Putting the Pieces Together: REMS Logic Model in REMS Design, Implementation, and Evaluation

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Learning Objectives

- Discuss the potential value of using a logic model in linking REMS design and assessment
- Explain the use of theories, frameworks, and logic models to assess the effectiveness of programs
- Describe the REMS logic model
- Apply the REMS logic model to a theoretical case

REMS Background

Risk Evaluation and Mitigation Strategy (REMS)

- Is a drug safety program to ensure the benefits of the medication outweigh its risks
- Is designed to achieve specific goals to mitigate risks associated with use of a drug
- May include a number of interventions to help mitigate the occurrence and/or severity of a serious risk(s)
- Interventions may include communicating, educating, or requiring certain safe-use behaviors
- Programs are assessed to determine if interventions are achieving the desired safety outcomes (i.e., is the REMS meeting its goal(s))

A REMS can include…

- Medication Guide or Patient Package Insert
- Communication Plan for healthcare providers*
- Certain packaging and safe disposal technologies for drugs that pose a serious risk of abuse or overdose[A]
- Elements to assure safe use (ETASU)[B]
- Implementation System[C]
- Timetable for submission of assessments*[D]

*applies only to NDAs and BLAs
A. Section 505-1(e)(2)-(4) of the FD&C Act.
B. See section 505-1(f) of the FD&C Act.
C. See section 505-1(f)(4) of the FD&C Act.
D. ANDAs are not subject to the requirement for a timetable for submission of assessments (section 505-1(i)), but FDA can require any application holder, including ANDA applicants, to submit REMS assessments under section 505-1(g)(2)(C).

REMS ETASU[E]

These are not mutually exclusive and can be used in combination to support safe use

- Certification and/or specialized training of healthcare providers who prescribe the drug
- Certification of pharmacies or other dispensers of the drug
- Dispensing/administration of drug only in certain healthcare settings
- Drug is dispensed/administered only with evidence of safe-use conditions
- Each patient using the drug is subject to certain monitoring
- Enrollment of treated patients in a registry

E. See section 505-1(f)(3) of the FD&C Act.

REMS and Assessments

Applicants must periodically evaluate their REMS to assess whether they are meeting goals and determine whether modifications to the REMS are required[F]

F. See Section 505-1(d) of the FD&C Ac and 505-1(g)(2) of the FD&C Act.

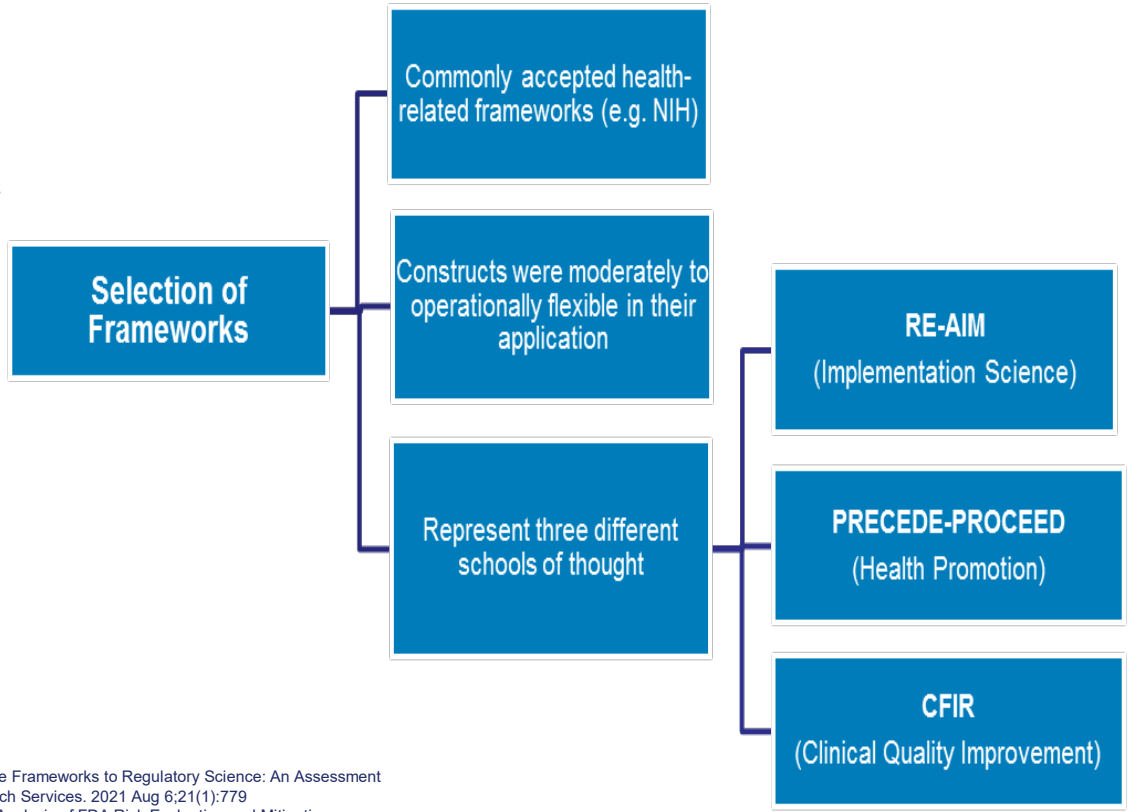
The REMS logic model (RLM) is a part of FDA's continuous process to improve and modernize REMS[1]

1. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 through 2022. (n.d.). Retrieved October 28, 2024, from https://www.fda.gov/media/99140/download

REMS Research Project[1,2]

Objectives:

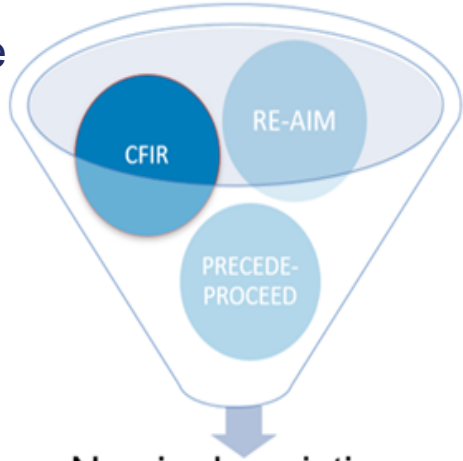
1. Determine feasibility and utility of applying scientific frameworks to REMS assessments
2. Characterize REMS assessment plans using commonly used and validated frameworks and identify areas for advancing methods for evaluating REMS programs



1. Huynh L, Toyserkani GA, Morrato HE. Pragmatic Applications of Implementation Science Frameworks to Regulatory Science: An Assessment of FDA Risk Evaluation and Mitigation Strategies REMS (2014-2018). BMC Health Research Services. 2021 Aug 6;21(1):779
2. Toyserkani GA, Huynh L Morrato EH. Adaptation for Regulatory Application: A Content Analysis of FDA Risk Evaluation and Mitigation Strategies Assessment Plans (2014-2018) Using RE-AIM. Front Public Health. 2020 Feb 25;8:43. doi: 10.3389/fpubh.2020.00043

REMS Research Project
Key Findings[1,2]

- Frameworks provide a logical, structured approach to determining outcome measures
- Identified areas where we can strengthen and advance REMS assessments:
  - Explicitly linking design assumptions with program evaluation metrics to validate assumptions, allow for necessary modifications, and improve program performance
  - Improving and increasing outcome and health impact measures
  - Identify measures to assess integration and sustainability of REMS into the health care system and clinical practice
    - This can inform on whether the REMS requirements can be eliminated
  - Identifying a primary outcome measure to determine whether the REMS goal is being met



No single existing unifying framework for REMS

REMS Assessment Commitments

PDUFA VII Commitments | Fiscal Years 2023 – 2027[2]

- Modernize and improve REMS assessments by incorporating assessment planning into REMS design
- Update relevant guidances with recommendations on:
  - linking the design with the assessments
  - ensuring sufficient and appropriate data collection
  - identifying key metrics for success

2. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027. (n.d.). Retrieved October 1, 2024, from https://www.fda.gov/media/151712/download?attachment

