Welcome to the training on the TransCelerate approach to Risk-Based Monitoring. This course will take you through five modules of information to introduce you to the concepts behind risk-based monitoring, the TransCelerate Approach, some hands on exercises and some information to provide to sites as well on tips for transitioning projects and studies into the new model.
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As noted, the course information will be broken down into five distinct modules. While information may overlap, the intent is to individually explore the concepts, tools and implementation of evaluating risk and implementing management and monitoring techniques. Each module will consist of three to four key objectives for the learners. The modules are as follows:

Module 1- Introduction to Risk-Based Monitoring (RBM). In this module we will introduce the concept of RBM, how it varies from traditional monitoring approaches and why we are focusing on implementing this methodology. We will also introduce you to definitions and assumptions underlying the TransCelerate Position Paper: Risk-Based Monitoring Methodology that was published May, 2013.

Module 2- Methodology and Team Members. The focus of module 2 will be to further explore the TransCelerate Methodology, introduce the RBM toolkit, discuss RBM team responsibilities within a company, and describe the on-site, off-site, and central monitoring activities in study oversight.

Module 3- Risk Assessment. In module 3 we will be focusing on how to identify and quantify risk and will address one of the key measurement tools, the RACT, in detail.

Module 4- Risk Management. Module 4 will further address risk management and how to define critical Risk Indicators and Thresholds in decision making. We will also talk about risk mitigation plans, activities, and risk response.

Module 5- Transitions. The focus of the final module is on the application and considerations of RBM plan implementation. In this section we will address a practical approach to implementation and management, as well as how to transition projects, protocols and sites into the RBM model.
Module 1

INTRODUCTION TO RISK-BASED MONITORING (RBM)

Our first module is an introduction to Risk-Based Monitoring, which we will refer to as RBM.
As previously stated, each module will have some key objectives. At the conclusion of this module, learners will be able to:

1. Describe the Risk-Based Monitoring (RBM) Model as compared to traditional monitoring methods
2. Explain the rationale for Risk-Based Monitoring (RBM)
3. Describe TransCelerate’s key assumptions and concepts

This course was designed to be very interactive and as we move through the materials we will ask you to challenge yourself and to share your knowledge. Many of you already probably know quite a bit about RBM and some of the questions we will be asking are designed to help you determine if there are areas in which you still have questions.
As noted, we will be asking a lot of questions and pushing you to challenge yourself and test your knowledge. Let’s go ahead and begin with a true/false question.

ANSWER: False

RBM is not fixed, it is an adaptive approach to clinical trial monitoring that directs monitoring focus and activities to the evolving areas of greatest need which have the most potential to impact subject safety and data quality. Each clinical trial requires its own customized monitoring approach to ensure that risks are minimized and sponsor responsibilities are satisfied. It is based on awareness that different trials, different data points/processes, and different sites represent differing risks to the product’s development.

Note to speaker: The answers are listed on each slide following the true/false question and may be hidden if you choose not to use.
As noted, we will be asking a lot of questions and pushing you to challenge yourself and test your knowledge. Let’s go ahead and begin with a true/false question.

ANSWER: False

RBM is not fixed, it is an adaptive approach to clinical trial monitoring that directs monitoring focus and activities to the evolving areas of greatest need which have the most potential to impact subject safety and data quality. Each clinical trial requires its own customized monitoring approach to ensure that risks are minimized and sponsor responsibilities are satisfied. It is based on awareness that different trials, different data points/processes, and different sites represent differing risks to the product’s development.
ANSWER: True

SDV can be thought of as a “transcription check” to ensure that data in source documents are accurately transcribed into the CRFs. One aspect of the TransCelerate risk-based monitoring methodology is a reduced reliance on SDV as a means of assuring patient safety and data quality. The TransCelerate Position Paper further defines another concept called Source Data Review, or SDR, which we will discuss in detail later.

