Manage Thinking & Writing at   
Population Health Partners

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# Introduction

This document supports the integration of a managed thinking and writing process within Population Health Partners (PHP) as a routine approach to complex documents. These processes are aimed at ensuring the right message and supporting data are delivered to the right person, at the right time, in the right way so that they can make the right decision, and take action efficiently based on the documents we provide.

The process follows the principles of good communication. In addition, the process uses the specific tools: MIRS, prototyping, document standards, and reviewing instructions which are summarized in this document. In general, the process encourages writers to create documents that are message-driven and issue-orientated and to put the main messages up front using deductive logic and structure. Deductive logic supports purposeful and persuasive business communication where the reader clearly understands what they are reading and why.

We will use internal (or occasionally external) facilitators to integrate these managed thinking and writing skills into our firm. Our overall goal however is to provide these skills to teams for their own use and measurement of results. Some team members may be trained as accredited and recognized facilitators.

# Ownership and Responsibilities

At PHP, documentation results from a collaborative process, and in that sense all employees are shareholders of the corporate messages. However, for each document authorial responsibility needs to be defined; i.e., the responsibilities of the lead writer versus key content contributors versus reviewers. These documents are likely to relate to our portfolio companies, and so the overall ownership may lie with a full-time member of the relevant company, or alternatively a Global Innovation Group member (GIG), albeit PHP might provide the writing expertise.

# The MIRS Process and Tables

## 1. Overview of MIRS

PHP has endorsed MIRS as the basic intellectual process/tool underscoring all corporate documentation. MIRS tables have proved themselves to be very effective in support of pharmaceutical developments. They are flexible and highly adaptive. They can be used everywhere from New Companies to designing programs, analyzing markets, through development and delivery steps even including investor relations or corporate communications press releases. Indeed, their value is limited only by the scope of imagination by the people who use them.

MIRS is both a process and a product. The process involves team ideation, defining and organising the main product **messages** (e.g. development conclusions, interpretations, label statements, promotional claims) and their associated **issues** (e.g. potential authority questions, objections, threats, adverse findings, inconsistencies) and then addressing each issue with a specific **response** (e.g. a scientific rationale based on known or published information, proposal for a new study or study design) and identifying the **support** (source of data/information which supports the message and/or response, e.g. study reference or other data source, publication). These are created as a table that includes cross-functional input and links to provide a common repository for the key features of the product and how they can be presented and supported.

MIRS tables provide an ongoing record of the current known information on the product as well as recording strategies for addressing concerns. In addition, MIRS tables identify messages that are yet to be proven but that represent the target for product development. By proactively identifying issues and the necessary support, the MIRS process can ensure that study designs and data collection are guided by the goals of development.

The content of the MIRS tables can be modified and updated as the project progresses and ultimately can serve as a data base for providing the content for internal presentations, regulatory and professional presentations, publication plans, business plans, regulatory strategy, protocol design, regulatory documents etc.

## 2. What is a MIRS Table?

A MIRS is table, sometimes called a MIRS Matrix, of information generated about a drug development. It is an intellectual snapshot of product knowledge at a particular moment in time. *A MIRS is not an end product; it is one step in the process of creating a document or other communication product* (See Appendix A).

MIRS is an acronym for “Messages”—“Issues”—“Responses”—“Support.” PHP often adds a fifth column (“Action”) to assign responsibilities, or it includes Actions as part of the Support column. Sometimes it is helpful to add “Rationale” to the title of the third column to prompt articulation of the scientific argumentation underpinning the message.

A blank MIRS Matrix is a simple table:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ref. No. | Message | Issue | Rationale/Response | Support | Action |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

A group of team members will complete the table by filling the cells with relevant information:

**Messages** are positive statements (such as label claims, marketing messages etc)

**Issues** are obstacles that stand in the way of the messages’ authenticity or impact

**Responses** represent the logic that we use to overcome the issues and/or to substantiate the message.

**Support** comprises the hard data that will support the logic and prove the messages

**Actions** are a record of “to-do” tasks and other notes.

MIRS can be constructed in many ways, but some are more efficient and lead to better outcomes:

* MIRS can be created (or seeded) by an individual then circulated for “fleshing out” and commentary.
* Projecting the MIRS via a PC and projector can be effective with relatively small groups (4-5 participants)
* For larger groups, the use of Sharpie pens, flipcharts and Post-it™ notes works well
* For geographically distributed teams, use of collaboration tools such as [Mural](https://mural.co/) works well.

Once the MIRS has been created, it needs an “owner,” someone to take responsibility to drive reviews, updates, and applications. The team also needs to define a review and updating process. An example MIRS table with format annotations to help guide its use is given in Appendix B.

## 3. Types of MIRS

There are at least three distinct types of MIRS used at PHP (for samples of different kinds of MIRS, see Appendix C):

* Product or Program MIRS
* Document MIRS
* Legacy MIRS/Due Diligence MIRS

A **Product or Program MIRS** is an overview of the intellectual knowledge of a development team at a given moment in time. It is used as a source document to record results and understandings as they develop. The MIRS should capture information that is not yet proven so that studies are designed to support messages and address issues. These MIRS should be updated as new knowledge becomes available.

