HealthSphere Strategy & Implementation

Planning for Trial Success

Product Development Boot Camp

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Introduction

Is your team prepared to react?

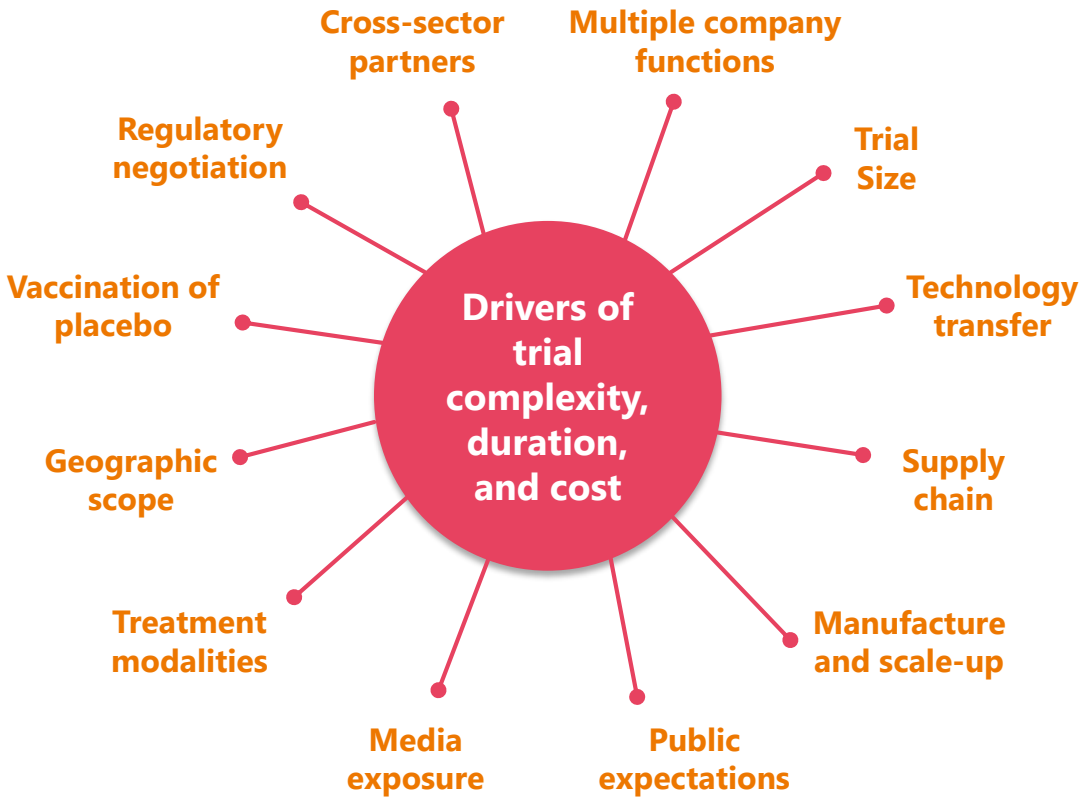
"[The company's] stretch of bad, ugly, not-good results just got longer. The pharma giant, which recruited more than 16,000 patients in a monumental postapproval effort … says that study **failed…its primary endpoint … and key secondary endpoints**."[1]

"researchers halted a trial of the vaccine … because it seemed to **increase the risk of HIV infection.** The failure of the trial **… was a serious setback** for AIDS researchers, who were **at a loss to explain its disappointing results**."[2]

Addressing unexpected trial results in the absence of a comprehensive, consensus-based plan can lead to a crisis situation and test the resolve of trial partners.

[1] Modified from: http://www.fiercebiotech.com/story/ropes-glaxosmithkline-admits-another-phiii-debacle/2015-09-08
[2] Modified from: http://www.nature.com/news/2009/090720/full/news.2009.707.html

Addressing the complexities inherent to clinical trials makes contingency planning critical—and also very challenging.



Contingency planning mitigates risks by anticipating the large array of issues that drive trial complexity, duration and cost.

Planning for trial success (and failure) should be proactive, systematic and collaborative.

These elements are often codified in a 'Contingency Planning Roadmap', which arms decision-makers with a 'playbook' for managing risks.

Elements of Planning for Trial Success

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2. **Define proactive and reactive responses in a prescriptive and unambiguous manner**
3. **Ensure that contingency plans set the stage for future product access**

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A wide net must be cast to identify all potential trial outcomes—those that are aspirational, realistic or unlikely.