Logic Models

Theories, Frameworks and their use in REMS

What is a Logic Model?[3-6]

- Tool commonly used in program design and evaluation
- Road map leading to the program's desired outcome
- Graphical 'causal pathway' diagram of human processes and behaviors
- Makes explicit the scientific evidence, assumptions, and underlying logic that support the program and the various processes behind it

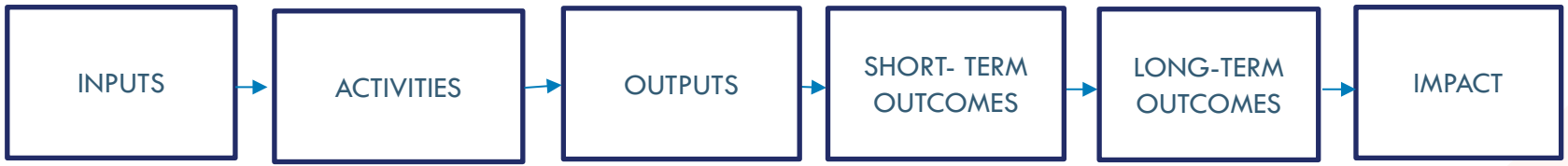
3. Renger R (2002). "A Three-Step Approach to Teaching Logic Models". The American Journal of Evaluation. 23 (4): 493–503. doi:10.1016/s1098-2140(02)00230-8.
4. Frechtling JA (2015). "Logic Models". International Encyclopedia of the Social & Behavioral Sciences. Elsevier. pp. 299–305. doi:10.1016/b978-0-08-097086-8.10549-5. ISBN 978-0-08-097087-5.
5. "Developing and prioritizing interventions," in Brownson RC, Baker EA, Deshpande AD, Gillespie KN (Eds) Evidence-Based Public Health (3rd Ed): Oxford University Press, 2018.
6. W.K. Kellogg Foundation framework. http://toolkit.pellinstitute.org/evaluation-guide/plan-budget/using-a-logic-model/

Why Use a Logic Model?

- Provides a systematic structure for the development, implementation, and evaluation of a program
- Helps clarify the relationship between your objectives, strategies, and your assessment results
- Identifies the evidence, assumptions, and uncertainties
- Maps out what the program (e.g., REMS) can and cannot accomplish
- Identifies what is important to measure

Types of Logic Models

- **Types**:
  - **theory of change model**[6] - general representation of how you believe change will occur
  - **program logic model**[7] - details resources, planned activities, and their outputs and outcomes over time that reflect the intended results
- The **REMS logic model** is a program logic model. However, its assumptions are built on the theory of change
- Key parts of a **program logic model** include:



6. W.K. Kellogg Foundation framework. http://toolkit.pellinstitute.org/evaluation-guide/plan-budget/using-a-logic-model/
7. Taylor-Powell, E., Jones, L., & Henert, E. (2002) Enhancing Program Performance with Logic Models, University of Wisconsin Extension Services Online course https://lmcourse.ces.uwex.edu/

Key Parts Of a Program Logic Model

Term	Inputs	Activities	Outputs	Outcomes (short & long-term)	Impact
Definition	What you need to operate the program	Actions completed by the program participants	Direct results of activities and inform how the program is operating	Changes in those participating in the program including specific changes in knowledge or behavior	specific type of outcome that is defined as the "*ultimate aim*" of the program
Application to REMS	The strategies and resources you need to implement the REMS	The actions that occur to fulfill the REMS requirements (e.g., certification, enrollment, monitoring).	The information collected about the REMS activities (e.g., communication received, number and types of healthcare providers certified)	Change in knowledge or behavior in healthcare providers about the risk and safe use of the drug X years after program implementation.	This is usually mitigating an adverse event associated with a drug.

When to use the Logic Model?

To develop a new REMS

- Use when REMS are initially being considered, before identifying the possible REMS goals and objectives
- Helpful to make explicit the evidence, assumptions and underlying logic of the proposed REMS to create a program that is effective and efficient

To evaluate and modify a REMS

- May be applied throughout the lifecycle of a REMS in evaluating and modifying a REMS, for example:
  - New data/evidence, changes assumptions or underlying logic of REMS
  - A REMS is not meeting its goals (to determine how the REMS should be modified)

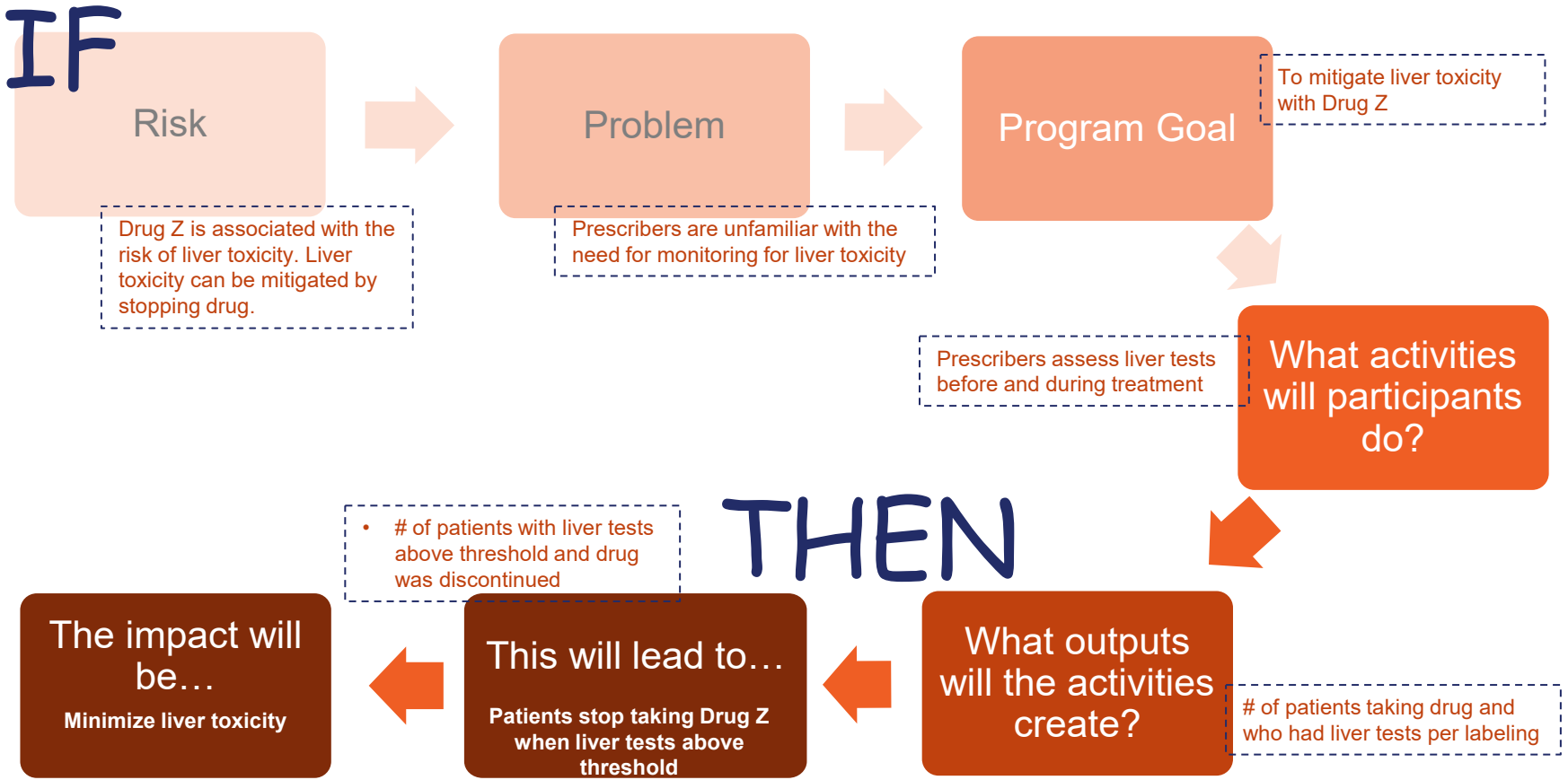
How does RLM fit into REMS Determination