For a Product MIRS, PHP uses the categories from the PHP Development Process: Efficacy, Safety, Dose, Risk/Benefit, Quality and Cost/Performance (Value).

A Product MIRS should contain **Links** that show where product knowledge is connected to other places in the MIRS. For example, many of the messages in Efficacy and Safety will connect clinical messages with non-clinical messages. The linking process will become particularly important if Product MIRS are used for Prototypes of NDA documents.

*Purpose for Product MIRS:* It is used as a source for content for all major internal and external communication about the product. The content is used to populate the Prototype (See Prototyping Section).

A **Document MIRS** is a snapshot of the knowledge necessary to create one communication product: a document, a slide set, a presentation, etc. Sometimes this MIRS needs to be generated by those involved in the creation of the Product as well as those responsible for the document. If a Product MIRS is available, then the Document MIRS is created by importing MIRS from the Product MIRS and the reviewing, refining, editing and adding detail as necessary to achieve the purpose of the document and meet the specific needs of the audience.

*Purpose for Document MIRS:*  It is used a source for the content of the prototypes of one communication product – quickly

**Due Diligence/Legacy Document MIRS** can be used as part of the process followed when PHP acquires assets (products) during later stages of development when considerable portions of development have been undertaken and/or completed, e.g. technical (CMC), preclinical (pharmacology, ADME, toxicology), early clinical development (e.g. clinical pharmacology). Focussed and effective review of these areas is important to:

* Ensure PHP rapidly understand and integrate fully the product knowledge generated to date into ongoing development and future marketing activities
* Identify where the information supports Product Messages and Responses to Issues
* Identify any specific Messages and Issues arising from within the specific development area
* Identify additional Responses and/or Support for Issues and responses in other areas of development
* Identify gaps in knowledge which require additional studies or other responses

*Purposes of Legacy and Due Diligence MIRS:* These enable PHP to complete development activities (if appropriate) and prepare regulatory dossiers supporting efficient product approval and to identify potential features and benefits of the product which support current or future product positioning and development activities.

## 4. MIRS Process Description

### Conducting a MIRS Session

At PHP creating a MIRS is a group process. Although it’s possible and seemingly efficient for one person to produce a MIRS table, this process in seclusion leads to the isolation of knowledge in the hands of the few. In addition, it puts the project at risk for delays because of lack of scientific consensus, or to error because of non-reviewed knowledge.

Typically, therefore, creating a MIRS matrix is a collaborative activity - although if circumstances dictate then it can be constructed in any number of ways. Participants convene in real time and in the same place (although given collaboration tools and Zoom-conferencing, a MIRS session can occur with participants connecting from different global venues).

### The Basic Process

The basic process normally involves the use of flipchart paper and Post-it™ notes. For best results, a meeting facilitator skilled in the MIRS process is required. The facilitator will direct the participants on how to fill-in the matrix and ensure balance and challenge to thinking.

The process allows for an initial ideation period where ideas can be created, captured, shared and expanded – there is no editing at this point. Only once have all participants have had the opportunity to participate in this phase does the process move on to allow evaluation, prioritization, organization and refinement of content.

One method is to tape flipchart pages (lengthwise or landscape) to the wall of a meeting room and to draw on the grid lines and headings with a simple marker:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **M** | **I** | **R** | **S** | **A** |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

Using Post-it™ notes, participants can then begin to fill in the table. Some groups prefer to go horizontally and work through each message line by line as described below.

In the following representation, the **Message** column contains a single message, perhaps making an efficacy or safety claim, for example.

Working horizontally, the **Issues** column contains three issues that are standing in the way of the message. (Each issue is captured on a single Post-it™.)

Likewise, the **Response** column contains four responses or ways in which to redress the issues.

Finally, a single Post-it™ defines the support needed for the message, and a single note captures the **Action** item in the final column. Note that the number of Post-its™ represented below is arbitrary. A message may have multiple issues, or it may have none. However, all issues need responses, and messages and responses must have support.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **M** | **I** | **R** | **S** | **A** |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

Participants write their notes on Post-its™ and place them on the chart; the ideas contained on the notes can then be logically and strategically aligned. Building the MIRS proceeds line by line.

Another similar approach works vertically. Participants might be asked to write down all of the messages that define a given project, trial or development, then place them into the **Message** column.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **M** | **I** | **R** | **S** | **A** |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

Once all of the draft messages are captured on the chart, then the participants can go back and reorder the notes according to logical structure or strategy, such as arranging safety or efficacy messages together or going from key critical messages to non-critical ones, etc.

Subsequently, once the **Message** column has been put in place, the participants can then work to complete the table:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **M** | **I** | **R** | **S** | **A** |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

Not every message requires an issue and so forth; however, having too many blanks may suggest that the thinking is faulty somewhere.

Some groups of participants doing MIRS prefer to start with the **Issues** column first instead of ideation from messages. Either way will work.