Note to speaker: The question is meant to allow the audience to gauge their understanding of the TransCelerate paper (if they did the pre-course work and read it) and to generate some interest in the material to be further clarified later. All companies will have different definitions or understanding of SDV, this question is focused on the TransCelerate approach as it will be defined later in the presentation.
ANSWER: True

SDV can be thought of as a “transcription check” to ensure that data in source documents are accurately transcribed into the CRFs. One aspect of the TransCelerate risk-based monitoring methodology is a reduced reliance on SDV as a means of assuring patient safety and data quality. The TransCelerate Position Paper further defines another concept called Source Data Review, or SDR, which we will discuss in detail later.

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ANSWER: True.

FDA Final Guidance on RBM identified the following as characteristics of the clinical trial monitoring:

- Wide range of monitoring practices
- Periodic, frequent visits with 100% source data verification
- Reactive and premised on retrospective detection of errors
- Oversight efforts not commensurate with risks
- May not optimally address significant risks to trial integrity, particularly systemic error
- Resource intensive
ANSWER: True.

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- Wide range of monitoring practices
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- Reactive and premised on retrospective detection of errors
- Oversight efforts are not aligned with risks
- May not optimally address significant risks to trial integrity, particularly systemic error
- Resource intensive

This is True.
Risk-Based Monitoring, or RBM, is not a new concept and there has been a significant amount of discussion around the topic for the past several years. Many sponsors and CROs have adapted to a type of RBM based on recent regulatory guidance documents circulated in the US and in Europe. In this module we will compare the RBM model to traditional monitoring methods in order to better understand the intent of RBM.
The term “monitoring” is used very loosely in the industry and has come to refer to a number of different activities conducted by sponsor and CRO personnel in clinical trials. We have seen it in the context of an individual that goes to the site to review data, or when data is checked by data management. Medical monitors and/or pharmacovigilance groups review safety data and this may be referred to as monitoring. And finally, there may be Quality Control monitoring by Sponsor and CRO internal processes and systems. However, for the purposes of our RBM discussion, the focus is on updating and revising “traditional” site monitoring approaches.

**Note to speaker: The next slide will ask the audience to tell us how they might define “traditional” site monitoring.**
Note to speaker: See Train the Trainer’s Manual for ideas on how best to solicit and track audience feedback. The intent of the question is to ensure the audience comes to a general consensus on what traditional monitoring means as everyone may have a slightly different interpretation and this should lead to some discussion. Some possible answers and examples you can provide are: Monitoring On-Site, monitoring on a set schedule, source verifying all data on site. The next slide will further define On-Site Monitoring which should be considered general traditional monitoring practice in the industry (although some companies may have taken a different approach, monitoring every 4-6 weeks, verifying 100% source documents on site has been very typical).
We generally think of traditional site monitoring as an approach consisting of monitoring all data, in person, on site. Traditional on-site monitoring can be defined as an in person evaluation carried out by sponsor or CRO representatives at the location where the study is being conducted. The visits are generally conducted based on a set visit window schedule such as every four to six weeks and all data is source verified 100% regardless of the type of study, safety risks, phase of the study, stage of the study, or experience of the individuals conducting the study.

On-site monitoring is conducted to identify missing data in source records and data entry errors in case report forms, assess compliance with protocol and investigational product accountability, and to evaluate investigator supervision. Remember that we were monitoring before there was technology, so there was little choice in the approach we could take to review the data other than reviewing it on site.

So, if RBM is an approach that updates our concept of monitoring from the “traditional” approach, how are they different?

While traditional monitoring is conducted in a “one size fits” all schedule and approach (every site is visited every 4-6 weeks), RBM customizes the monitoring approach to each individual trial based on risk assessment to identify potential issues.

RBM makes use of all available technology to allow sponsors/CROs to supervise study conduct without having to be at the site location.

RBM involves many different functions and roles of the sponsor/CRO, not just Clinical Research Associates or Monitors. It includes a recognition that monitoring is a cross-functional responsibility.

