Trust in Data

RBQM Case Studies

EXPLAINING WHY MyRBQM PORTAL WAS USED

Marketing | January, 2022

INTRODUCTION

Some of the major challenges (risks!) in clinical trial conduct include delays in data entry, misconduct at the site, degradation of data quality (due to lost-to-follow-up cases/Informed Consent withdrawn cases), etc.

Risk Based Quality Management has evolved through the use of data in order to mitigate these risks. For e.g. using **audit trails** from the EDC systems to check for data integrity, and by **establishing timelines** of important events.

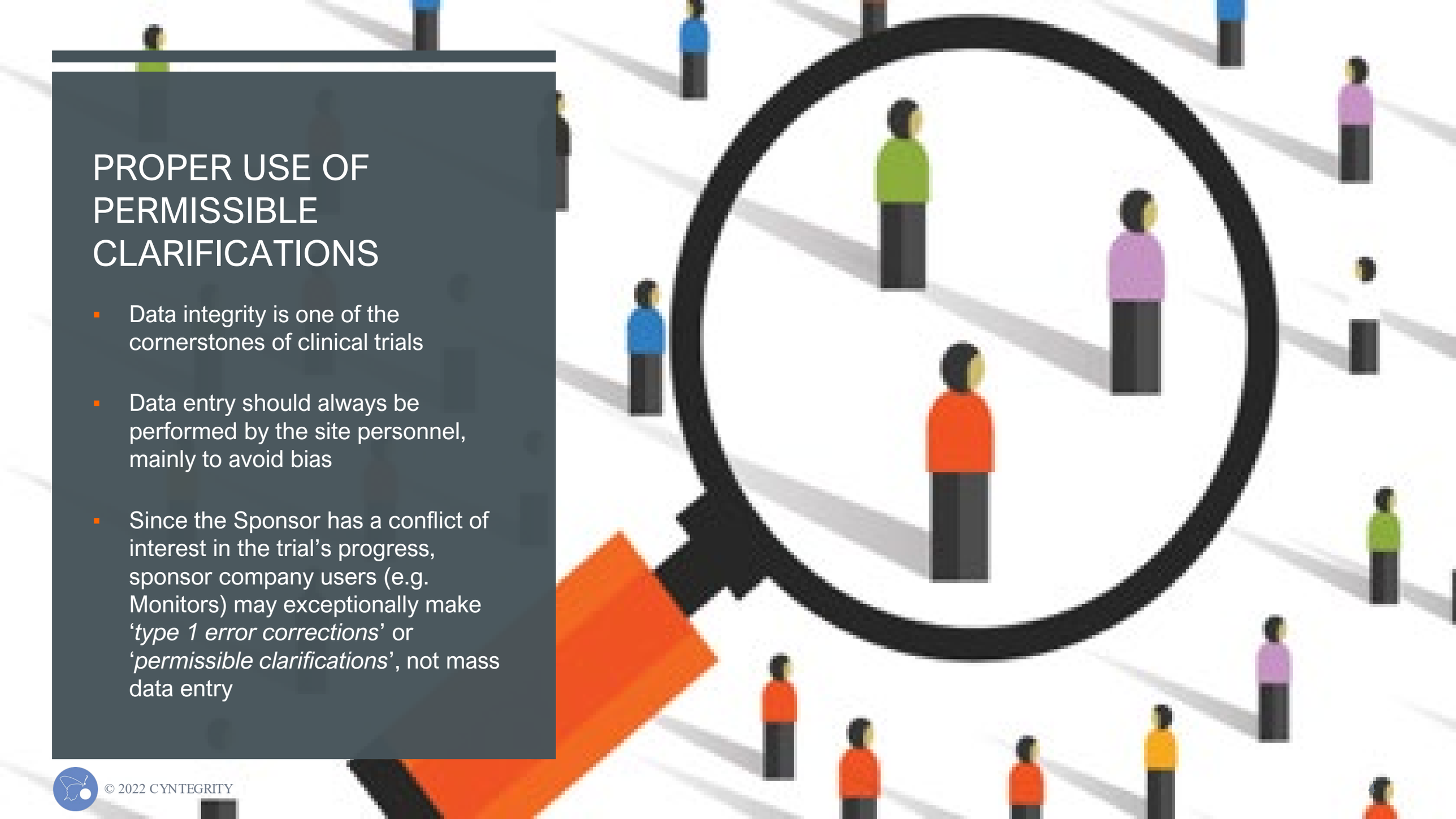
The following case studies illustrate how the **MyRBQM®** system helped solve these problems using the principles of Risk Based Quality Management.