Developing the MIRS horizontally is especially good when a limited amount of time is involved. That way, participants can work through as many lines as time will allow and can quickly pick up the logic at a future meeting. Working vertically allows everyone in a group to participate and it tends to be more comprehensive but sufficient time needs to be available to ensure that the MIRS contains sufficient detail, especially in the response and support columns.

### Variation

The MIRS process is very flexible, so there may be much variability in how sessions work among various groups and for different purposes. For example, an alternative to using Post-its™ is to use a platform such as Mural to enable real-time collaboration for those geographically distributed. While this approach may be relatively easy logistically, it can be less dynamic than the paper approach. In addition, this approach tends to allow more verbal personality types to dominate the discussion. Capturing the flow of the discussion can also be an issue. Generally, due to distraction, the person operating the keyboard can not participate in the discussion; indeed, only the most practiced, polished and skillful facilitators have success doing the typing/phrasing as well as moving the meeting ahead at the same time. An inexperienced typist might slow down the progress of the meeting unbearably.

### Time Commitment

A MIRS matrix session can be as long or as short as required. Normally, the session can run from an hour or two up to an entire day or more depending on the intensity and importance of the discussion, although having frequent short sessions (up to a half-day) may be more desirable than creating MIRS matrix in a single marathon session - as structured strategic thinking can be quite demanding. Creation of a Project or Program MIRS at the outset needs a 2-day meeting in order to capture the breadth and detail necessary. Having an overnight break also allows for time for reflection and further thought which often catalyzes decisions and issue resolution.

### Follow-up

Normally, a MIRS session will produce a draft MIRS; that is, unless the participants are well-versed in the process and experienced, the information captured in the matrix will need refining and polishing. Hence, each MIRS needs to have a designated “driver” to ensure that the completed MIRS is logical, comprehensive, and applicable to its target, which is the creation of a development strategy, label, report, publication etc. The process works best when an experienced MIRS facilitator works with one or more of the participants designated as "corporate or scientific partner(s)" to prioritize, revise, and distribute the completed MIRS matrix.

### Points Worth Further Consideration

* For best results, use an experienced facilitator.
* Do your homework before the session. Come equipped with relevant information and supporting data.
* Ensure that the MIRS has a specific target, such as a defined publication, label, report, marketing strategy etc; otherwise, the discussion can become too general. And understand how to characterize the likely reader of the document.
* Know how the MIRS fits in with the project as a whole so as not to duplicate effort. Get all the right cross-functional expertise in the room.
* MIRS can be done via Zoom-conferencing, but all participates need to be able to see the matrix (via screensharing, or collaboration platforms such as Mural etc).
* Establish clear timelines, drivers, and applications and practice good meeting behaviors.
* Remember that the MIRS is a thinking process and not an end product in itself. It is a process tool that moves the critical thinking and shared knowledge of teams toward specific targets, such as documents or presentations.
* Consider having a basic structure to the meeting via use of a MIRS template. (Some facilitators prime the pump by conducting one-on-one interviews with team members or meeting with a subset of the whole group before the meeting to identify initial Messages and related Issues, which may then be inserted into the MIRS.)
* In addition to Messages and related Issues that the team may identify, be sure to address the key questions of drug development (list available to assist teams) so that nothing gets overlooked.
* Consider Issues from the perspective of an outsider, so use external sources such as Health Authority questions, Summary Basis of Approval for competitor products, questions from customers, Advisory Boards/Committee minutes etc to help make the Issues comprehensive. (Note: New members of teams often ask the best questions as they have no previous context.)
* Consider linking graphics (or presentation slides) that may be used in later documents (or presentations) to specific Messages or Issues identified in the MIRS. Use the Support column in the MIRS Matrix.
* Move the discussion toward a complete MIRS with descriptive Messages and related Issues, Responses, and Support.

### Create a Parking Lot

If an Action column is put in MIRS, the owner of each section of the MIRS or the overall MIRS owner must regular check for progress and the team must be informed and the MIRS updated. If this does not happen, then the Action column becomes another bureaucratic obstacle to moving forward.

## 5. Special Processes for a Legacy or Due Diligence review

These two approaches to due diligence and legacy products are each relevant and appropriate to assessing an asset and appropriately developing it to realise its maximum value. As an initial assessment of a product (e.g. due diligence, initial product strategy setting), the top-down approach provides a targeted and efficient method to analyze and assess legacy data. However, it does not analyze a program in detail and potentially significant issues not associated with pre-defined major product messages may be missed.

The bottom-up approach enables a broad and deep understanding that is essential ultimately to successfully develop a product, but it takes considerable time and effort to complete and so should be started as soon as possible after an asset is required.

When analyzing legacy data, MIRS tables can be used in two synergistic ways: Top-down and Bottom-up.

*Top-down analysis* is a targeted assessment process aimed at identifying whether the study program conducted either supports or refutes primary Product Messages that have already been defined (e.g. in a Product MIRS, Target Product Profile, Draft Labelling). In addition, this assessment should identify where there are significant Issues (including significant missing data) where the program would be expected to support a key product message (e.g. toxicology data to support a specific dose regimen).