And finally, as opposed to depending primarily on activities conducted at the site (on-site monitoring), RBM relies more heavily on central and off-site monitoring activities. Let’s look next at what is meant by central or off-site monitoring.
As technology has evolved we have been enabled to conduct less on-site monitoring and focus more on centralized and off-site monitoring techniques. Central monitoring involves a review of centralized data not just reviewing data from a central location. Off-site monitoring (sometimes called remote monitoring) is an evaluation carried out by sponsor personnel or representatives at a location other than the investigative site.

Both of these techniques may be used to check that data is consistent and complete, identify unusual distribution of data, identify higher risk sites to target additional monitoring, and to ensure routine review of data is completed in real time. In other words, we can do a significant amount to be proactive in addressing issues before ever going on site and identifying study risk factors and potential indications of risk.

Ensuring that data is consistent and complete and identification of unusual distributions of data can be realized through analytics and visualization of data across the study, across regions, across a site and across a patient. Also, in order to be able to ensure that data is consistent and completed, there will need to be emphasis on the ability to integrate data from disparate sources.

Central monitoring may be carried out by the same individual that would conduct on site monitoring such as a Clinical Research Associate or Clinical Monitor, or by other functional roles such as a data manager or statistician.
According to data from the Clinical Trials Transformation Initiative, even though many sponsors have access to centralized data, 33% or fewer sponsors use centralized data monitoring to guide, target, or replace site visits. So this leads us to considering further changes to our monitoring approach to make better use of technology and our resources.
In addition to being able to review data from a remote location, we are further adapting our processes to work smarter and focus on what really matters instead of trying to look at everything. RBM provides sponsors with an ability to evaluate and plan for risks before a study starts and continuously adapt monitoring activities to areas that have the most potential to impact patient safety and data quality.

An RBM approach may utilize a variety of monitoring types, such as on-site and central monitoring, to fit the needs of the program and individual studies, and even to manage each site. The process includes three key ideas.

First, the sponsor assesses the risks at the program, protocol, and site levels. Then the sponsor determines the Critical Variables (Critical Data and Processes) for the trial.

Once the Critical Variables are identified, it is important to know what to look for as an indication of the risk turning into an actual issue, these are called Risk Indicators and Thresholds to determine what type of action needs to be taken.

The last step is to clearly define the monitoring approach within an Integrated Quality Risk Management Plan or IQRMP which includes various functional plans (e.g. the Monitoring Plan, Data Management Plan). We will discuss all of these steps in detail later, but the take away message is that risk must be assessed, Critical Variables identified, and a plan documented for addressing risks that may include a change in
the monitoring approach.
So let’s see what you think. Based on our experiences in the industry and the definition we just discussed for RBM, can you identify at least four differences between traditional monitoring and RBM?

**Challenge Yourself- Traditional Monitoring vs. RBM**

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<thead>
<tr>
<th>Traditional Monitoring</th>
<th>RBM</th>
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<td>1.</td>
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*Can you identify four differences between traditional monitoring and RBM?*

**Note to speaker:** Allow group to come up with potential ideas on what might differ in RBM based on the definition provided on the last slide. The answer key is on the next slide and may be hidden if you choose not to use it.
## Answer Key - Traditional Monitoring vs. RBM

<table>
<thead>
<tr>
<th>Traditional Monitoring</th>
<th>RBM</th>
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<tbody>
<tr>
<td>1. Fixed approach</td>
<td>1. Adaptive approach</td>
</tr>
<tr>
<td>2. Reactive</td>
<td>2. Proactive</td>
</tr>
<tr>
<td>3. On-site Monitoring</td>
<td>3. On-site, Off-site, and Central Monitoring Activities</td>
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<tr>
<td>4. Paper based</td>
<td>4. Technology based</td>
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Answer Key
Challenge Yourself

Which of the following statements are true when discussing the concept of centralized monitoring? (select all that apply)

A. Defined as a remote evaluation carried out by sponsor personnel or representatives at a location other than the investigative site.

B. Used to identify unusual distribution of data.

C. Used to identify higher risk sites to target additional monitoring.

D. Used to ensure routine review of data in real time.

So, let’s see what you’ve learned so far. [Read slide]

ANSWER: All statements are true definitions, potential uses, and/or appropriate applications of centralized monitoring.