CASE STUDY 1

When conflict-of-interest is a hidden factor of **potential bias**

PROPER USE OF PERMISSIBLE CLARIFICATIONS

- Data integrity is one of the cornerstones of clinical trials
- Data entry should always be performed by the site personnel, mainly to avoid bias
- Since the Sponsor has a conflict of interest in the trial's progress, sponsor company users (e.g. Monitors) may exceptionally make '*type 1 error corrections*' or '*permissible clarifications*', not mass data entry

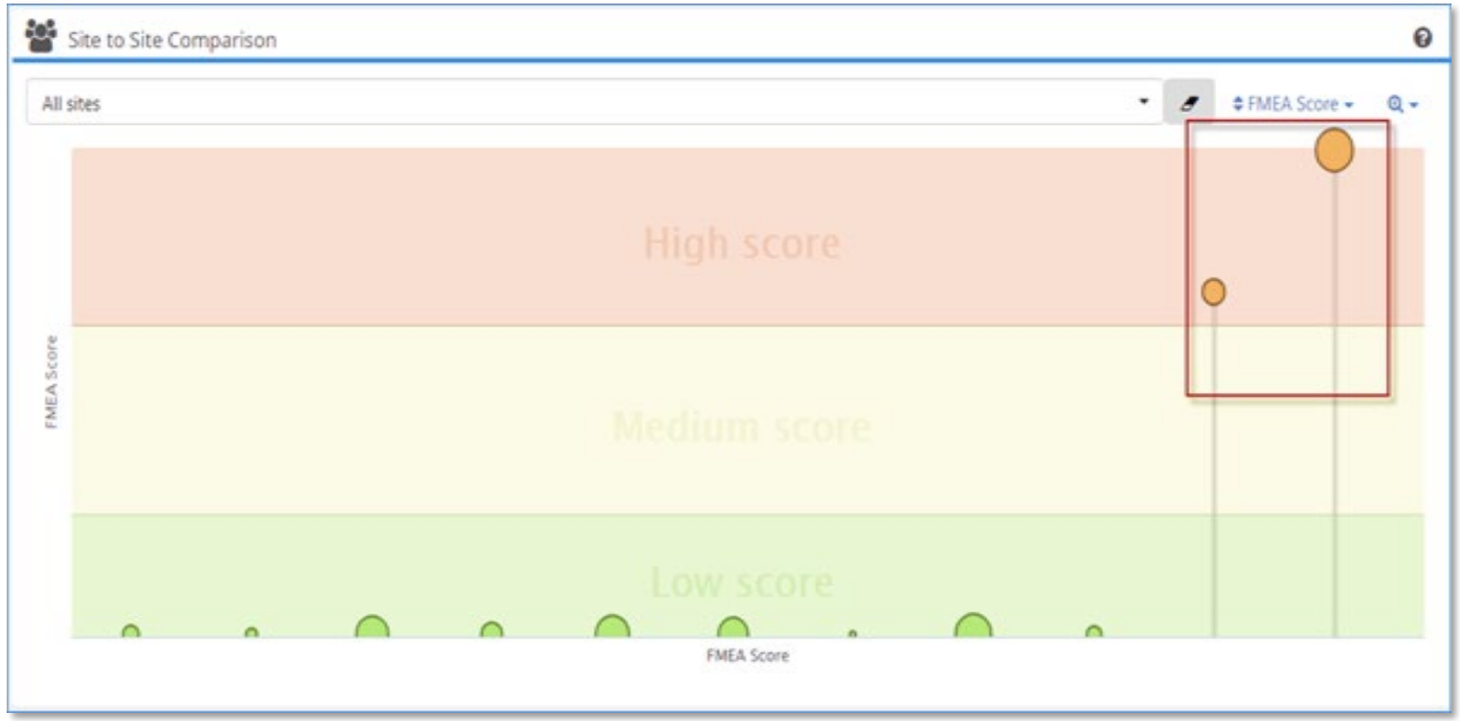


WHAT WENT WRONG?