In this case, the Product MIRS is being used as a tool to guide the assessor to specific parts of the program and assess the adequacy and robustness of the data therein.

*Bottom-up analysis* is where the MIRS process and tables are used to capture the key information about a product obtained during the analysis of the study program. This will define what messages can be said based on the data and where are the significant issues in the program as conducted. The MIRS tool provides a format to summarise and capture to what extent Messages can be supported and whether or not the Responses to Issues are adequate. To complete the MIRS requires that an analysis of the program be conducted by appropriate specialists as a team and the output of this analysis be shared with the broader project team to identify key links and prioritise and manage issues.

In this case the MIRS process is aimed at capturing the knowledge contained within the area of development to enable a broad understanding of the area, what needs to be done to complete the development to a defined standard (e.g. for US and EU regulatory approval), and where are the significant issues which require support from other areas of development.

## 6. Reviewing a MIRS

When a MIRS is first generated, it can be general and raw. Therefore, the MIRS needs to be reviewed and refined to be complete and logical. MIRS should be kept up to date when projects reach periodic milestones.

The MIRS owner should send a review request to, at the minimum, the key knowledge holders on the team. It’s also a good idea to involve key decision-makers in this review process. If they accept the product or document knowledge at this stage in the process, it will save review time and rewriting - even rethinking the project - at later stages.

In this initial review the focus should be on content issues, on content that needs to be added, deleted, or changed. At PHP reviewers should use the questions in the PHP Drug Development Process.

Since the production of an initial MIRS focuses on generation and creativity, it is important to conduct a MIRS review soon after the MIRS session:

* Messages should be prioritized and the Issues assessed for potential impact. Check to see if Messages belong in more than one section.
* Responses should provide the main logic and rationales to develop a Message or refute an Issue.
* Support should contain specific references to locations of data. As you write the documents, you will have to know the data and the sources.
* Link material from one section to that in another whenever there is an overlap, or one is needed to support the other.
* Avoid stylistic, grammatical, and punctuation comments.
* Avoid comments on format. The format will eventually be standardized.

If key team knowledge holders were not at the initial MIRS meeting, the MIRS owner should check with them and ensure that they understand how the MIRS provides content for the product program or document.

There should be a half-day review meeting to discuss comments and agree to changes. Participants should come prepared with specific comments either marked on the tables or added as revision marks. Once changes have been discussed and agreed, they will be made to the master versions. (See Appendix E.)

# 

# Prototyping

## 7. What is Prototyping?

Prototyping at PHP is the process of envisioning the outcome of a document at the beginning of the process of its creation.[[1]](#footnote-1) It involves creating a compelling and convincing document **structure** through creating and testing a variety of structures. In this way, the document helps to shape thinking as well as communicating knowledge. Prototyping allows the creation of complex documents, with multiple contributors, to be created efficiently and to speak with a single voice. But it is **not** a draft document.

At PHP we use the MIRS Matrix to supply the content of the different sections of a prototype. The MIRS also help contribute to the thinking as the prototype is created. We can prototype a document, presentation, marketing plan, investor pitch, investor meeting, or other communication event in such a way that messages and issues are effectively managed and structured into an emerging document.

Prototypes take the information from the MIRS and create an outlined visualization of a draft paper or presentation. Prototyping sessions are designed to lead group consensus regarding content, structure, length, space utilization and argumentation logic at a macro level before a writer creates a prose version of the project. An early outline might look like an outline of ideas placed on flipchart paper. Only a very advanced prototype begins to look like a finished draft.

## 8. What is a Prototype?

A document prototype is a model for a document. At any point in its refinement, the model is not 100% accurate, but it:

* Represents the best guess at that moment.
* Anticipates data and reserves space for their presentation in appropriate tables or figures.
* Establishes the arena for considering important information and drawing conclusions.

The final “prototype” is the completed document. It has the following characteristics:

* The organization makes information accessible.
* All potential issues have been identified and investigated.
* Study data have been analyzed.

Prototypes differ from ‘outlines’, ‘lists of contents’ etc in that in addition to listing key headings in order, they contain actual content, comments and notes to aid the writer, as well as represent the structure of the final document (e.g. number of pages – total and in each section; location and type of visuals). Most regulatory documents have ICH content pages and instructions which dictate the prototype structure. But again, don’t think “draft report” too early.

## 9. Conducting a Prototyping Session

Prototypes are visual representations of pages that allow writers to envision structure and logic flow. Once a MIRS has been created, polished, and refined, it gets put into an initial prototype, which goes through subsequent drafts and reviews until it becomes a finished document. While individuals can create prototypes by themselves, the process works best when done by the relevant group of people necessary to buy in to the structure, strategy, content, and argument of the document.

### The Basic Process

As with the MIRS process, creating a prototype at its most basic involves the use of flipchart paper and Post-it™ notes. As also with MIRS, a meeting facilitator skilled in the prototyping process is required for best results. The facilitator will direct the participants on how to build the initial prototype.