Safety

- Suboptimal monitoring and reporting of adverse events
- Trial stops due to observed serious adverse events
- High frequency of adverse events reported; trial continues

Operational

- Trial stops due to insufficient enrollment, acquisition, retention
- Data collection issues at certain sites impact overall data quality
- Supply chain disruptions impact trial timelines

Efficacy

- Trial stops due to efficacy futility
- Trial concludes within several possible efficacy ranges
- No correlate of protection identified

The scenarios listed above are only examples of the dozens of safety, operational and efficacy scenarios that could transpire.

Shift HEALTH

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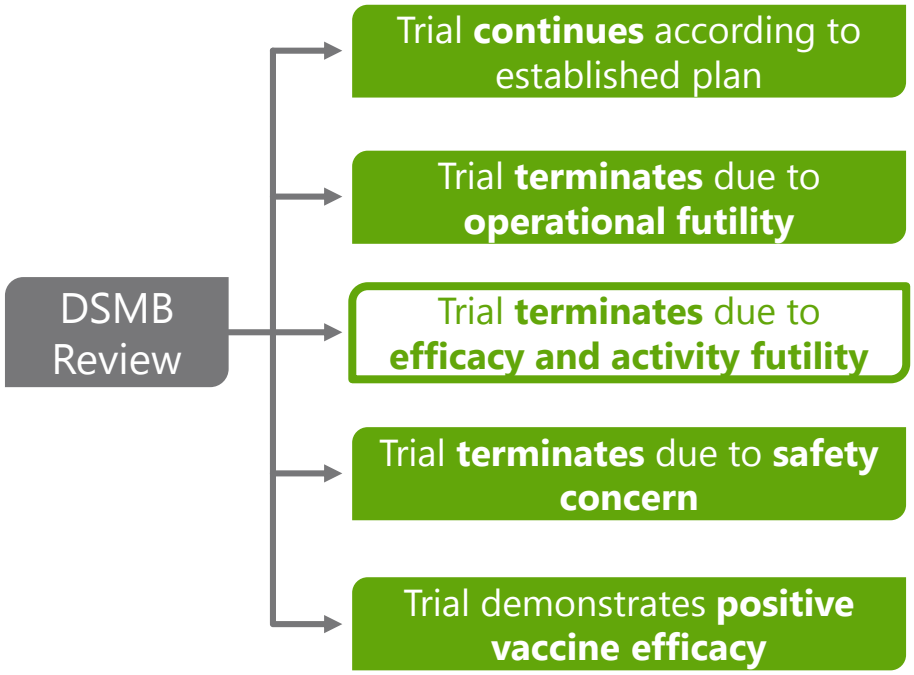
Case Study: Five potential scenarios were developed to prepare the HVTN 505 study team for an upcoming DSMB review meeting.



- The contingency plan established specific response plans for various outcomes.
- The sudden termination of the trial triggered implementation of a multi-pronged communication strategy, including dissemination of tailored materials to trial volunteers and the media.

The contingency plan provided the trial team with a clear plan of action to respond to the DSMB recommendation and communicate effectively with the media and participants.

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2 Effective response plans are informed by a disciplined reflection on priorities and constraints.

When to Act?

- Defining specific triggers and thresholds for action/escalation provides clarity on timing.

What to Focus On?