- FDA's determination whether a REMS is necessary is a complex, drug-specific inquiry reflecting an analysis of multiple, interrelated factors[8]
- Concepts in the benefit-risk framework[9], statutory factors that are considered when a REMS is necessary[8], and the REMS logic model are complementary
- REMS logic model principles may assist Applicants with elucidating the benefits, feasibility, and challenges of requiring additional risk mitigation measures beyond labeling.
- Once a serious risk is identified…
  - Use information from the benefit-risk framework to inform the REMS logic model
  - REMS logic model is a *complementary process* to the benefit-risk framework

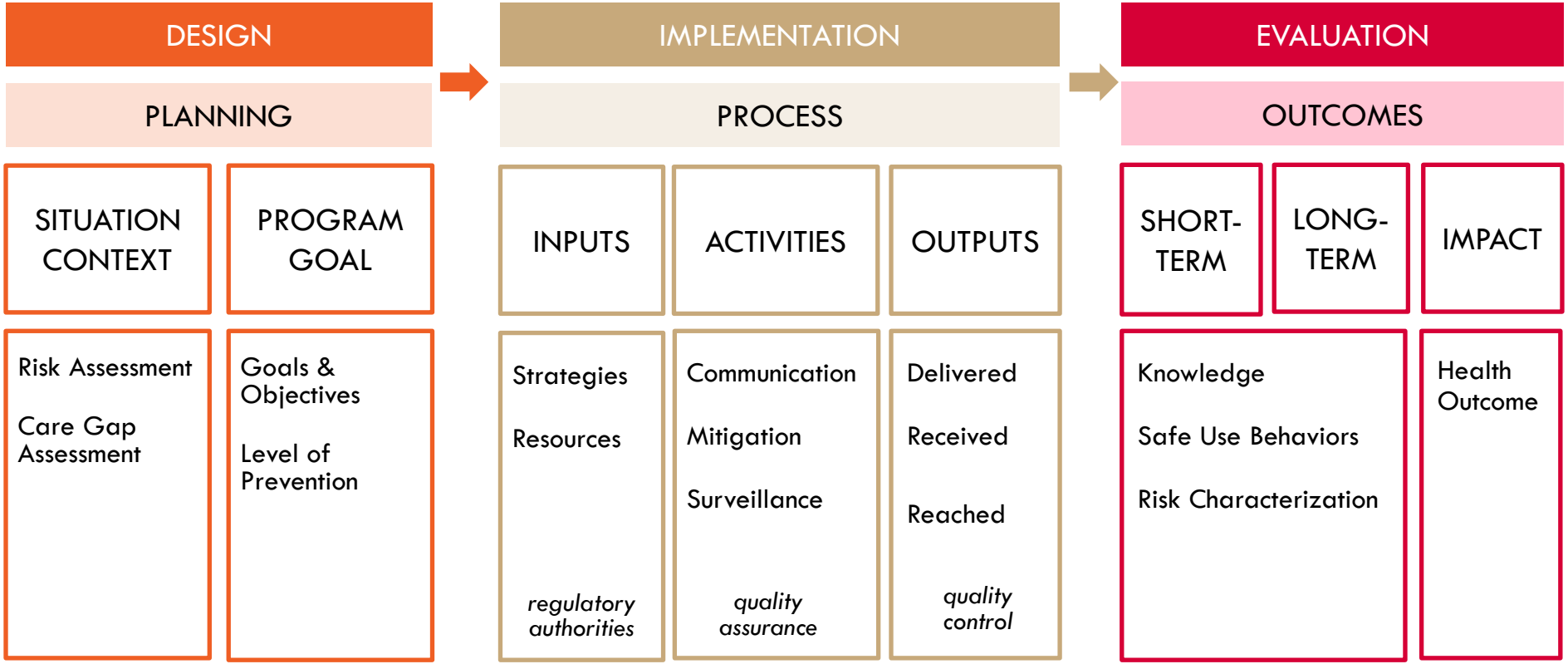
8. FDA's Application of Statutory Factors in Determining When a REMS Is Necessary, Guidance for Industry. (2019). U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER). https://www.fda.gov/media/100307/download
9. Benefit-Risk Assessment for New Drug and Biological Products, Guidance for Industry. (2023). U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER). https://www.fda.gov/media/152544/download

FDA's REMS Logic Model

General Example of REMS Logic Model



REMS Logic Model



REMS Logic Model

- Although visually linear, intended to be an **iterative process** that involves toggling between steps to address uncertainties, validate assumptions, incorporate new information, and refine the REMS program
- Toggling assists with continually verifying the relationship between the goal, objectives, strategies, and intended outcomes of a REMS

Situation Context

DESIGN

PLANNING

SITUATION CONTEXT

Risk Assessment

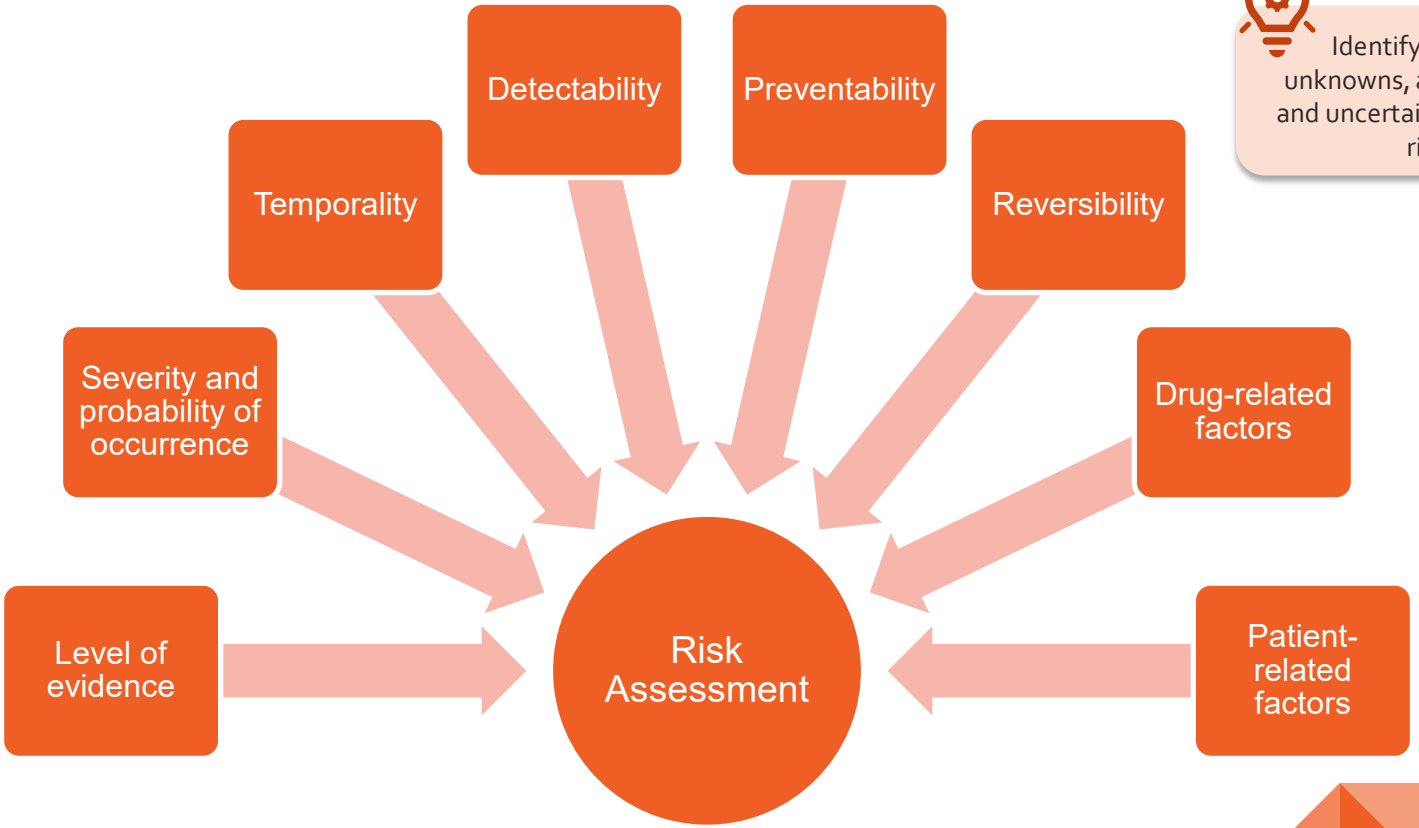
Care Gap Assessment

Risk Assessment | *Characterization of the risk*

Sources of information (for example):