One method is to tape flipchart pages to the wall of a meeting room and to outline the various sections of the target document. Using Post-it™ notes allows for easy moving and restructuring of comments, ideas, and information - usually previous captured via MIRS.

|  |  |  |  |
| --- | --- | --- | --- |
| **Page 1** | **Page 2** | **Page 3** | **Page 4** |
| Summary  ¼ Page  Introduction  ¾ Page | Methods  ½ Page  Results | Discussion  1 Page | Conclusion  ½ Page |

The example above is for a short 4-page document. Prototypes can be as long or as short as necessary in order to budget the relative lengths of the document’s sections. A good initial prototype allow for group consensus on the development of the document (or slides etc): content, space allocation, visuals and so forth.

Of course, paper prototypes can involve regular size paper spread out on a table. The most important element of this early stage of prototyping is to be able to visually represent sections and ideas and to be flexible so that they can be re-arranged quickly and conveniently.

An electronic way to prototype is to convert a MS Word MIRS table to text and to list the MIRS information via bullet points as in the following example. The approach is readily done via an PC projector.

| Ref No. | MESSAGE | ISSUE | RESPONSE | SUPPORT | ADDENDA |
| --- | --- | --- | --- | --- | --- |
| 1 | There is no need to adjust doing of Angiomax in renally impaired patients because the 1.75 mg dosage is appropriate for everyone except for the patients on dialysis. | Creatinine clearance is not a good predictor of bleeding, so is there an alternative way to calculate clearance? | We need to change clinical practice. | The data support not adjusting the dose—not to adjust. *[Note: What specific data?]* |  |

***Introductory Section [1/2 page]***

### Main Message

There is no need to adjust doing of Angiomax in renally impaired patients because the 1.75 mg dosage is appropriate for everyone except for the patients on dialysis.

**Issue to Resolve**

Creatinine clearance is not a good predictor of bleeding, so is there an alternative way to calculate clearance?

**Response**

We need to change clinical practice. *[Note: We need to spell out the specifics here!]*

**Supporting Data**

The data support not adjusting the dose—not to adjust. *[Note: What specific data?]*

While building an initial prototype electronically may have some advantages, one major drawback is a tendency to limit group interaction and spontaneity. Logistically, it also depends on the skill of the person handling the keyboard and the meeting facilitator to drive the meeting effectively; otherwise, the prototyping session can bog down.

### Points to Consider

* Prototyping sessions should be dynamic and not static; that is, people should stand up, move around, and discuss concepts and strategies. They should try out different structures and not be afraid to move Post-it™ notes.
* The emphasis of prototyping is on visualizing structure, trying out argumentative/rhetorical strategies, and budgeting section and page lengths; therefore, it should not bog down in matters of phrasing or stylistics etc.
* Participants should come prepared by having reviewed MIRS and with relevant data and information in hand whenever possible.
* Documents structures need to reflect their Purpose, the Audience and their Content. Often there are guidelines (e.g. for regulatory documents), good examples (internal or external to PHP) and/or recent precedents which can help illustrate different strategies.
* Initial prototyping can be combined with MIRS via specialized MIRS templates, such as a Clinical Study Report MIRS; however, breaking down MIRS and prototyping into separate steps is preferred because MIRS can focus on content and prototyping on presentation.
* Follow-up prototypes should take on the appearance of drafts leading to a finished document.
* A with MIRS, a prototype needs a “designated driver” - normally, the primary writer of the document.
* Reasonable deadlines should be agreed on, set, and observed when creating MIRS, developing prototypes, and drafting documents through final review and acceptance.

## 10. Reviewing Prototypes

Reviewing prototypes helps to improve the document, and ensure that key contributors, reviewers and those responsible for sign-off, get the chance to add their comments and advice before a writer expends considerable time and effort in crafting text and adding large amounts of content, visuals etc.

The principles of reviewing prototypes and the use of Document Standards to ensure quality are the same as for reviewing drafts and final documents. These are discussed below.

# 

# Reviewing Documents

Drug development reporting must be done via persuasive documents grounded in sound science and medicine. Ideally, what the writers intend to communicate in these documents is what the readers perceive. In addition, these reports, whether written for internal or external readers, should have the following characteristics:

* Science as evidence
* Infallible logic
* Coherent story from the first page to the last
* Interrelated parts
* Reader-oriented structure (leading the reader or reviewer to critical issues and putting them into proper context in order to grasp key concepts quickly)
* A common vision that has guided research and development

These characteristics clearly overlap; it is impossible to separate one from another. For example, a coherent story is connected to both interrelated parts and to a common vision. Taken together, they reflect a larger issue - quality. We review documents to ensure that all PHP documents contain these characteristics.

## 11. Types of Reviews

Reviews can add extra value to the communication process when they are used other than just at the final stages of document production. The following are examples of such reviews:

* *Strategy reviews* where authors and reviewers reach an understanding of the document strategy and how to address in the text
* *Prototype reviews* to ensure major MIRS and document structures are appropriately addressed
* *Cross-document reviews* to uncover inconsistencies, for example CTD Overview documents (quality, nonclinical, clinical)
* *Graphics/visuals reviews* - are they clear, do they sell, too few/too many, link with text, is the data accurate?

