2025_v1`.
- Each study records which rule versions were applied.
- Adding new jurisdictions = adding new rulepacks, not mixing into India profile.