Instead of site personnel, the **sponsor company monitor entered the majority of the data** of two Japanese sites into the EDC system using his user ID for ‘permissible clarification’ or ‘type 1 error correction’.

HOW WAS IT DETECTED?

- The MyRBQM® Portal had been set up such that the **entries done** by the various parties involved in the study and having access to the EDC system **had been counted**
- **It used the audit trail** of the EDC system and checked for the sponsor company users entering or modifying data



HOW WAS THIS RISK ADDRESSED?

- **Implementation of a Key Risk Indicator** (KRI) for User-ID from sponsor company staff and the use of it for data entry
- **With a threshold**, i.e. in case of more than 0.5% usage of the user-ID for data entry, an alert was triggered

WHY…

MyRBQM® Portal was used?

- Non-adherence was spotted proactively, instead of retrospectively
- So that misconduct could be mitigated on time using a specific KRI

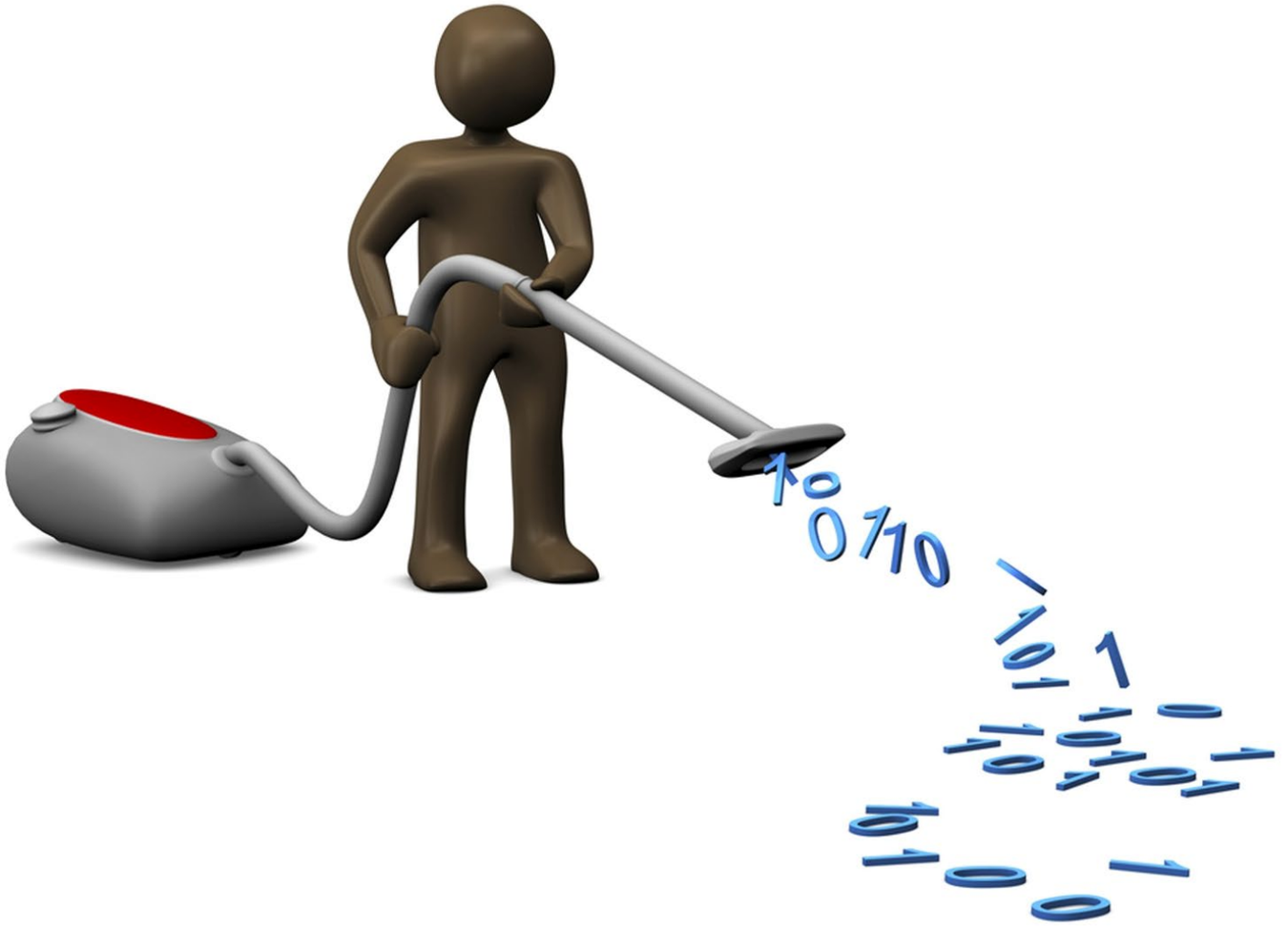
CASE STUDY II

When **early prediction** is the key to a trial's success

PROACTIVE DATA CLEANING

In traditional clinical trial settings, **accurately predicting important events is difficult**.