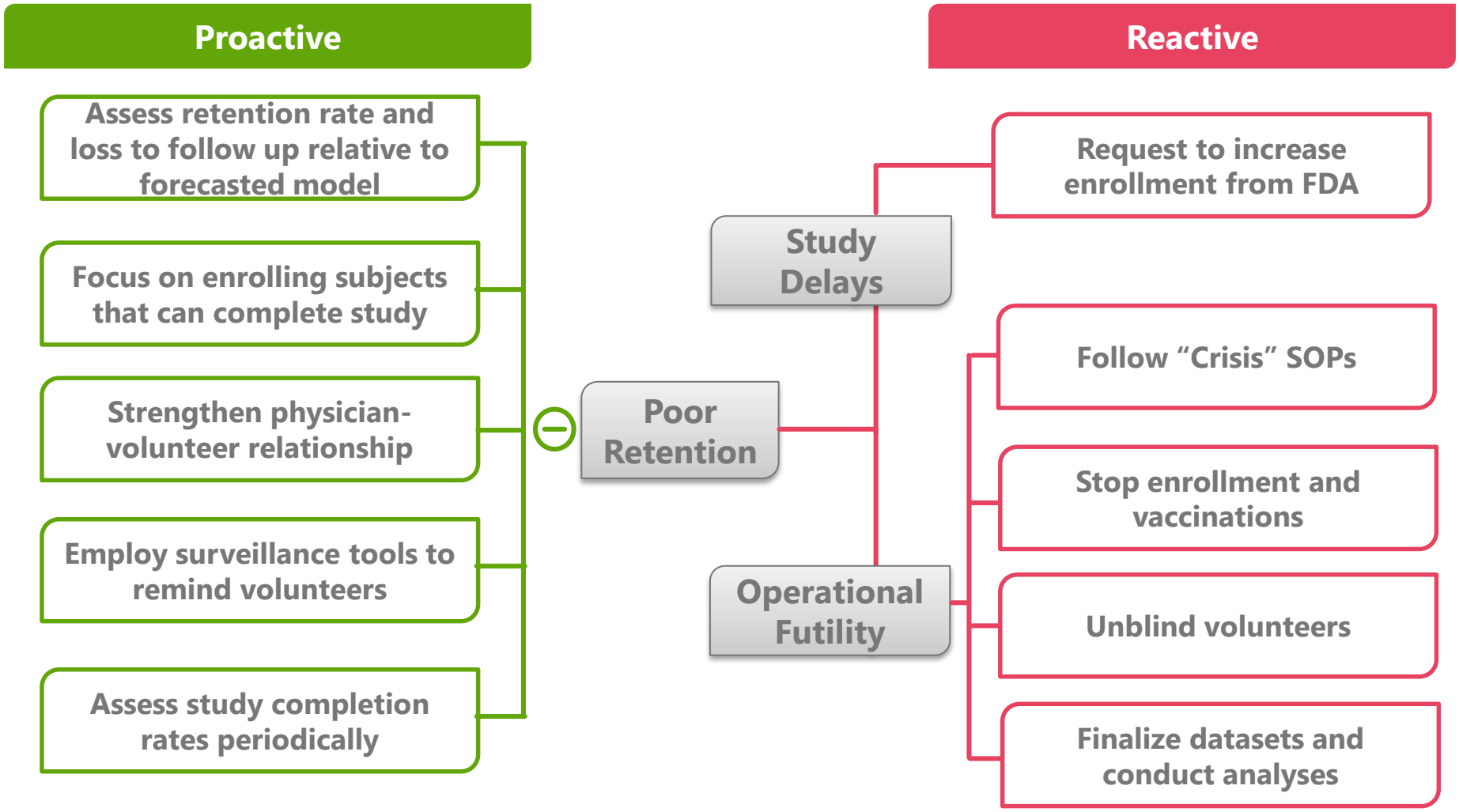
- Reflecting on likelihood and impact focuses attention on high-risk events and responses.

What is Needed?

- Outlining detailed responses provides an understanding of resource requirements and gaps.

Responses should be proactive and reactive—proactive to avert and minimize risks; reactive to respond to and manage risks.

2 A single scenario can be associated with multiple proactive and reaction actions.



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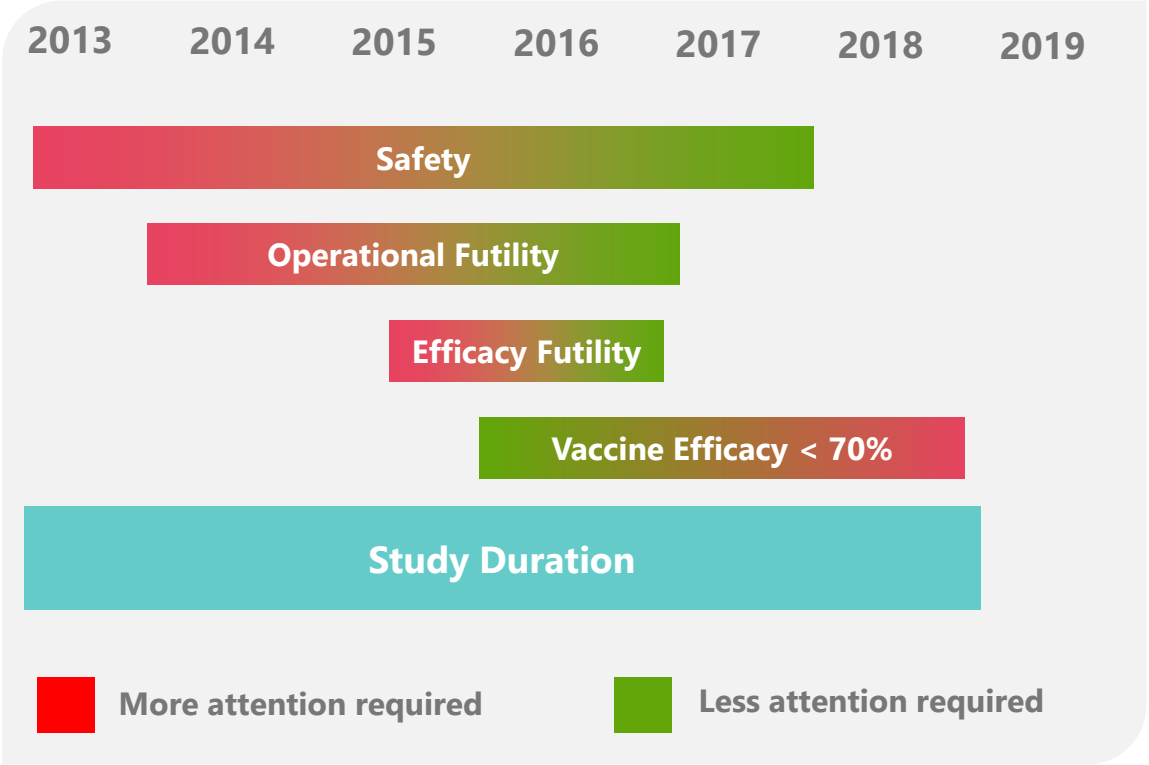
Case study: Contingency planning to prepare for outcomes, risks and scenarios of a Phase 3, multinational vaccine clinical trial.