Note to speaker: Answer key is on the next slide if you would like to show it
So, let’s see what you’ve learned so far. [Read slide]

**ANSWER:** All statements are true definitions, potential uses, and/or appropriate applications of centralized monitoring.
Now that we understand how RBM differs from traditional monitoring, what is driving the adoption and move towards risk-based monitoring in the clinical trials industry?
As you can see based on the timeline on the screen, there have been a number of actions taken that are directed towards modifying our monitoring approach.

The 1988 FDA Guidance on Monitoring of Clinical Investigations stressed personal contact between the monitor and investigator. This was withdrawn by FDA in 2010 as evidence grew for the need of a shift in our approach to monitoring.

The 1996 ICH E6 (GCP Guideline) provided flexibility in how trials are monitored; centralized monitoring alone appropriate only in exceptional circumstances.

In 1998 there was an FDA Guidance issued in which the agency suggested more flexibility in what’s considered acceptable monitoring and provided data standards for studies with minimal on-site monitoring.

In 2007 at the IFPAT meetings (GMP Manufacturers), Janet Woodcock, Chief Medical Officer of CDER/FDA talked about the intersection of Process Analytical Control (PAT) in GMP and Quality by Design (QbD) in clinical development. Additionally, Helen Winkle (Director, Office of Pharmaceutical Science, CDER/FDA) gave a presentation on QbD in September 2007.

In 2009 CTTI was formed with the mission to identify practices that through broad adoption will increase quality and efficiency of clinical trials. 120 members from FDA, academia, industry, government, and patients/investigators participating. One of the earliest projects was to identify current monitoring practices and apply Quality by Design (QbD) principles to clinical trials.

Between 2009 and 2010 we saw more FDA Warning Letters to Sponsors with findings of failure to adequately monitor clinical investigators. This finding includes improper selection of investigators who subsequently fail to meet GCP requirements, failure of monitors to find protocol compliance issues, and/or failure of sponsors to promptly take actions to correct deficiencies when identified through monitoring.

In 2011 two draft documents were issued from the FDA and the EMA, and can be considered a clear indication that we are being encouraged to modify our practices.

In 2013, the FDA finalized its guidance document.
Some of the documents mentioned on the timeline include the Clinical Trials Transformation Initiative, the FDA Guidance for Industry, A Risk-Based Approach to Monitoring, and the EMA Reflection Paper on Risk Based Quality Management in Clinical Trials. These three documents provide a framework for some of the concepts that are driving the industry to change. We will not be spending a great deal of time discussing these documents, but it is important to understand that there is a regulatory drive to adapt our practices according to risk and move away from the idea of “one size fits all.”

The CTTI project focused on gathering data, confirming the current industry approaches to monitoring, and verifying that our primary focus should shift from post-hoc inspection to incorporation of quality into the scientific and operational design of a trial. CTTI stated there is not one single approach that is appropriate or necessary in all circumstances, and that the monitoring approach for a given clinical trial should be tailored to the needs of the trial and may combine several methods of monitoring. Furthermore, the CTTI participants agreed that the quality of the protocol is likely an important determinant of the quality of monitoring.

The FDA Guidance was intended to assist sponsors in developing risk-based monitoring strategies and plans tailored to the specific human subject protection and data integrity risks of the trial. It included a focus on critical study parameters, encouraged the use of a combination of monitoring activities and promoted greater reliance on centralized monitoring practices, where appropriate.

The EMA Reflections Paper focused on Risk Based Quality Management through assessment of the use of risk identification and control. The key points were to develop a plan at the start of a program, adapt protocol by protocol, build on experience gained with each study and build on technical, regulatory, and other advances.
Discussion Point

Take a couple of minutes and see if you can name at least three reasons why the industry’s traditional monitoring approach may need to be changed.

