Preclinical Risk Review

ENDPOINT PRECLINICAL

Use this discussion guide before finalizing your preclinical strategy to identify assumptions that could affect study quality, regulatory confidence, timelines, and downstream development decisions.

Start With the Strongest Possible Plan

Before evaluating the proposed strategy, establish the reference point.

If time, budget, and operational constraints did not exist, what evidence would give the team the greatest confidence in the program?

Consider the studies, endpoints, models, time points, analyses, regulatory interactions, and supporting data that would make the strategy most complete and defensible.

The strongest evidence plan would include:	What question would it answer?

Where Has the Strategy Been Streamlined?

Compare the strongest evidence plan with the strategy currently being proposed.

Where has work been reduced, combined, substituted, or deferred?

Strategic decision	Why was this decision made?

Common examples:

- ☐ Studies combined
- ☐ Sample size reduced
- ☐ End/time points removed
- ☐ One model used for many questions
- ☐ Evidence substituted for new testing
- ☐ Pathology/analytical work limited
- ☐ Testing deferred
- ☐ Regulatory delayed/avoided
- ☐ Other:

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Surface the Assumption

Every simplification rests on an assumption. Complete the sentence:

This decision is acceptable because we assume...

Strategic decision	Assumption supporting the decision

Stress-Test the Assumptions

Work through the questions below for each major assumption identified

1. If This Assumption Is Wrong, What Changes?

What data, conclusions, claims, timelines, or regulatory milestones would be affected?

2. When Would We Find Out?

- ☐ Before the study begins
- ☐ During study execution
- ☐ During pathology or data analysis
- ☐ During report preparation
- ☐ During regulatory review
- ☐ During clinical use
- ☐ Other: _____

3. Could We Recover Without Repeating Major Work?

What would the recovery path require?

- ☐ Additional analysis
- ☐ Additional animals or procedures
- ☐ Supplemental testing
- ☐ A new study
- ☐ Revised regulatory rationale
- ☐ Design or manufacturing change
- ☐ Additional regulatory interaction
- ☐ Other: _____

Notes:

4. What Would Recovery Cost?

Potential Impact	Low	Moderate	High
Time	☐	☐	☐
Budget	☐	☐	☐
Animal Use	☐	☐	☐
Submission Timing	☐	☐	☐
Regulatory Flexibility	☐	☐	☐
Scientific Confidence	☐	☐	☐

5. Make the Decision

Accept
The assumption is understood, the consequences are limited, and the program can recover if needed.

Mitigate
Additional evidence, analysis, documentation, rehearsal, or oversight can reduce the risk.

Clarify
Regulatory feedback or expert input is needed before the strategy is finalized.

Redesign
The potential consequence is too significant, costly, or difficult to recover from later.

Decision Owner: _____ Target Date: _____

Agreed Next Step:

Final Check

Could your team confidently defend this assumption to a regulator six months from now?

☐ Yes
☐ Not yet

The goal is not to eliminate risk. It is to ensure every major assumption has been discussed before it becomes a costly surprise.

Need an Independent Strategy Review?

Every development program makes tradeoffs. The challenge is knowing which ones strengthen the strategy—and which introduce unnecessary risk.

Our Regulatory & Risk experts work with medical device teams to review preclinical development plans, identify hidden assumptions, and strengthen study strategies before protocols are finalized.

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