- *5-year Phase 3 study involving 250 clinical centres*
- *Detailed response plans, with proactive and reactive components*
- *Preparation based on likelihood of occurrence and potential impact*



The contingency plan has guided a number of proactive manoeuvers and will continue to direct activities during the course of the trial.

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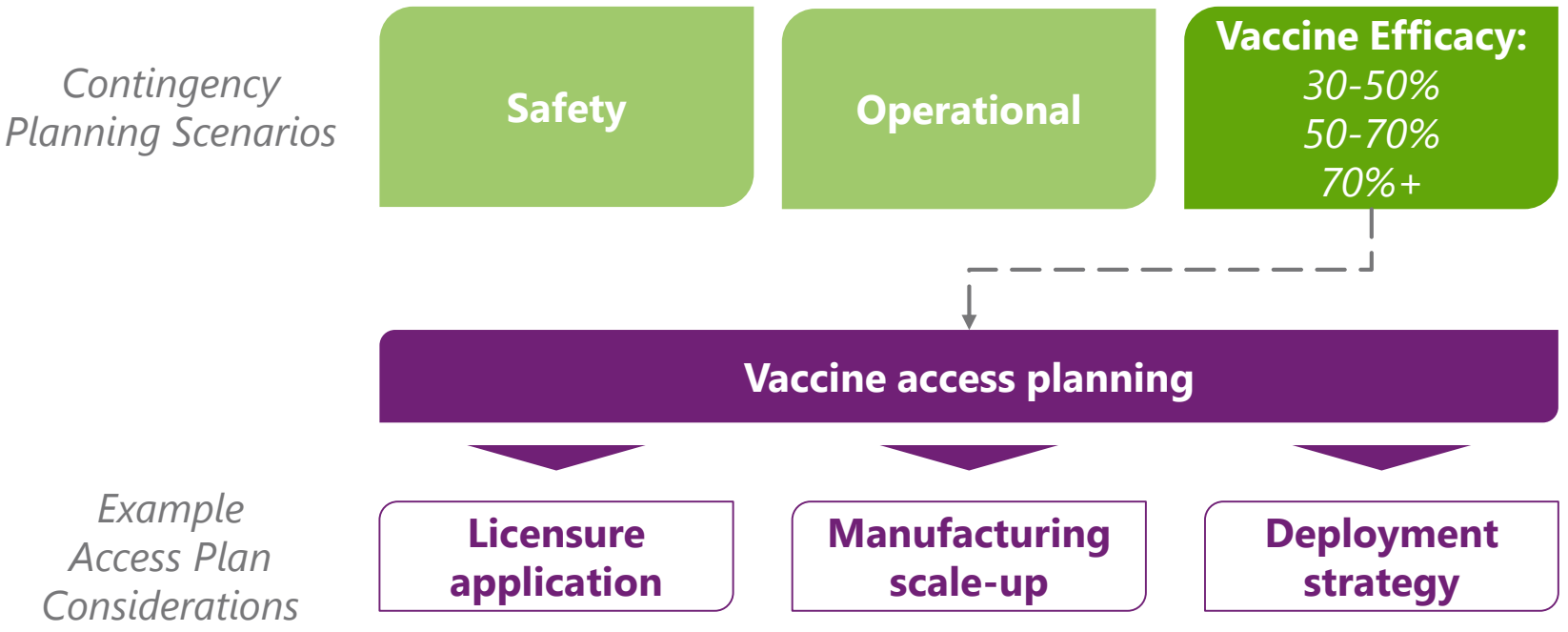
3 Contingency planning has broader access implications when predetermined efficacy levels are demonstrated.



