Are we at the tipping point of RBQM widespread adoption?

Abhishek Ghosh M Pharm, PMP
Executive Director – Clinical Dev Ops
Premier Research India
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<tbody>
<tr>
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Regulatory landscape and RBM/RBQM

Clinical Trials Management – RBQM & Non-RBQM Approach

Pandemic as Tipping Point for RBQM Adoption

Post Pandemic will RBQM Adoption keep up its momentum?

Why RBQM Adoption is the Need of the Hour?

Lessons from Covid-19 vaccine development, for embracing RBQM in Post-Pandemic times?
Regulatory Agencies & RBM/RBQM Guidelines

- **1906**
  - Pure Food & Drug Act

- **1938**
  - Food, Drug & Cosmetics Act

- **1990**
  - ICH

- **1995**
  - EMA

- **2003**
  - MHRA

**1996 ICH**
- ICH GCP E6

**2013 FDA, EMA**
- RBM/RBQM Guidelines, Quality by Design Approach

**2016 ICH**
- ICH GCP E6 (R2)

**2019 FDA**
- Risk Based Approach Q&A Draft Guidelines

**2021 ICH**
- ICH GCP E6 (R3) & E8 (R1)

**2022 MHRA**
- RBM Guidelines

**August 2013**
- FDA Guideline: A Risk Based Approach to Monitoring

**November 2013**
- EMA Reflection Paper on Risk Based Quality Management in Clinical Trials

**November 2013**
- EMA & FDA jointly release guidance on Quality by Design (QbD) Approach

**November 2016**
- Integrated Addendum to ICH E6 (R1) and E6 (R2) – Quality Risk Management, Quality-by-Design process & Risk-based monitoring

**January 2022**
- MHRA Risk Adopted Approach to Clinical Trials and Risk Assessments

**October 2021**
- ICH E8 (R1) Quality by Design (QbD)

**April 2021**
- ICH E6 (R3) work in progress version

**March 2019**
- FDA Risk Based Approach to Monitoring of Clinical Investigations Q&A Draft Guidelines

- **1990**
  - FDA Guideline: A Risk Based Approach to Monitoring

- **2013**
  - EMA Reflection Paper on Risk Based Quality Management in Clinical Trials

- **2016**
  - EMA & FDA jointly release guidance on Quality by Design (QbD) Approach

- **2019**
  - Integrated Addendum to ICH E6 (R1) and E6 (R2) – Quality Risk Management, Quality-by-Design process & Risk-based monitoring

- **2021**
  - MHRA Risk Adopted Approach to Clinical Trials and Risk Assessments

- **2022**
  - FDA Risk Based Approach to Monitoring of Clinical Investigations Q&A Draft Guidelines
### Contrasting Before & After RBQM Guidelines

<table>
<thead>
<tr>
<th>RBQM Guidelines</th>
<th>Before RBQM Guidelines</th>
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<tbody>
<tr>
<td>Proactive Risk Management (Cross-functional)</td>
<td>Frequent Site Visits</td>
</tr>
<tr>
<td>Quality Tolerance Limits (QTLs)</td>
<td>100% SDV</td>
</tr>
<tr>
<td>Key Risk Indicators (KRIs)</td>
<td>Reactive Issue Management, Lag indicators</td>
</tr>
<tr>
<td>Quality-by-Design (Protocol, CRF, Sites, Personnel)</td>
<td>Systematic errors, Trends not identified</td>
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<tr>
<td>Leveraging Technology</td>
<td>No customization of time &amp; efforts, based on trials</td>
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<tr>
<td>Optimization — Focus monitoring activities on critical study parameters</td>
<td>High labour hours (resource intensive trials)</td>
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<tr>
<td>Centralized Monitoring</td>
<td></td>
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<tr>
<td>Off-site/Remote-site Monitoring</td>
<td></td>
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<tr>
<td>Reduced SDV &amp; SDR</td>
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RBM/RBQM Adoption Trend during Pandemic

Reasons for slow adoption of RBM between 2013 till 2019:
- Resistance to change (maintain status quo)
- Challenges in understanding, implementation, execution
- Misconception about RBM

Reason for faster adoption of RBM between 2019 to 2020:
- Pandemic – tipping point
- Need (Necessity is the mother of all invention)

2019 ACRO Landscape Survey Results
6513 ongoing studies, 7 CROs in 2019

2020 ACRO Landscape Survey Results
5,987 ongoing studies, 6 CROs in 2020. 908 study started in 2020

Source: Therapeutic Innovation & Regulatory Science https://doi.org/10.1007/s43441-022-00387-z
RBM/RBQM Adoption Trend During Pandemic

Adoption of Individual RBM/RBQM Components

- Cross-Functional Risk Assessments: 53% Pre-Pandemic 2019, 33% During Pandemic 2020
- Quality Tolerance Limits: 10% Pre-Pandemic 2019, 11% During Pandemic 2020
- Reduced SD Review: 8% Pre-Pandemic 2019, 16% During Pandemic 2020
- Reduced SD Verification: 15% Pre-Pandemic 2019, 20% During Pandemic 2020