Note to speaker: Possible solutions/answers are on the next slide. Wait until participants generate/provide some of their own ideas before displaying next slide. Suggestion for activity is to have each person write down their three ideas and then share with the group or write up to three ideas on individual sticky notes and they are all passed forward for speaker to read.
From the sponsor perspective, there may be multiple and varied reasons for changing our approach to monitoring. The rationale for change may vary depending upon everything from the size of the sponsor to the type of study being conducted.

The endorsement of a change in monitoring by key regulatory authorities serves as a rationale for looking at monitoring in a different way. These regulatory authorities are communicating that monitoring can and should be designed and customized to meet the specific needs of the program and study.

Some challenges facing the industry, such as protocol complexity, focus on cost-benefit ratio, and limited resources, just to name a few, are also serving to help drive a shift in our monitoring philosophy.

Finally, changing our monitoring approach potentially provides benefits such as improved risk mitigation, adapting monitoring to the needs of the trial or site, and more effective use of current state technology.
“Application of risk based quality management approaches to clinical trials can facilitate better and more informed decision making and make the most use of the available resources.”

EMA Draft Reflection Paper on Risk-Based Quality Management in Clinical Trials, August 2011

This quote from the EMA paper stresses that applying risk based quality concepts to clinical trials can help us maximize the use of resources and result in better, more informed decisions and conduct of our trials.
Take a look at this question in regards to the factors contributing to a focus on RBM.

ANSWER: C is not part of the rationale or focus for RBM. Roles and responsibilities may change but this is not why RBM is being implemented.

Note to speaker: Answer is on the next slide if you would like to show it.
Take a look at this question in regards to the factors contributing to a focus on RBM.

ANSWER: C is not part of the rationale or focus for RBM. Roles and responsibilities may change but this is not why RBM is being implemented.
So, you may be wondering – what exactly is TransCelerate? Why did TransCelerate develop a RBM methodology? And what are the core concepts of that methodology?
You may have already heard quite a bit about the TransCelerate initiative in the news. We will be spending the rest of the presentation expanding upon one of their key initiatives, developing a model approach for RBM.

**Note to speaker:** The TransCelerate detail slides may be hidden depending on your audience and their background. Slides have been left in the presentation in the event you would like to use them.
TransCelerate BioPharma Inc. is an independent non-profit organization focused on accelerating the development of new medicines.

- TransCelerate was founded with a mission to identify and solve common drug development challenges with the end goals of improving the quality of clinical studies and bringing new medicines to patients faster.
- TransCelerate was launched on September 19, 2012. At that time, the organization chose to focus on five initiatives related to clinical trials – designed to increase efficiency, reduce costs and enhance patient safety.

Note to speaker: The TransCelerate detail slides may be hidden depending on your audience and their background. Slides have been left in the presentation in the event you would like to use them.
As you can see a number of industry leaders are members of TransCelerate and have contributed to the improvement of the way we do things in the industry. This is an unprecedented industry collaborative effort that is fully supported and encouraged by the FDA. For example, FDA representatives reviewed the RBM position paper and provided feedback prior to its publication and release.

Note to speaker: The TransCelerate detail slides may be hidden depending on your audience and their background. Slides have been left in the presentation in the event you would like to use them.
As you can see, this is an industry wide initiative and not just a sponsor or CRO driven initiative. Involved parties include regulatory bodies, industry initiatives, patient advocacy, and research and CRO community organizations.

**Note to speaker:** The TransCelerate detail slides may be hidden depending on your audience and their background. Slides have been left in the presentation in the event you would like to use them.
TransCelerate BioPharma Inc. developed a methodology that shifts monitoring processes from an excessive concentration on Source Data Verification to comprehensive risk-driven monitoring.

The TransCelerate RBM team started from an understanding that by building quality and risk management approaches into the scientific design and operational conduct of clinical trials, risks can be mitigated and issues can be detected early or prevented entirely.

Additionally, the TransCelerate partners recognize that although current on-site monitoring practices do provide a level of control, advances in risk-based approaches and technology provide an opportunity for a more holistic and proactive approach.