Contingency planning will inform parallel access planning efforts and ensure that partners are prepared to provide access to a successful product in a timely manner.

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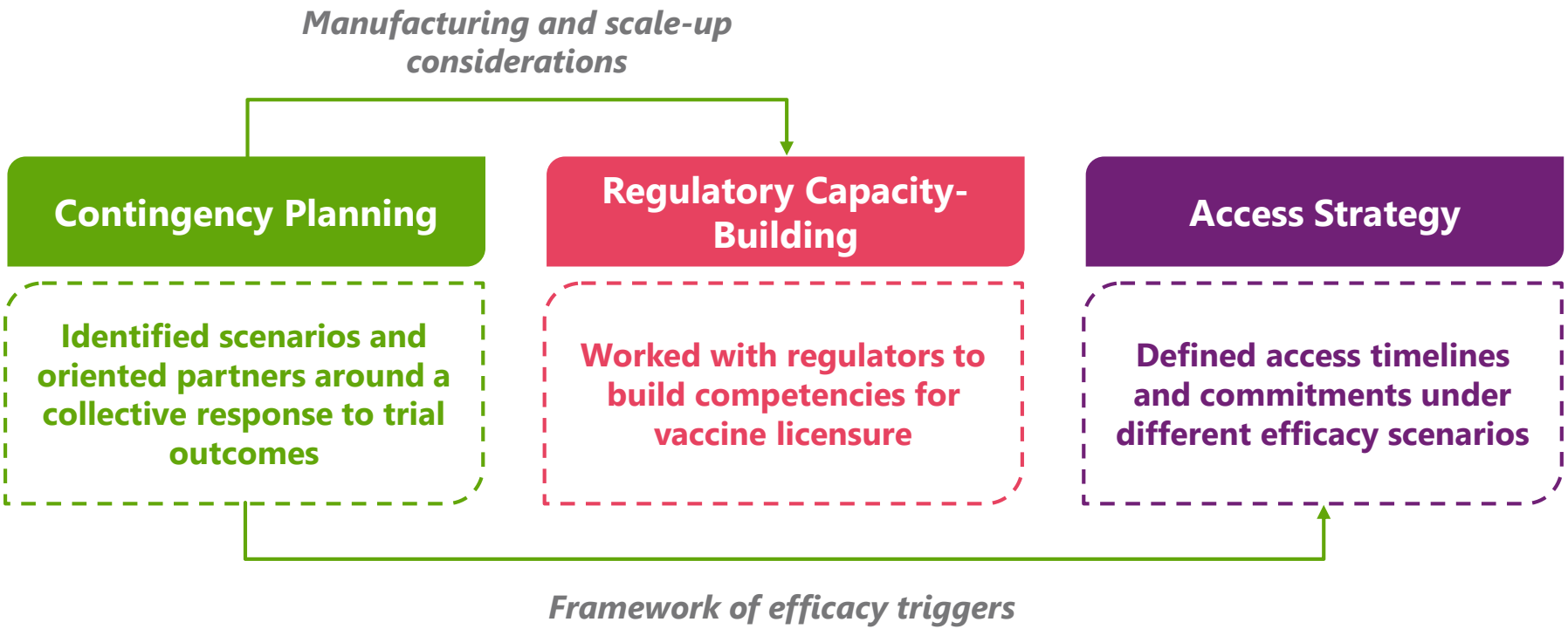
Case Study: RV144 set a precedent for the importance of multi-faceted and timely planning in a complex HIV vaccine trial.



Contingency planning is a critical mechanism for compelling partners and stakeholders to have discussions around key issues that will have implications for overall planning efforts and eventual vaccine access.

Success Factors and Impact

Key success factors

Contingency planning must be:

- ***Comprehensive*** in assessing all potential events and outcomes—whether *positive* or *negative*—regardless of initial perceived likeliness
- ***Consensus-driven*** to align expectations and secure commitments across diverse partners and stakeholders
- ***Coordinated*** through a central point of contact and/or project manager to ensure timely communication and harmonization of activities across partners and stakeholders
- ***Flexible*** to enable adjustments in response to new information and/or evolving partner commitments

Impact

- Ensures that all ***stakeholders are prepared to respond*** and act in a unified and decisive manner
- ***Streamlines implementation*** of the appropriate scientific, clinical and operational responses
- Manages public expectations by ***guiding communication*** of trial events with volunteers, the public, and medical community

Ultimately, effective contingency planning will result in cost-effective trial management, comprehensive risk mitigation and efficient coordination of partners, participants and the public.

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