## 12. Focused Review

Reviews with multiple contributors located in multiple locations can involve complexities and complications that cause review time to extend beyond the time needed to create the draft under review.

Problems with reviews include:

* People reviewing out of their expertise
* Arguments about style
* Iterative review cycles in chained sequence
* Decision makers enter into review at late stages
* No established end cycle or level of quality established

## 13. PHP Document Standards

One way to ensure this level of document quality is to review to a common set of document standards. The following table summarizes these standards that can help to focus reviews and give a common language for comments:

|  |  |  |
| --- | --- | --- |
| **Standard** | **Evaluation Criteria** | **Assessment\*** |
| Overall Message | How well do readers understand early on what they are reading and why? |  |
| Context | Can a reader understand how the information fits into the overall picture of the development? |  |
| Logic | How apparent is the writer’s use of deductive versus inductive reasoning? Does the data support the conclusions and are these linked to the objectives? |  |
| Content | How well are the audience needs and expectations understood and met? Is the document MIRS oriented? |  |
| Organization | Are the key messages readily apparent, and is the information accessible and easy to follow? Are organizational devices used effectively? |  |
| Presentation | How well does the writer take advantage of visuals, bulleted listing, white space etc in making the information accessible and persuasive to the audience? |  |
| Language | Is the language used appropriate to the audience? Is the language scientific without being arcane and clear without being too informal? If the document has been written by multiple authors, is one clear, clean, and concise style in evidence? |  |

\* One approach to assessment is to use a numerical assessment (such as, for example 1-5); this kind of quantification allows for averaging among a group of reviewers, which creates a kind of objectivity. However, readers need to agree on what qualities the numbers represent. Hence, using a qualitative, evaluative measurement (e.g. good, acceptable, not acceptable) can work just as well.

The following sections provide more information on each standard.

### Overall Message

The overall message is stated early in the document and at the beginning of the appropriate main sections (e.g., Results, Discussion, Efficacy, Safety etc) of the appropriate documents. The message often answers the broader question of “so what?”. The overall message should be related to the main purpose of the research and/or the document.

Using deductive logic, the writer should place the messages as high as possible, as in the beginning of paragraphs, sections, abstracts, introductions and so forth. Messages should come across as explicitly as possible and not be left for the audience to infer.

Documents at PHP are MIRS-generated and MIRS-based. (See MIRS Process Overview.)

### Context

The purpose of documentation at PHP is to have an impact on the audience leading to a favorable outcome; i.e., approval, adoption, changes in practice etc. Thus, each document should provide a clear context for the message, providing a relevant view into the background necessary to understand issues and their impact. PHP documents are convincing and persuasive.

The introduction or problem statement describes the disease, its treatment, the therapeutic need, demographics, economic impact, etc and so is a key section for context.

The context in PHP documents makes the connections between various functions of the development program. Topics might include efficacy variable, consistency of study design, and evolution of understanding as the program progressed, information available from pre-clinical and CMC areas. Discussions address inconsistencies and try to resolve them.

### Logic

***PHP documents reach conclusions that are consistent with data.***

The information presented in the document provides a logical, coherent picture of the drug and issues leading to its successful scientific development.

As a general rule, documents should use deductive rather than inductive logic whenever expedient. Deductive argumentation states the conclusion first, then discusses issues and presents supporting data. (Inductive logic presents information first from which a conclusion is then drawn; most scientists are trained in inductive logic, so using deduction may require effort and practice.) If, for whatever reason, inductive reasoning must be used, then the writer should consider setting off the concluding message in a paragraph by itself.

Messages, objectives, measurements, data/results, conclusions, interpretations are logically connected to one another. In particular, conclusions interpret results and state their significance in relation to the program objectives.

### Content

The document addresses all reader expectations (critical analysis, suggested outline topics, adequacy of studies to GCP, etc) for content. The writer must analyze the prospective needs of audience carefully in anticipation of the readers’ intellectual expectations as well as their fears, uncertainties, and doubts. The content reflects the MIRS table and is shaped according to the document prototype that has been generated by the MIRS. (See Prototyping section above)

The scope of detail must be appropriate to the document type. When possible, content is presented in a logic hierarchy to promote accessibility - with summary information first and very detailed information left to tables and appendices. Data and content should be immediately understood by the reader and crafted and presented in meaningful ways.

### Organization

The document contains organizational devices within the text that help readers navigate the document. Headings, cross-references, “road maps,” page numbering, appendices, etc are used effectively and consistently. The organization reflects audience needs and document purpose and supports different reading styles.

Organizational devices and cues help readers access supporting information in the publication.

### Presentation

Information is presented in the most appropriate way, whether texturally or visually. Visual balance helps readers’ access important information. Visuals are of high quality and clearly related to the text. Like the text, visuals should focus on specific messages and issues. Titles are a good location to place the main message for the visual.

All documents and presentations produced at PHP should use the appropriate templates and formats developed for their specific purpose.

### Language

Save declarative sentences for main ideas and for points of emphasis. In general, paragraphs should focus on one main point and, thus, avoid becoming unduly long and wordy.