- Preclinical and clinical development
- Literature evaluation
- Post-marketing data
- Epidemiologic studies
- Real-world data

Risk Assessment



Identify what are unknowns, assumptions, and uncertainties with the risk

Situation Context

DESIGN

PLANNING

SITUATION CONTEXT

Risk Assessment

Care Gap Assessment

Risk Assessment | *Characterization of the risk*

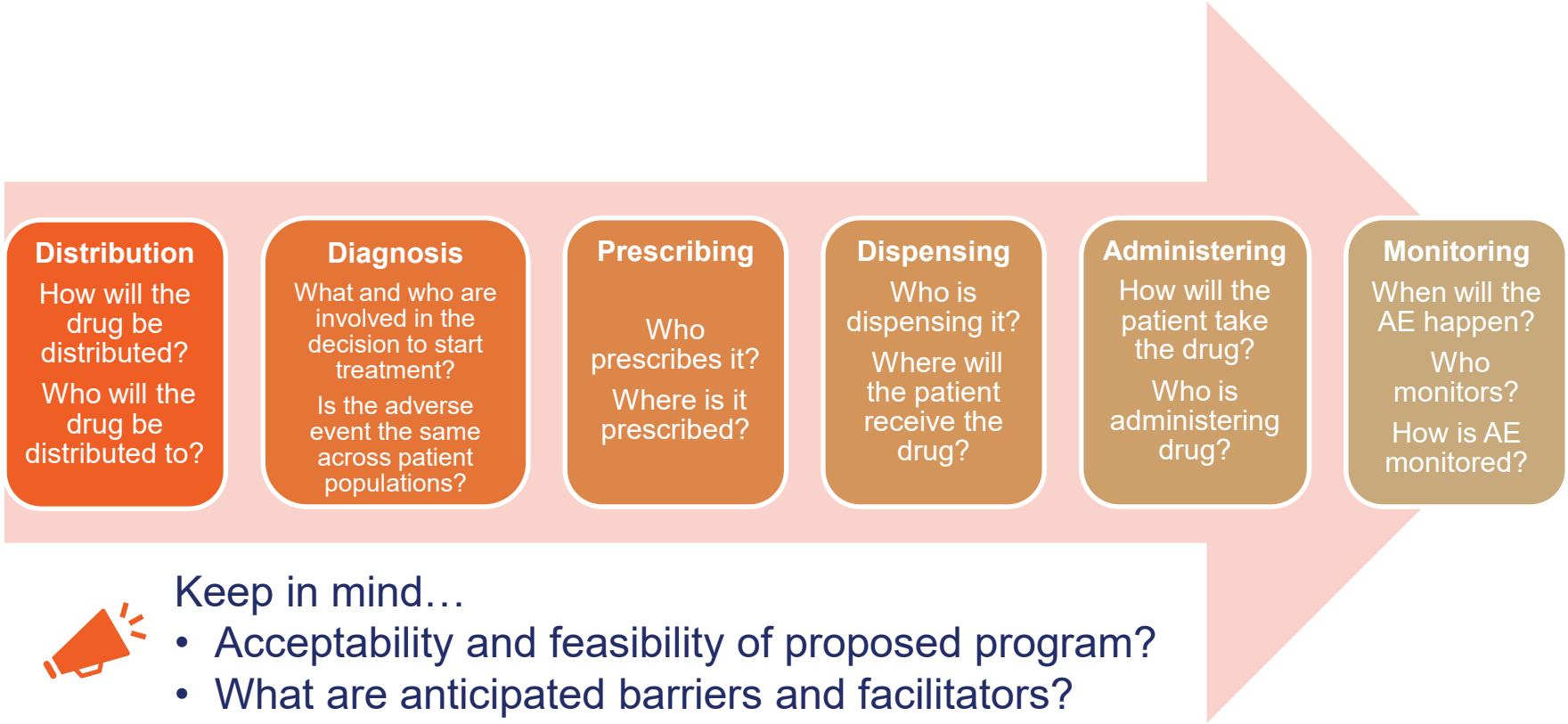
Sources of information (not exhaustive):

- Preclinical and clinical development
- Literature evaluation
- Post-marketing data
- Epidemiologic studies
- Real-world data

Care-Gap Assessment | *Potential discrepancies in risk mitigation between clinical trials, best practices and real-world care*

- Medication use process mapping
- Baseline risk knowledge, attitudes and beliefs
- System level impacts

Medication Use Process



Keep in mind…

- Acceptability and feasibility of proposed program?
- What are anticipated barriers and facilitators?

Baseline Risk Knowledge, Attitudes and Beliefs

- May create or influence care gaps
- Consider self-efficacy and readiness for change of stakeholders
- Qualitative research, literature reviews may inform