2019 - 2020 ACRO Landscape of RBM/RBQM Implementation

- Initial Risk Assessment: 33% 2019 Ongoing Studies, 33% 2020 Ongoing Studies
- Ongoing Risk Assessment: 10% 2019 Ongoing Studies, 11% 2020 Ongoing Studies
- QTL: 27% 2019 Ongoing Studies, 15% 2020 Ongoing Studies
- KRI: 19% 2019 Ongoing Studies, 16% 2020 Ongoing Studies
- Centralized Monitoring: 25% 2019 Ongoing Studies, 10% 2020 Ongoing Studies
- Remote Monitoring: 8% 2019 Ongoing Studies, 16% 2020 Ongoing Studies
- Reduced SDR: 39% 2019 Ongoing Studies, 36% 2020 Ongoing Studies
- Reduced SDV: 40% 2019 Ongoing Studies, 20% 2020 Ongoing Studies

Source: Therapeutic Innovation & Regulatory Science https://doi.org/10.1007/s43441-022-00387-z
Mirroring DCT Solutions Adoption During Pandemic

DCT Solutions Adoption

- **Telemedicine**: 22% (Pre-Pandemic) vs. 57% (During Pandemic)
- **eConsent**: 41% (Pre-Pandemic) vs. 65% (During Pandemic)
- **Wearables**: 39% (Pre-Pandemic) vs. 48% (During Pandemic)
- **Home Visits**: 37% (Pre-Pandemic) vs. 61% (During Pandemic)
- **Home Tx Delivery**: 20% (Pre-Pandemic) vs. 64% (During Pandemic)
- **Remote Monitoring**: 43% (Pre-Pandemic) vs. 70% (During Pandemic)

**Source**: Tufts CSDD May 2022, N = 54 Companies Keynote Speaker Ken Gentz, Executive Director & Professor Tufts CSDD, RBQM Live 2022, Keynote: How the Evolving RBQM Landscape Will Reinforce The Way We Improve Efficiencies The Way We Improve Efficiencies And Add Value.
Pandemic The Tipping Point for RBQM Adoption!

47% to 77% jump in at least one RBM component from 2019 to 2020

33% to 53% jump in Cross-Functional Risk Assessment from 2019 to 2020

33% to 93% jump in Initial & Ongoing Risk Assessment from 2019 to 2020

33% to 60% jump in DCT adoption during pandemic (comparison of average of the six DCT components from previous slide)
Survey forecasts decline in momentum of DCT adoption post pandemic. Will similar sentiments mirror for RBM/RBQM adoption post pandemic?

Source: The Avoca Group, 2021 (N = 145 Sponsors and 84 CROs), Keynote Speaker Ken Gentz, Executive Director & Professor Tuffs CSDD, RBQM Live 2022, Keynote: How the Evolving RBQM Landscape Will Reinforce The Way We Improve Efficiencies The Way We Improve Efficiencies And Add Value.
Why Continue to Embrace RBQM in Post Pandemic Times?

- Pandemic was the Tipping Point for RBQM adoption
- However, post pandemic momentum of RBQM adoption, may not take an auto-pilot mode!
- We must take conscious decision to continue embracing RBQM, post pandemic for the following reasons:

1. **Increasing Complexity of CT**
   (protocol, procedures, endpoints)

2. **Increasing Number of CT**
   (y-o-y registered CT is growing in numbers)

3. **Technological Advancement**
   (opportunities for alternative monitoring & data analysis)

4. **Globalization of CT**
   (customized approach needed across different participating countries)

5. **Integrated Risk Identification & Mitigation**
   (Holistic, Proactive Project Management)
## Covid-19 Vaccine Development - HOPE & TRIUMPH For RBQM Adoption

<table>
<thead>
<tr>
<th>Name of Pandemic</th>
<th>Timeframe for Vaccine Development</th>
<th>Duration</th>
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<tbody>
<tr>
<td>Spanish Flu</td>
<td>1917 – 1942</td>
<td>25 years</td>
</tr>
<tr>
<td>H2N2 Asian Flu</td>
<td>Feb 1957 – June 1957</td>
<td>&lt; 5 months</td>
</tr>
<tr>
<td>H3N2 Hong Kong Flu</td>
<td>July 1968 – Nov 1968</td>
<td>&lt; 5 months</td>
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<tr>
<td>SARS</td>
<td>2003 – present</td>
<td>19 years (ongoing)</td>
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<tr>
<td>Ebola</td>
<td>1976 – 2019</td>
<td>43 years</td>
</tr>
<tr>
<td>AIDS</td>
<td>1981 – present</td>
<td>41 years (ongoing)</td>
</tr>
<tr>
<td>H1N1 Swine Flu</td>
<td>Apr 2009 – Sep 2009</td>
<td>6 months</td>
</tr>
<tr>
<td>MERS</td>
<td>2012 – present</td>
<td>10 years (ongoing)</td>
</tr>
<tr>
<td>Coronavirus (Covid-19)</td>
<td>Jan 2020 – Dec 2020</td>
<td>11 months</td>
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How We Made Unprecedented Covid-19 Vaccine Development Possible?

- Trust, Collaboration, Sharing of Information
- Proactive Regulatory Engagement & Guidance
- Public Private Partnership for the larger good
- Mobilization of Cross-Functional Resources (Breaking Silos)
- Leveraging On New Science, Technology, Methods & Approaches
- Government Funding, Shared Development Risk
- Proactive, Agile Project Management
- Parallel Activities of Vaccine Development & Clinical Trials
- Emergency Use Authorization (EUA), Digital Platforms for Decision making
Our attributes which made us triumph over the pandemic, can propel us from this Tipping Point towards widespread adoption of RBQM in post-pandemic times for addressing the Needs of Present Day and Future Clinical Trials.
THANK YOU