## 14. How to ask for Reviews

More time is lost in reviewing documents than in any other phase of the writing process. However, reviews are essential to producing quality documentation that meets the author’s purpose and are often part of sign-off processes required for regulatory compliance. The product of several minds, if focused, is usually better than the product of a single mind. The problem is how to go about reviewing.

The following can help shorten the review process and improve the quality of the input:

1. *Provide specific instructions for reviewers.*

Don’t just send out a document and attach a note that says: “For your review and comment.” Give reviewers written direction. Tell them exactly what you want them to do. Tell them where you are having difficulties or where you feel the document needs input.

1. *Provide time limits for the reviewers.*

Give reviewers sufficient time but make a date for the review and stick with it. Planning review timelines during the early prototyping of documents can help ensure reviewers keep time free in their schedules in the knowledge that a document will be sent out for review.

1. *Remind the reviewers of what they are NOT supposed to do.*

In your instructions, besides telling reviewers what to do, tell them what not to do. If documents will have a final editing and QA process, tell reviewers not to check data in tables or spelling.

1. *Get reviewers involved early.*

The best time to begin the review process is at the early stages, such as MIRS and/or at prototyping. In this way, the reviewer will have comments incorporated before the document is written.

1. *Use review meetings to gain agreement.*

Use review meetings where complex documents are involved and/or reviewers have divergent opinions. Use a RFT facilitator for meetings to allow authors and reviewers to be fully engaged in the discussion.

1. *Use MIRS and Document Standards as review tools.*

MIRS tables will summarize the key content of the document, so reviewers should use them to check that the MIRS are clearly represented and appropriately located in the document. Document Standards allows for the document to be assessed and described using a common language, away from personal opinions.

# 

# Conclusion

Managed thinking and writing principles and processes impact the PHP and portfolio companies’ business by providing means to expedite drug development and particularly the quality and effectiveness of our thinking and writing – it is not just “a better way to write a draft report”.

The overall goal is to plan and evaluate accurately, decide correctly, put together an accurate and compelling story, and enable readers to act on what they read in the document decisively to provide high-quality medicines for patients who need them. The approach can also reduce the emotional and intellectual stress within team members at PHP and portfolio companies – potentially turning a devastating emotional project into one which is full of good teamwork and learning.

# Appendices

**Appendix A: MIRS as Source Document**

**Target PI/SmPC**

**Regulatory Documents   
and Meetings**

**Marketing Materials**

**Sales Training**

**Publications**

**Education**

**Investor Relations**

**Slide Kits**

|  |  |  |  |
| --- | --- | --- | --- |
| **M** | **I** | **R** | **S** |
|  |  |  |  |
|  |  |  |  |

**Appendix B: PHP MIRS Table Formatting with Annotation**

| **Message** | **Issue** | **Rationale/ Response** | *[Make sure that you have a heading on each page]*  **Support** |
| --- | --- | --- | --- |
| A. The MIRS process is a powerful tool for drug development and marketing team | *[Not every Message has a direct Issue]* |  | Testimony of wide number of drug development experts from a wide variety of companies |
|  | It demands fairly complex logistics. | The MIRS Workshop helps a company harmonize the MIRS process. Helps teach team members the processes | ACTION: Schedule MIRS Workshop *[Although Actions can be listed as part of a MIRS table, they should be moved to a Project Plan. If the MIRS is assigned other purposes as well as its primary one, it becomes too complicated to use]* |
|  | Debate about which technical format to use. Most often a Word Table; however, some teams have used a spread sheet | Word tables are easier to read as a group, but spreadsheets are easier to use for subordinate structures. | Experience of investigators recorded in testimony |
| A.1. MIRS is as powerful as its structure |  | A team should get the assistance of a digital expert to design the forms *[Sometimes material will appear in more than one category]* | Is there someone in PHP who could fulfill this role? |
| **A.2.** A team should get the assistance of a digital expert to design the forms [Sometimes Responses will be elevated to the category of Message, with their own IRS] | This adds cost to the project. | An IT expert saves valuable time for the other team members. | Study GWMV 2003, ongoing, measures time spent by MIRS team w/o IT support compared to one with. |
| **B.** [Numbering messages can help with cross-referencing] **The MIRS is also a powerful Knowledge product.** |  |  | Experience in use in Pharmaceutical Communication for over 10 years. |
|  | It requires structures that avoid confusion. | * MIRS can be aligned by rows, by numbers, by bullets, or a combination of all. * A MIRS team should get the assistance of a computer expert to design the forms * Keeping high level messages separate from one another helps readability | **LINK**: See PHP SharePoint as a possible structure  *[Often a topic needs to appear in more than one section of a MIRS table either because it belongs in different documents or is part of consideration in a variety of areas]* |
|  | It takes too much time to create and maintain. | * It saves time when writing an NDA because it gives a head start on content * It improves quality of company communication. | Reference: Article in 1998 issue of CCCC, p. 299  *[Often support will come from already published material]* |
| **B.1.** A MIRS improves quality of company communication. |  | MIRS used to review documents and other communications ensures that company messages are included at all possible opportunities. | McCulley-Cuppan White Paper, Archive |
|  |  |  |  |