This philosophical shift in monitoring processes employs Centralized and Off-site mechanisms to monitor important study parameters holistically and uses adaptive On-site Monitoring to further support site processes, subject safety, and data quality. Through modernization, including use of technology enablers, efficiencies can be gained without impacting subject safety by implementing quality risk management approaches to clinical trial oversight.
To better understand the impact of existing SDV approaches on overall data quality, TransCelerate member companies evaluated data discrepancies for completed studies to determine the rate of queries identified via SDV as compared to all queries for a study. Those queries were then further assessed to determine what percentage of SDV-generated queries were found in Critical Data.

Nine sample studies from 6 member companies were analyzed. Despite variability in the way companies manage their data review activities, all companies were similar in the low rate of SDV-generated queries. The average percentage of SDV queries generated was 7.8% of the total number of queries generated. The average percentage of SDV queries that were generated in Critical Data as represented as a part of the total number of queries was 2.4%.

The rate of SDV-only discrepancies in Critical Data (2.4%) suggests that SDV has a negligible effect on data quality. These data help support the TransCelerate methodology which recommends shifting the on-site monitoring focus from 100% source data verification (SDV) to a risk-driven level of SDV and source data review (SDR).

**Note to speaker:** The Value of SDV slide may be left hidden depending on your audience and their background. Slide has been left in the presentation in the event you would like to use it.
There are 9 assumptions underlying the TransCelerate monitoring methodology promoted in the May 2013 position paper.

1. Central and off-site monitoring form the foundation of monitoring, complemented by targeted, risk-based on-site monitoring activities.
2. Monitoring activities should be responsive to issues/risks identified and increased in a targeted, temporary manner. The goal should always be to return to the baseline level of monitoring. Root cause analysis is critical to prevent identified issues from recurring.
3. Monitoring methodology and activities must be tailored to the technology available for the program, study, and/or site.
4. Since central/off-site monitoring is the foundation of sponsor oversight, timely data entry and query resolution are critical. Sponsors should establish expectations in site contracts.
5. The IQRMP is a living document and should be revised/amended throughout the study as needed in response to changes in the study, identified risks, etc.
6. It is acceptable to define risk-based monitoring standards in associated SOPs rather than within each study-specific IQRMP.
7. The defined methodology is applicable to all phases of studies, types of studies, and stages of clinical trials.
8. Communication plans should be tailored or customized in whatever way is necessary to maximize effectiveness.
9. Risk assessment should be completed prior to protocol and CRF finalization as a means to address and minimize risks before the trial starts. Then, monitoring strategies can be used to oversee and manage risks that cannot be prevented via protocol/CRF design strategies.
TransCelerate’s RBM methodology embraces the concept of building “Quality by Design” (QbD) into clinical trials starting with protocol development and extending across all aspects of a trial. A well-written protocol and CRF are important facets which may impact the success of the RBM methodology.

Quality refers to the ability to effectively and efficiently answer the intended question about benefits and risks while assuring subject safety. Decisions are supported by quality data which is not considered error-free data, but rather fit-for-purpose data that sufficiently supports conclusions equivalent to those derived from error-free data.

QbD includes a focus on identifying key risks to subject safety, data quality, and GCP/regulatory compliance. QbD also involves the application of an efficient monitoring approach to rapidly detect and correct issues while the study is ongoing and developing a quality risk management plan that focuses on factors that are at high risk for generating errors.

It is also critical to apply monitoring strategies that are tailored to risks, permit timely oversight (through central/off-site monitoring and use of technology), and are focused on Critical Processes and Critical Data. On-site interventions should be targeted in nature.

In summary, QbD provides a basis for implementation of RBM and is a fundamental principal of the TransCelerate methodology and tool application as we will discuss in later modules.
As you can see, Building QbD is the first step in the TransCelerate approach. TransCelerate developed a model approach for RBM that can be adopted for any type, phase, and stage of trial. The TransCelerate RBM methodology improves efficiency by changing the focus to Central or Off-site Monitoring activities that are intended to identify potential issues sooner than a monitoring strategy that relies primarily on site monitoring visits.