This may lead to extension of the study, inaccuracy in data and delays in the approval process.



WHAT WAS THE PREDICTION?

- In an Oncology trial the RBQM system **predicted the number of events required to run an interim analysis** were going to occur around Christmas
- This was important to the trial's progress as one of the **main efficacy parameters is the 'time-to-event' which can only be run on rather clean data**

HOW WAS THE RISK PREDICTED?

- **Using the KRI = number of events (deaths) over time** along prediction feature in the MyRBQM® Portal
- On the time-scale it showed that the number of events very likely will be reached around Christmas, which then helped to work against that target date accordingly

WHY…

MyRBQM® Portal was used?

- The Sponsor could **proactively intensify the data cleaning**
- All queries were ‘On Schedule’ for interim analysis which lead to risk minimisation
- **Study could be stopped early due to a positive outcome**

CASE STUDY III

When late data entry could **delay trial completion**

ENSURING TIMELY ENTRIES & RESPONSES

Timely data entry and response to queries are integral parts of a clinical trial.

A huge number of open queries can result in the delay of a clean database which is undesirable.

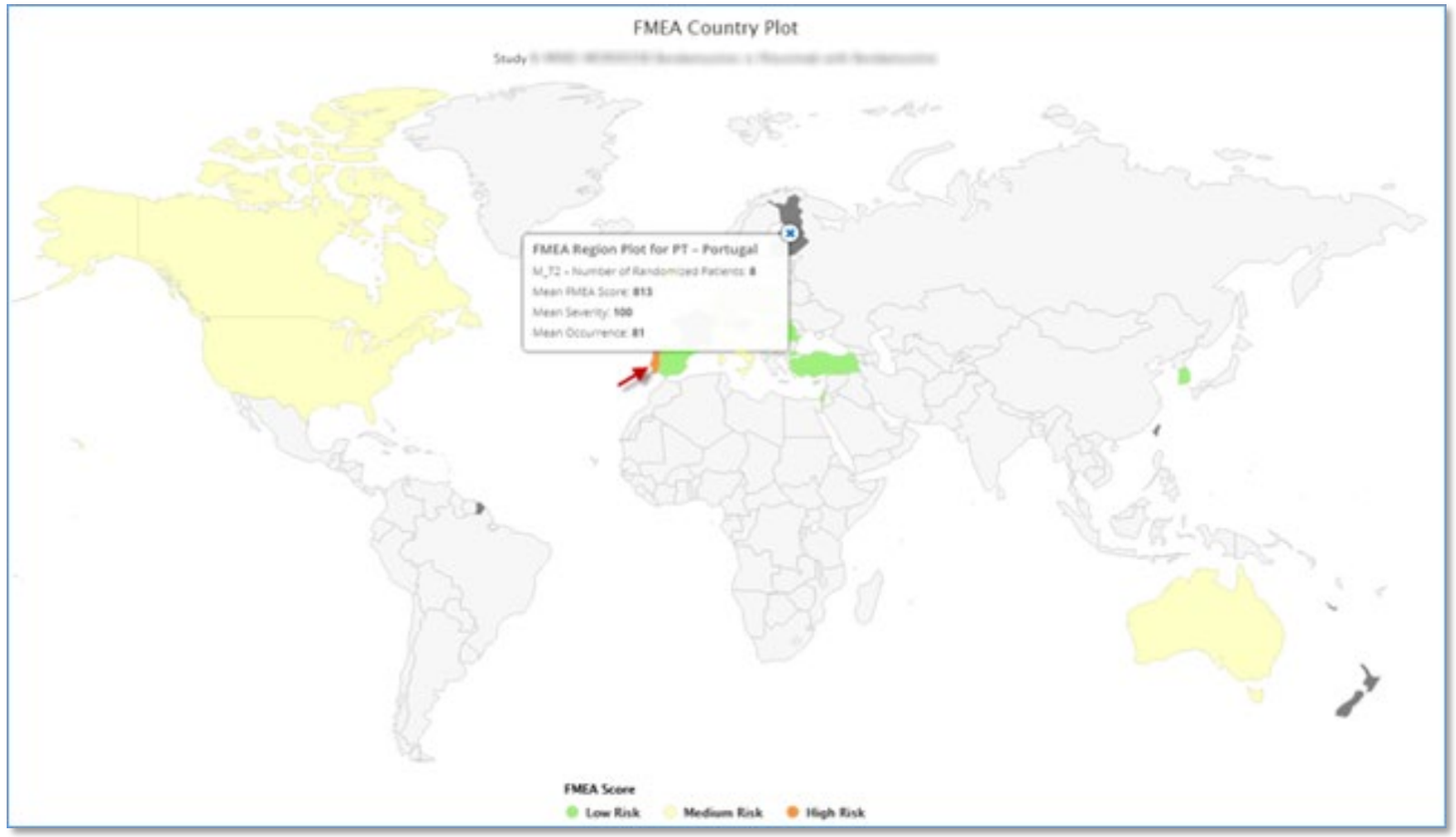
WHAT WENT WRONG?