Potential System-Level Impacts

State and Federal laws and regulations

Clinical Practice Guidelines

Fragmentation of care

Disparities in accessing healthcare

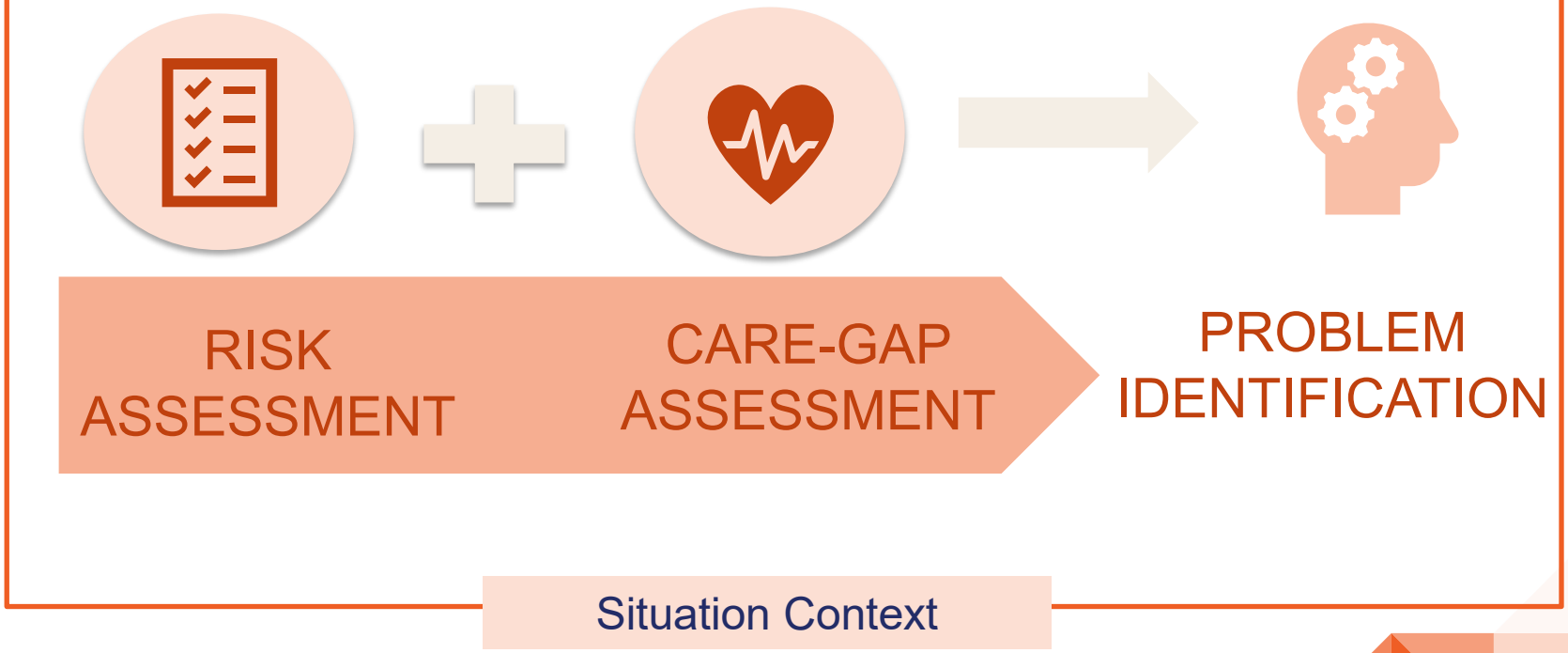
Accrediting organizations' standards

Medical Institutional Guidelines

Insurance coverage decisions

Lack of shared decision making

Defining Problems that may be addressed by a REMS



Program Goals

DESIGN

PLANNING

PROGRAM GOAL

Goals & Objectives

Level of Prevention

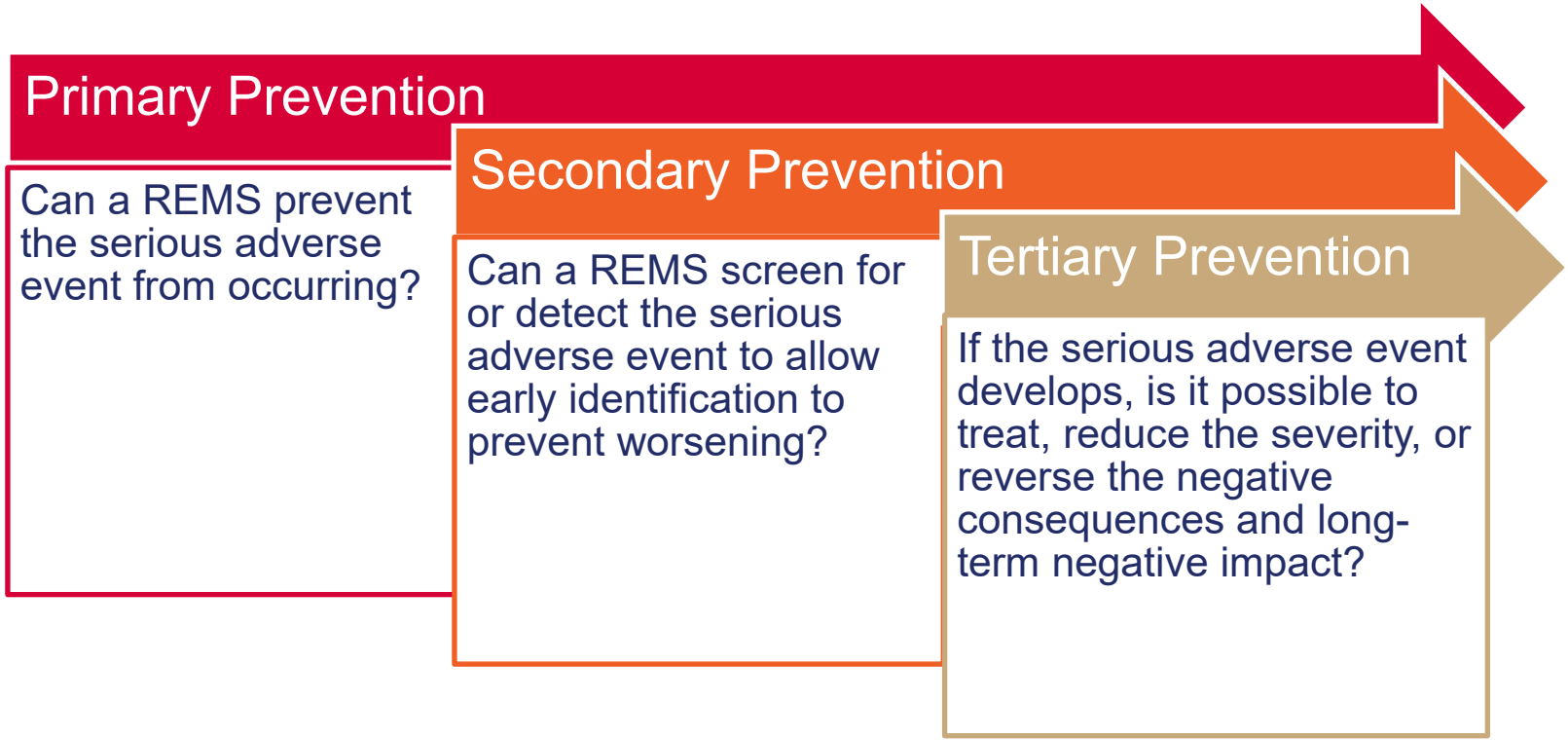
Goals & Objectives

- Broad statement about the expectation of what the program intends to achieve
- Drug-specific
- Risk aligns with labeling
  - (typically, a Boxed Warning)

Level of Prevention

- Consider the prevention level the REMS could target
- Informs selection of the program's **K**ey **P**erformance **I**ndicator (KPI)

Levels of Prevention and REMS Considerations



Levels of Prevention and Design Considerations

- Identify the earliest achievable stage of prevention
  - When feasible or practical, design the REMS to target the earliest prevention level
  - Ultimately the REMS may include a combination of prevention levels
- If targeting at least one of the prevention levels is not feasible or practical, the REMS may need to be designed to ensure **informed benefit-risk decision-making** (i.e., the patient's and prescriber's decisions are based on appropriate information)

Key Performance Indicator (KPI)

- We won't know what success looks like unless we define it
  - At the time of developing goals and objectives, begin to consider program evaluation

- Every REMS needs a defined program outcome that can be measured
  - A Key Performance Indicator (KPI) is an indicator that can be used to determine if REMS goals are being met.
    - Similar to defining a primary endpoint in a clinical trial
    - Identifies *a priori* expectations for program success

Challenge Question #1

All of the following are reasons to use a logic model <u>except</u>:

A. Provides a systematic structure for the development, implementation, and evaluation of a program

B. Helps clarify the relationship between your objectives, strategies, and your assessment results

C. Maps out what the program (e.g., REMS) can and cannot accomplish

D. Ensures the best solution without the need for further evaluation

Challenge Question #2

You are designing a REMS for Drug B. The serious adverse event of concern can only be mitigated with the use of another drug to lessen the negative effects of Drug B. Your REMS should be designed with which level of prevention in mind?:

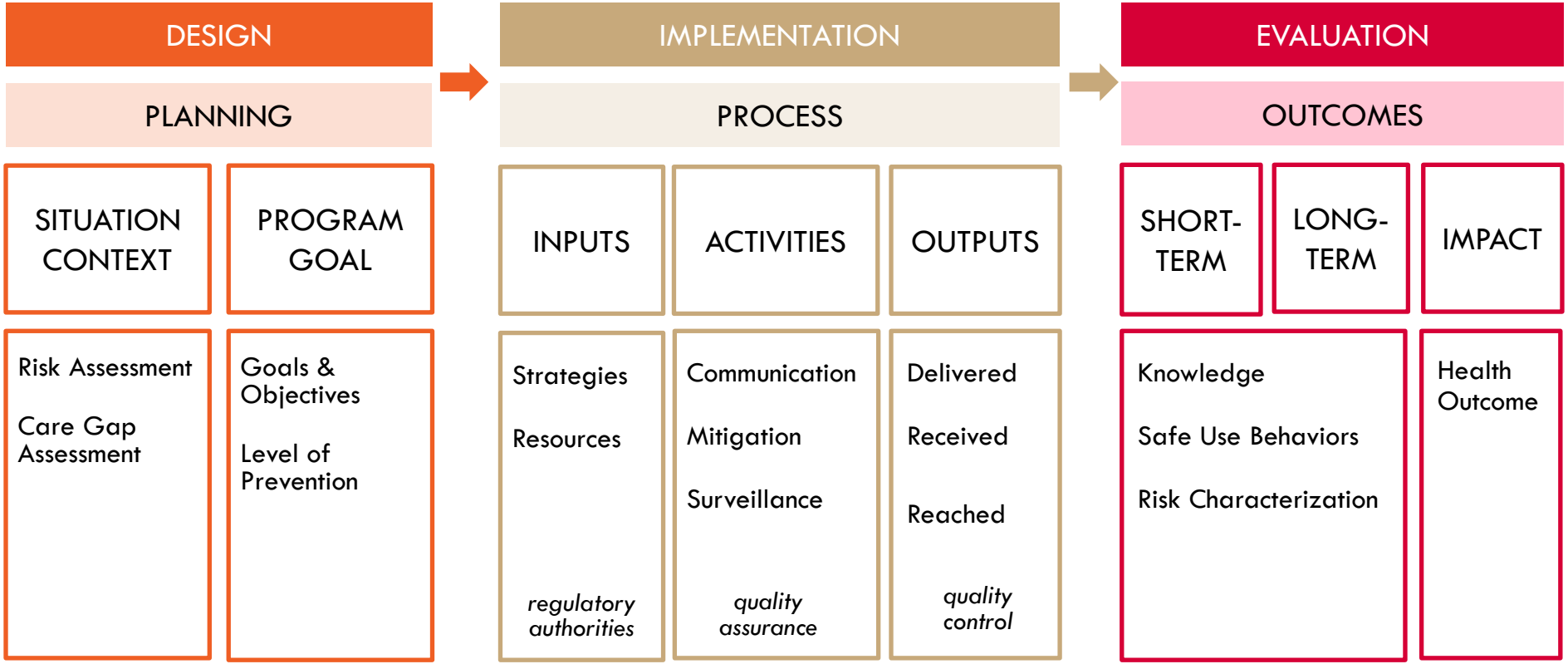
A. Primary prevention

B. Secondary prevention

C. Tertiary prevention

D. informed benefit-risk decision-making

REMS Logic Model



Inputs

What the applicant needs to operate a program

IMPLEMENTATION

PROCESS

INPUTS

Strategies
Resources

regulatory authorities

Strategies

- Align with regulatory authority
- What you are doing as it relates to the elements of a REMS as outlined in the FD&C Act[G]

G. See section 505-1(e) and 505-1(f) of the FD&C Act

A bit more about Strategies

Strategy	Substrategy
To affect knowledge *Communication Strategies*	• Medication Guide • Communication Plan • Training (e.g., prescriber, pharmacy, healthcare setting) • Certification (e.g., prescriber, pharmacy, healthcare setting)
To affect safe-use behaviors *Mitigation Strategies*	• Healthcare setting requirements necessary for dispensing (e.g., equipment, personnel) • Documentation of safe use behaviors (e.g., verifying completion of lab testing) • Monitoring (e.g., observation, assessing results of lab testing) • Packaging (e.g., unit of use) • Disposal systems (e.g., mail back envelopes)
To inform risk characterization/mitigation *Surveillance Strategies*	• Patient Registry

Inputs

What the applicant needs to operate a program

IMPLEMENTATION

PROCESS

INPUTS

Strategies
Resources

regulatory authorities

Strategies

- Align with regulatory authority and precedent
- What you are doing as it relates to the elements of a REMS as outlined in the FD&C Act

Resources

- **People**: anyone involved in implementing and participating in the REMS
- **Materials**: communication materials, training materials, enrollment forms, medications, equipment
- **Technologies**: websites/portals, authorization systems, databases, text messaging, phone, fax

Activities

Actions to achieve the program's goal and objectives

IMPLEMENTATION

PROCESS

ACTIVITIES

Communication
Mitigation
Surveillance
quality assurance

Activities

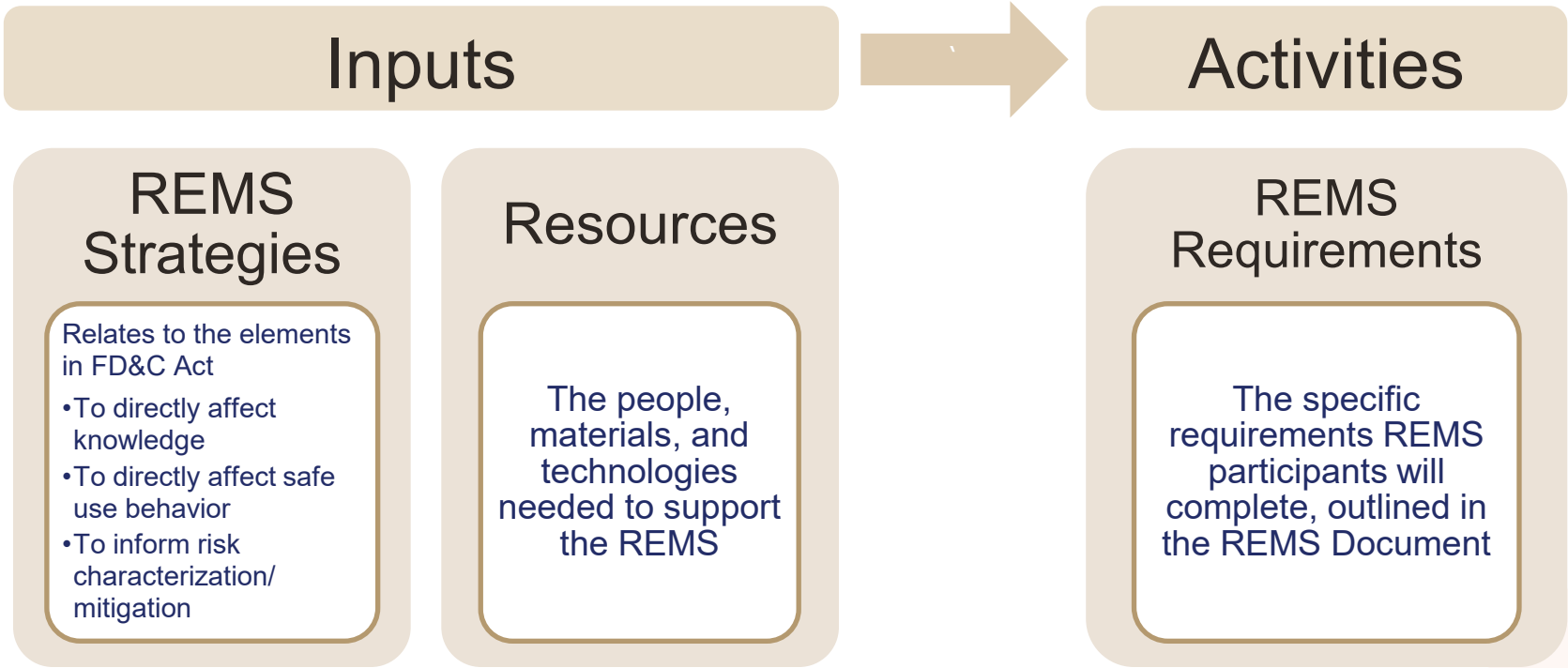
- Actions completed by participants as well as applicant(s)
- ***For REMS:***
  - Same as "REMS requirements"
  - Described in the REMS Document[10-11]

- Support your strategies:
  - Communication-related strategies
  - Mitigation-related strategies
  - Surveillance-related strategies

- Based on the defined inputs (strategies) you will select corresponding activities

10. Format and Content of a REMS Document, Guidance for Industry. (2023) U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER). https://www.fda.gov/media/77846/download
11. REMS Document Technical Conformance Guide. (2023) U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Biologics Evaluation and Research (CBER). https://www.fda.gov/media/164344/download

How Inputs & Activities Relate



Example Activities

Activities support the REMS strategies you selected

Strategy	Sub-strategy Examples	Activity Examples
To directly affect knowledge *communicate*	Training	• Applicant must provide training to healthcare providers who prescribe… Training includes the following educational materials
To directly affect safe use behavior *mitigate*	Healthcare setting requirements necessary for dispensing, administering and monitoring	• Have resuscitative equipment and medications onsite
To inform risk mitigation *surveillance*	Patient registry	• Establish and maintain a registry which includes a reporting and collection system for all patients to provide information on….

