



Looking Beyond 95%: A New Data-Driven Framework to Assess Regulatory Approval Risk

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What this Is and Is NOT?

IS:

- A real case
- About Decision Quality Deployment
- About Innovation and Change Management

IS NOT:

- Academia talk on how to evaluate Probability of Regulatory Success (neither Eric nor Lan is regulatory expert)

How this Get Started?

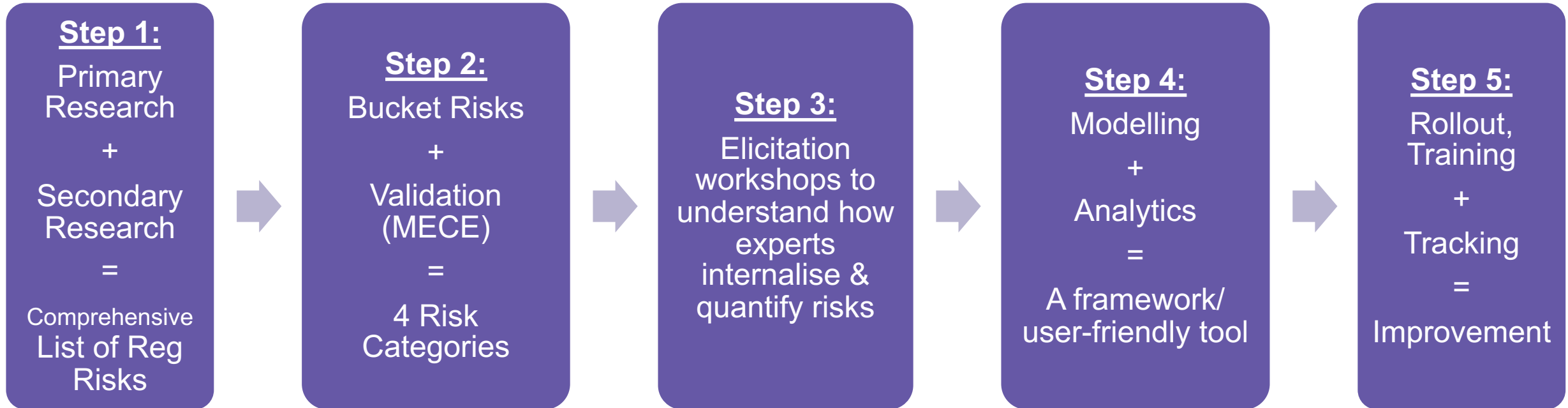
Problem Statements:

- 95% PRS (industry benchmark) was widely used and lack of consistent approach for adjustments.
- People internalize risks differently. Challenging discussions were observed at governance as lack of agreement on how to quantify regulatory risks.

Mission:

- A cross- functional working force was formed to develop a **robust** framework and process to capture the key regulatory risks and guide teams to **systematically** evaluate and quantify regulatory probability of success.

Key Steps Leading Towards the New Framework?



Output: PRS Assessment Framework

Regulatory Factor 1: Regulatory Considerations: *'Do we have clear regulatory path*? Does the programme follow the regulatory path?'. Any opportunity to shape the regulatory environment or guidelines? Any known upcoming policy change?*

** Regulatory path include regulatory guidelines, precedents and/or obtained health authority feedbacks.*

Regulatory Factor 2: Unmet Needs: *'Is there clear unmet needs? Will high unmet needs increase regulatory flexibility?'*

Regulatory Factor 3: Clinical Data Package: *'any potential perceived gaps from HAs?'*

Regulatory Factor 4: Pre-Clinical & CMC Data Package: *'any potential perceived gaps from HAs?'*

Within each regulatory factor, we provided a list of risks for consideration and developed **Red**, **Amber**, **Green** statements. Details are not included due to business confidentiality.

Examples of Regulatory Factor Scenarios and Associated PRS Based on Elicitation Results

Regulatory Factor Scenarios*	Regulatory Considerations	Unmet Need	Clinical Data Package	Pre-Clinical & CMC Data Package	Estimated PRS
1. No perceived regulatory risks likely to impact approvability	Green	Green	Green	Green	95%
2. Development plan broadly aligned with regulatory path, but some outstanding issues	Amber	Green	Green	Green	84%
3. As in 2. but also high unmet need	Amber	Hyper-Green	Green	Green	89%
4. Development plan, trial design etc. is not aligned with existing regulatory path and there is important misalignment and/or disagreement	Red	Green	Green	Green	61%
5. Clinical, pre-clinical and CMC data packages are likely to have some small gaps.	Green	Green	Amber	Amber	70%

Bringing Framework to Life - A Web-based User-friendly Tool

GSK PRS Evaluation Tool

Calculator

Description

Risk Profile Selection

Project ID

001

Project ID: 001

Risk Factor 1: Regulatory Considerations

Amber

Risk Factor

Risk Category

Description

Regulatory Considerations

Amber

Clear regulatory path, and the development plan, trial designs and/or key endpoints etc are broadly aligned with the existing regulatory path, but there are some outstanding issues/reservations/risks

Risk Factor 2: Unmet Need

Green

Unmet Need

Green

Neutral scenario (e.g. no regulatory designation or significant benefit vs well established SoC) without adjustment to PRS

Risk Factor 3: Clinical Data Package

Green

Clinical Data Package

Green

The planned Clinical data package is deemed to be sufficient for filling

Risk Factor 4: Pre-Clinical & CMC Data Package

Green

Pre-Clinical & CMC Data Package

Green

The planned pre-Clinical & CMC data package is deemed to be sufficient for filling

PRS Estimate 84%

95% Confidence Interval 82%, 86%

Tool provides team with recommended PRS for their selected regulatory profile

Potential Risks & Mitigation Strategies

Risks	Prob / Impact	Mitigation strategy
Systematically driving portfolio level PRS away from 95%	M/H	<ul style="list-style-type: none"> • Communicate the tool provides <u>directional</u> reference • Tool is intended to support decision not to direct it (Mindset change)
Team miscategorising the risk	M/M	<ul style="list-style-type: none"> • Training • Facilitated discussion and assessment
Team commonly deviating from the PRS number recommended by tool	M/M	<ul style="list-style-type: none"> • Boost confidence (tool was built based on elicitation with over 30+ experienced experts across Therapeutic Areas) • Continuously track, periodically review and appraise

A Few Thoughts on...

- Innovation
- Push vs. Pull
- Stakeholder Management
- Matrix Team: Forming & Performing
- Disagreements