A long-term study with many patients was supposed to be completed prior to summer break.

The study lock would be delayed by one country, together with the sites with **many unaddressed open queries**.

HOW WAS IT DETECTED?

- The **MyRBQM® Portal identified the rate-limiting sites** (investigators) and highlighted the risks around late data entry and delayed responses to queries
- Since these data were made available via the MyRBQM® Portal, **the particular sites could be identified** and mitigation action could be implemented to eliminate the backlog of open queries



HOW WAS THIS RISK ADDRESSED?

By implementation of two KRIs:

- **KRI = time between visit and data entry (audit trail)**, i.e. sites that took frequently more than 3 days (72 hours) for data entry were highlighted
- **KRI = time between query posting manually / automatic query generation by the EDC system and the time to respond to those queries**, i.e. when greater than 3 days, an alert was triggered to the Sponsor company

WHY…

MyRBQM® Portal was used?

- Study management was able to respond successfully to the situation by hiring an additional resource to assist with the data cleaning at those sites
- To ensure the **timely availability of a clean database**

CASE STUDY IV

When lost-to-follow-up could **lead to non-acceptance**

ACCEPTANCE BY HEALTH AUTHORITIES

A high number of lost-to-follow-up or IC withdrawn cases causes **a reduction in the effective sample size** as the investigators will be missing outcome measures on those who are lost.

It may lead to bias if the follow up rates are different among comparison groups and if attrition is related to the outcome.

Additionally it can also **lead to non-acceptance** by the health authorities/ regulatory bodies.

WHAT WENT WRONG?

In a large Cardiovascular outcome trial with 8000 patients, the MyRBQM® Portal predicted the study would end up with **1300 cases of lost-to-follow-up or informed-consent-withdrawn cases**.

HOW WAS IT DETECTED?

With its prediction feature the **MyRBQM® Portal predicted an outcome**, which was how many patients would likely have withdrawn their informed consent **based on a few data early in the study**.

HOW WAS THIS RISK ADDRESSED?

By implementation of KRIs:

- The KRI = number of patients lost to follow up / informed consent withdrawn was used to **trigger an alert** the moment the ratio between the number of patients in the study and the **number of patients lost to follow up and/or informed consent withdrawn exceeded 1%**
- In addition, the prediction feature was used to demonstrate that in **the worst case** – the number of informed consent withdrawn / lost to follow up **cases would be about 1300**

WHY…

MyRBQM® Portal was used?

- The organization could take appropriate mitigation actions and ensure that at least a follow up call with the patient could be established
- To ensure that the number of those particular drop out cases **remained at an acceptable level**, so that sufficient information about the outcome could still be collected for the analysis

Cyntegrity

Trust in Data

Cyntegrity Germany GmbH

Headquarters
Altenhöferallee 3
D-60438 Frankfurt am Main
o. +49 (0)6192-470-113-50

Office USA
220 Juana Avenue
San Leandro, CA 94577
o. +1 888.812.RBQM

Contact Us
post@cyntegrity.com