**Appendix C: Different Kinds of MIRS and Adaptability of MIRS**

**Sample from Program MIRS**

| **Ref No.** | **Message** | **Issue** | **Rationale/ Response** | **Support** | **Comments/ Action Items** |
| --- | --- | --- | --- | --- | --- |
| 3 | Angiomax results in fewer complications (i.e., fewer calls + patient quality of life) | Some physicians thinks that bleeding is not important | Too much Heparin results in high ACT → bleeding → death | R-2 Multivariate analysis, Cohen et al. AHA abstract, closure device papers—patient satisfaction.  R-2; TIMI 18  Kenard 5.4%  R-2; EPISTENT, ESPRIT |  |

**Sample from a Document MIRS**

| **Ref No.** | **Message** | **Issue** | **Rationale/ Response** | **Support** | **Comments/ Action Items** |
| --- | --- | --- | --- | --- | --- |
| Note: This MIRS is to prepare an FDA briefing document & protocol, which should demonstrate the following regarding prevention, prophylaxis & treatment. Request meeting with FDA and submit ~6-page briefing document by mid-February. | | | | | |
| **1** | HIT/TS is deadly & frequent | How often?  How deadly? | 20,000 patients in the U.S. are being treated, which is the tip of the iceberg.  Death rate = 20% | Warkenten, post-marketing data etc. | Warkenten, post-marketing data etc. |
| **2** | Anti-thrombin is essential to treat HIT/TS | Why? | Otherwise 52% will have thrombosis | Same as above. | Same as above. |
| **3** | Current therapeutic options are sub-optimal | But they are FDA approved. | Refludan (R) = high bleeding, antibodies, renal issues  Argatron (A) = Lack of effect, hepatic issues & INR | PI’s & publications  Note: find citations in the literature; see *Contemporary Cardiology* article. | PI’s & publications  Note: find citations in the literature; see *Contemporary Cardiology* article. |
| **4** | Angiomax is better | In what way? Prove it. | Comparative studies are needed:  R—less bleeding, no renal issues etc.  A—better than hep. & no hepatic issues. | Gosslin publications | Gosslin publications |

**[A picture containing text

Description automatically generated](https://www.fda.gov/media/71271/download)Appendix D: Creating a Specialized MIRS Document Template   
(such as for a Clinical Study Report (CSR)):**

| **Ref No.** | **Message** | **Issue** | **Rationale/ Response** | **Support** | **Comments/ Action Items** |
| --- | --- | --- | --- | --- | --- |
| **1-6. Front Matter** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **7. Introduction** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **8-9. Study Objectives & Investigational Plan** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **10. Study Patients** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **11. Efficacy Evaluation** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **12. Safety Evaluation** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **13. Discussion & Overall Conclusions** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **14. Tables etc. not included in the text** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **15. References** | | | | | |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
| **16. Appendices** | | | | | |
|  |  |  |  |  |  |
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**Appendix E: MIRS Review**

*Following is a sample agenda for a first review of an initial MIRS:*

**Angiomax® (bivalarudin) Cardiac Surgery MIRS (A) Tables**

**Review Instructions**

The following are the MIRS (A) tables resulting from the meeting on 10th – 11th November 2003. For review purposes these are being distributed as separate files:

The main MIRS (A) tables are based on the following key questions of drug development from The PHP Development Process: Efficacy, Safety, Dose, and Value. The Risk/Benefit MIRS (A) has yet to be completed.

In addition to these main MIRS (A) tables, there is information which was collected at the meeting but not discussed in detail nor included in the appropriate MIRS (A) tables. These are collected in two additional tables (‘Marketing + Parking Lot Issues’ and ‘Medical Need’)

Please review these tables focussing on the following points:

* Avoid stylistic, grammatical, and punctuation comments.
* Avoid comments of format. The format will eventually be standardized.
* Look for content that needs to be added, deleted, or changed. In particular, review the Messages/Issues captured under ‘Marketing/Parking Lot’ and ‘Medical Need’ which were not specifically reviewed or incorporated into the appropriate MIRS(A) tables at the meeting
* Review against the questions in PHPs Development Process.
* As you review, remember the multiple purposes of a program MIRS (A) as well as its multiple audiences.
* Check for understanding. Ensure that people who were not at the meeting can understand how the MIRS (A) provides content for the Angiomax program.
* Make sure that the Support column contains specific references to locations of data. As you write the sNDA, you will have to know the data and the sources.
* Make sure that the Rationale/Response column contains the main logic to develop a Message or refute an Issue.
* Check to see if Messages belong in more than one section.
* Link material from one section to that in another whenever there is an overlap or one is needed to support the other.

There will be a half-day review meeting to discuss your comments and agree changes. Please come prepared with specific comments either marked on the tables or added as revision marks. Once changes have been discussed and agreed, they will be made to the master versions.

**Target PI/SmPC**

1. We use the term “document” for simplicity. Any communication product, from a slide kit to an FDA Advisory Committee presentation can be prototyped. [↑](#footnote-ref-1)