Outputs

The direct results of the activities and inform how the REMS is operating

IMPLEMENTATION

PROCESS

OUTPUTS

Delivered

Received

Reached

quality control

- Reflects whether the program's strategies or activities are being implemented as intended and whether design assumptions are valid

Risk Mitigation Activities Delivered

- Lab test results reviewed
- Dispense authorizations

Communication Received

- Communication reach (by channel), frequency
- Number disseminated (by audience)

Participants Reached

- HCPs certified
- Patients enrolled

Indicators

- A way to measure outputs
  - Can be qualitative or quantitative
- Provide signals about change, not necessarily why a change occurred
- Categorized as
  - Process indicators
  - Outcome indicators

Process Indicators

- Determine how well a program is being implemented and operated
- Can include REMS applicant and recipient (i.e., REMS participants) outputs
  - e.g., extent to which REMS materials reach stakeholders, who is participating, compliance requirements
- Should include measures of burden and patient access
- Inform quality control (manner of evaluating fidelity of REMS program activities)

Quality Assurance vs Quality Control

Quality Assurance

The **proactive** plans, protocols, and procedures established to ensure the required activities are implemented as intended.

Quality Control

The **retrospective** process of verifying that activities have occurred or been fulfilled.

Outcomes

The specific change the REMS is intended to achieve as a result of the program strategies and corresponding activities

EVALUATION

OUTCOMES

SHORT-TERM

LONG-TERM

Knowledge

Safe Use Behaviors

Risk Characterization

Risk Knowledge

- Awareness
- Understanding

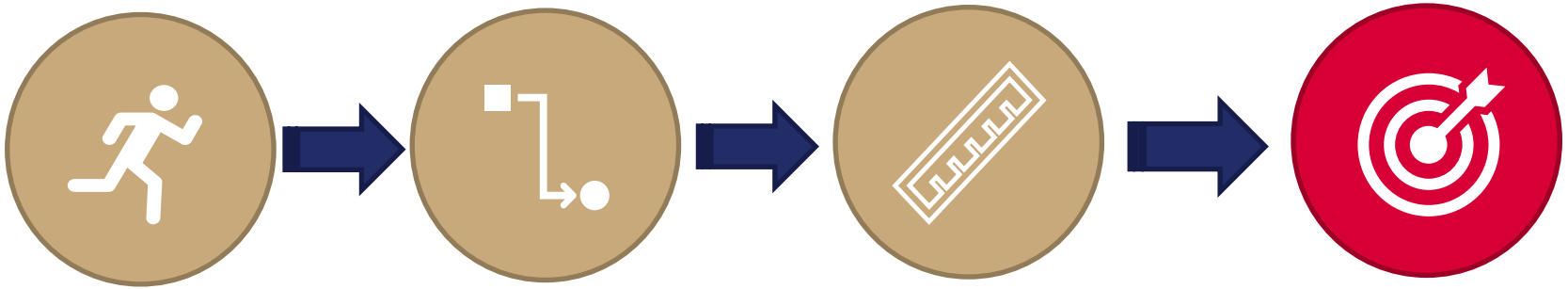
Safe Use Behaviors

- Changes in behavior of stakeholders
- Adoption of safe use behaviors e.g., appropriate patient selection, monitoring, early recognition of adverse drug reactions and appropriate intervention

Risk Characterization

- Incidence, severity and frequency of risk
- Prevalence of risk
- Factors that impact risk
- Appropriateness of risk mitigation measures

Outcomes



IF we pursue these required ***activities***

THEN we produce these ***outputs***

AND we measure the ***outputs*** using indicators

We **GET** these ***outcomes***

Outcome Indicators

- Determine if a program is achieving its intended results
- Consider influencing factors such as healthcare providers' and patients' attitudes and risk perception and system level factors when selecting outcome measures
- Can be subdivided as
  - Program Outcomes
    - KPI(s)
  - Health Impact

Thresholds

- Threshold = target value that, if achieved, indicates that the REMS is performing as intended
  - Pre-REMS data (if applicable), clinical trial data, literature, and/or other drugs
  - Identifying the threshold is part of defining the KPI
  - If the REMS KPI(s) meet the established threshold then we may consider the REMS to be meeting its goal, assuming program is operating as intended

Impact

The long-term expectation of what the program intends to achieve

Impact

- Distal outcome measure; may take time for the result of the program to be observed
- Relationship between the program and the impact may not be direct
- For REMS - Impact aligns to the health outcome or serious adverse event the REMS intends to mitigate

Health Outcome

- Incidence of serious adverse drug event relative to a comparator
- Incidence of surrogate health outcome measures
- Sustainment of knowledge and risk mitigation including incorporation into medical practice

Relationship Between REMS Program Outcome and Impact

	Reassuring Health Impact	Concerning Health Impact
Program Outcome Met	• Indicators of health impact are reassuring • REMS program outcome (KPI) is met	• Indicators of health impact are concerning • REMS program outcome (KPI) is met
Program Outcome Not Met	• Indicators of health impact are reassuring • REMS program outcome (KPI) is not met	• Indicators of health impact are concerning • REMS program outcome (KPI) is not met

REMS Logic Model in Action

REMS Logic Model in Action

- Drug X is indicated for a rare neurologic condition but also carries a serious risk of cardiac valvulopathy.
- A situation context assessment with a multidisciplinary team has occurred and takeaways include…

Defining Problems that may be addressed by a REMS

RISK ASSESSMENT

- Cardiac valvulopathy was seen at a rate of 25% during clinical trials
- Routine echocardiogram screening can mitigate the risk by detecting changes so that Drug X can be discontinued

CARE-GAP ASSESSMENT

- Likely prescribers are neurologists who do not routinely monitor echocardiograms
- Patients would likely not have routine cardiac monitoring as part of management of their disorder

PROBLEM IDENTIFICATION

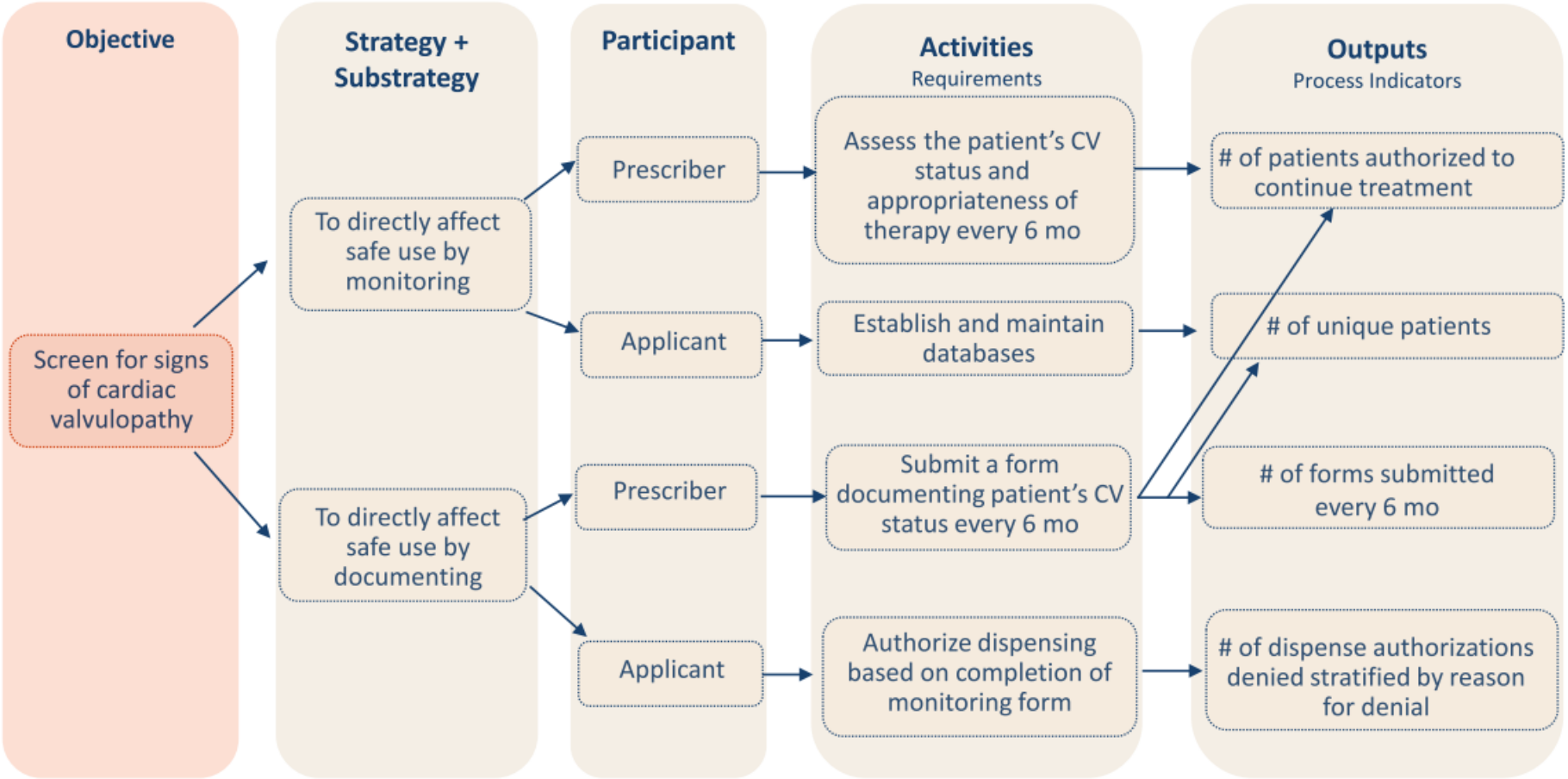
- Neurologists may not monitor echocardiograms as part of their routine practice