TransCelerate’s RBM methodology uses quality risk management as a foundation in ensuring subject safety and data quality through the implementation of the following: (1) building QbD into trials, (2) early and ongoing risk assessment, (3) a focus on Critical Processes and Critical Data, (4) use of Risk Indicators which are Critical Data and other study variables to be assessed (in many cases by comparing across program / protocol / country / site) and Thresholds, defined as the level, point, or value associated with a Risk Indicator that will trigger an action. Details surrounding the Risk Indicators and Thresholds will be documented in the various study plans, which fall under the Integrated Quality and Risk Management Plan, or IQRMP, (which we will discuss in detail in a later module) and (5) adjustment of monitoring activities based on the issues and risks identified throughout the study.

By monitoring available data Off-site or Centrally, On-site Monitoring can be targeted to activities which cannot be assessed remotely. Additionally, TransCelerate has adopted the term Source Data Review (SDR) which describes review of source data for protocol compliance, quality of documentation, as well as site processes in contrast to transcription checking, referred to as Source Data Verification (SDV).

The TransCelerate RBM methodology is aligned with the QbD paradigm, and with the monitoring and study oversight expectations of health authorities; when RBM methods are
used, applicable ethical standards, subject rights, laws and regulations are expected to be followed. Further, TransCelerate’s methodology is being developed concurrent with the transition to risk-based inspection processes by health authorities.
In future modules, we will be further breaking out how RBM should be implemented, what tools can be used and how risk assessment should be completed. We will define key Risk Indicators and address tasks to be performed on site or centrally. We will also focus extensively on quality plans and Risk Indicators for adjusting the type and amount of monitoring based on metrics.
As we move through the remaining modules in our presentation we will be using a number of terms from the TransCelerate Position Paper. To make sure you are comfortable with the definitions, go ahead and match the term with the correct definition on this slide and on the next one. If you are not sure of a definition, they can be found in the TransCelerate Position Paper on pages 13 and 14.

**ANSWERS:**

1 is B
2 is C
3 is A
As we move through the remaining modules in our presentation we will be using a number of terms from the TransCelerate Position Paper. To make sure you are comfortable with the definitions, go ahead and match the term with the correct definition on this slide and on the next one. If you are not sure of a definition, they can be found in the TransCelerate Position Paper on pages 13 and 14.

**ANSWERS:**

1 is B
2 is C
3 is A
Let’s check our understanding of a few more definitions. Again, if you are ever lost on a term or definition, these can all be found in the position paper.

**ANSWERS:**

4 is B  
5 is D  
6 is A  
7 is C
Let’s check our understanding of a few more definitions. Again, if you are ever lost on a term or definition, these can all be found in the position paper.

**ANSWERS:**

4 is B  
5 is D  
6 is A  
7 is C
In summary, the RBM Model varies from traditional monitoring methods through using a combination of On-site, Off-site, and Central Monitoring and risk assessment to identify critical study points and plan an individualized approach for monitoring based on the risks of the study.

The rationale for RBM is based on changes in the industry driven by protocols, technology, and resources.

TransCelerate’s key assumptions and concepts include a focus on a proactive approach to monitoring through quality protocols and case report forms, and shifts monitoring processes from an excessive concentration on SDV to comprehensive risk-driven monitoring based on risk assessment, mitigation and management.
Links

TransCelerate Home Page
http://www.transceleratebiopharmainc.org

FDA Guidance for Industry Oversight of Clinical Investigations - A Risk-Based Approach to Monitoring [Final].

EMA Reflection Paper on Risk Based Quality Management in Clinical Trials (EMA/INS/GCP/394194/2011).

Clinical Trials Transformation Initiative. Effective and efficient monitoring as a component of quality.
https://www.ctti-clinicaltrials.org/project-topics/study-quality/effective-and-efficient-monitoring-as-a-component-of-quality

The links for the documents referenced in this portion of the presentation are included on this slide for your reference.
Any questions?