Situation Context

REMS Logic Model in Action

- A REMS may mitigate the risk of cardiac valvulopathy by attaining the following **objective**:
  - Patients are screened by echocardiogram for early detection of signs of cardiac valvulopathy

REMS Logic Model in Action | Design and Implementation Phases



CV = cardiovascular

REMS Logic Model in Action | Evaluation Phase

Outputs

Process Indicators

# of forms submitted every 6 mo

# of unique patients

# of patients authorized to continue treatment

# of dispense authorizations denied stratified by reason for denial

Compliance

Effectiveness

Efficiency

Outcomes

KPI: >99% of patients treated had an echocardiogram to screen for cardiac valvulopathy at recommended intervals among all patients treated

$$\frac{\text{\# patients with rx dispense authorizations}}{\text{\# patients with rxs dispensed}}$$

Impact

Rate of valvulopathy consistent or lower than the rate in the clinical trial

REMS Logic Model in Action | Evaluation

	Reassuring Health Impact	Concerning Health Impact
Program Outcome Met	The rate of cardiac valvulopathy is low (< trial data) and monitoring is being reported to the REMS → - No changes needed - Continually reevaluate B:R and need for REMS	The rate of cardiac valvulopathy is high (> trial data) and monitoring is being reported to the REMS → - Broad re-evaluation of monitoring recommendations in labeling and REMS - Differences in real world use vs trial? - How are we measuring the rate of cardiac valvulopathy? - Modify REMS?
Program Outcome Not Met	The rate of cardiac valvulopathy is low (< trial data) and monitoring is not being reported to the REMS→ - External factors influencing monitoring? - Is REMS not functioning as designed? If not, why not? - Revisit KPI? - Reassess B:R?	The rate of cardiac valvulopathy is high (> clinical trial) and monitoring is not being reported to the REMS → - Broad re-evaluation of REMS - How are we measuring the rate of cardiac valvulopathy?

B:R = Benefit-Risk profile

REMS Logic Model in Action | Evaluation

	Reassuring Health Impact	Concerning Health Impact
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Program Outcome Not Met	The rate of cardiac valvulopathy is low (< trial data) and monitoring is not being reported to the REMS → - External factors influencing monitoring? - Is REMS not functioning as designed? If not, why not? - Revisit KPI? - Reassess B:R?	The rate of cardiac valvulopathy is high (> trial data) and monitoring is not being reported to the REMS → - Broad reevaluation of REMS - How are we measuring the rate of cardiac valvulopathy?

B:R = Benefit-Risk profile

REMS Logic Model in Action | Evaluation

	Reassuring Health Impact	Concerning Health Impact
Program Outcome Met	The rate of cardiac valvulopathy is low (< trial data) and monitoring is being reported to the REMS → - No changes needed - Continually reevaluate B:R and need for REMS	The rate of cardiac valvulopathy is high (> trial data) and monitoring is being reported to the REMS → - Broad reevaluation of monitoring recommendations in labeling and REMS - Differences in real world use vs trial? - How are we measuring the rate of cardiac valvulopathy? - Modify REMS?
Program Outcome Not Met	The rate of cardiac valvulopathy is low (< trial data) and monitoring is not being reported to the REMS → - External factors influencing monitoring? - Is REMS not functioning as designed? If not, why not? - Revisit KPI? - Reassess B:R?	The rate of cardiac valvulopathy is high (> trial data) and monitoring is not being reported to the REMS → - Broad reevaluation of REMS - How are we measuring the rate of cardiac valvulopathy?

B:R = Benefit-Risk profile

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REMS Logic Model | Tips and Reminders

- Problem identification and appropriately targeted program strategies are key.
- Ensure your strategies and intended outcomes are aligned.
  - For example, strategies to affect knowledge should be measured by knowledge-based outcomes indicators.
- The model is an iterative process.
  - Expect to go back and forth between steps as you get more information.
- RLM doesn't do the analysis for you. The quality that's put in is what you get out.
- You may not know everything needed for the model and that's OK.
  - The model also helps identify what you don't know, which is also imperative for decisions about REMS design and program improvement.
- The model may evolve as we gain more experience using it.

Challenge Questions

Challenge Question #3

Which of the following best describes the steps of the *REMS logic model*?

A. Situation Context, Goal, & Activities

B. Situation Context, Goal, Inputs, Activities, Outputs, Outcomes, & Impact

C. Situation Context, Strategies, Resources, Requirements, & Impact

D. Situation Context, Goal, Indicators, & Outcomes

Challenge Question #4

Which of the following is true regarding the relationship between REMS program outcomes and impact of the program?

A. If the REMS has met the desired program outcomes, the desired health impact is always achieved.

B. If the REMS has not met the desired program outcomes, there is no way that the desired health impact could be achieved.

C. Once a REMS meets the desired program outcome, a REMS is no longer needed.

D. If the REMS has met the desired program outcomes and the desired health impact is achieved, the REMS and overall risk-benefit of the drug should continually be re-evaluated.

Resources

1. Draft Guidance for Industry: REMS Logic Model: A Framework to Link Program Design With Assessment
2. REMS@FDA
3. Introduction to Program Evaluation for Public Health Programs: A Self-study Guide (Centers for Disease Control and Prevention)
4. Theory at a glance: A Guide for Health Promotion Practice (National Institutes of Health, National Cancer Institute)
5. Huynh L, Toyserkani GA, Morrato HE. Pragmatic Applications of Implementation Science Frameworks to Regulatory Science: An Assessment of FDA Risk Evaluation and Mitigation Strategies REMS (2014-2018). BMC Health Research Services. 2021 Aug 6;21(1):779. doi: 10.1186/s12913-021-06808-3. PMID: 34362367; PMCID: PMC8348874.

Considerations for Applying the REMS Logic Model

- Provides a systematic, structured framework to guide linking REMS design, implementation, and evaluation
  - Helps to identify the evidence, assumptions, and uncertainties
  - Maps out what a REMS can and cannot accomplish
  - Helps identify what should be measured
- Use of the model does not guarantee intended results
  - Should revisit the logic model as new data becomes available
- Establishes a common approach that can enhance efficiency during FDA review of the REMS proposals and assessments

Summary

- The REMS logic model provides a systematic, structured approach to the design, implementation, and evaluation of a REMS.
  - Facilitates communication between FDA and Applicants
- The aim of applying the model is to optimize REMS design and improve the way REMS are assessed by developing clear goals, objectives, and strategies that align with the intended outcomes of the REMS.

Closing Thought

Success must be defined before it can be achieved

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Questions?

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REMS Logic Model: A Framework to Link Program Design With Assessment


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