Risk Management for Medical Devices

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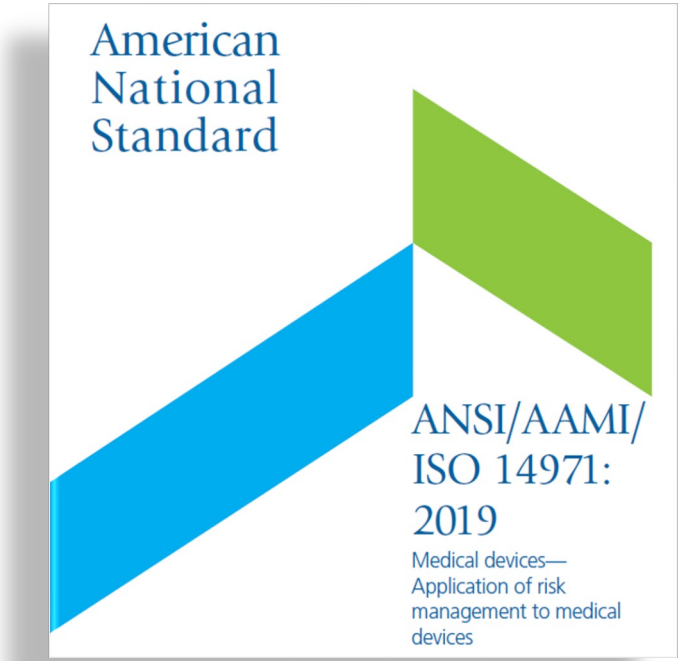
Chair - ISO TC210

Quality management and corresponding general aspects

for products with a health purpose including medical devices

ISO 14971 and ISO TR24971
Risk Management for Medical Devices



Medical device manufacturers around the world are compliant to ISO 14971 Risk Management Standard (it is also referenced in ISO 13485).

ISO 14971 and ISO TR 24971

- ISO 14971 is a widely recognized risk management standard for medical devices
  - Standard itself is short
  - Informative annexes make up the bulk of the document
- ISO 24971 is a guidance that provides additional direction

Many other medical device standards use ISO 14971 as a normative requirement

Scope

- The standard specifies a process for medical devices and IVDs
  - Identify hazards
  - Estimate and evaluate risks
  - Control risks
  - Monitor effectiveness of control
- Risk management is incorporated throughout the entire lifecycle of a medical device
  - From early development activities to post market surveillance
- The Standard does **NOT**
  - Apply to clinical decision making
  - Specify any acceptable levels of risk
  - Business risk management

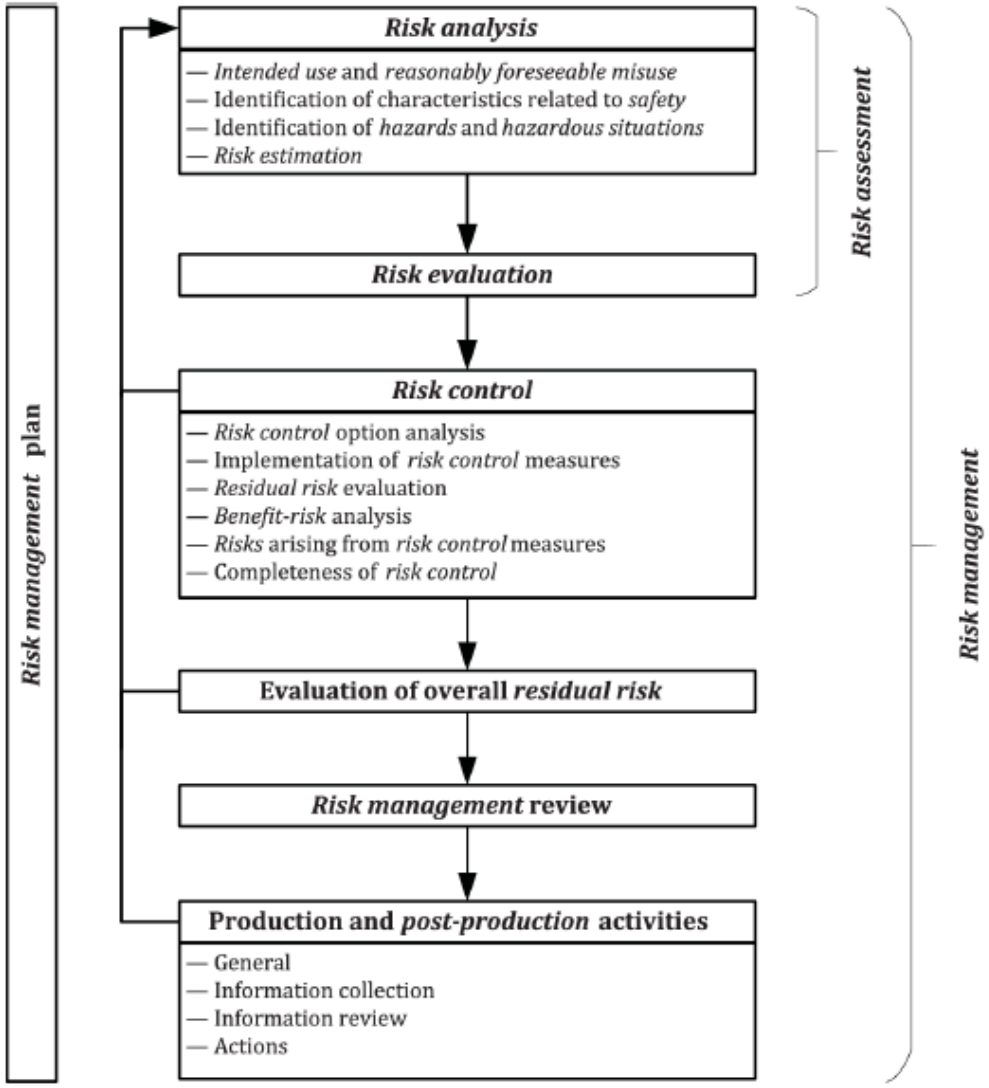
Risk Management Overview

1. What are you trying to do?

2. What can go wrong?

3. What are you going to do about it?

4. Did it work?



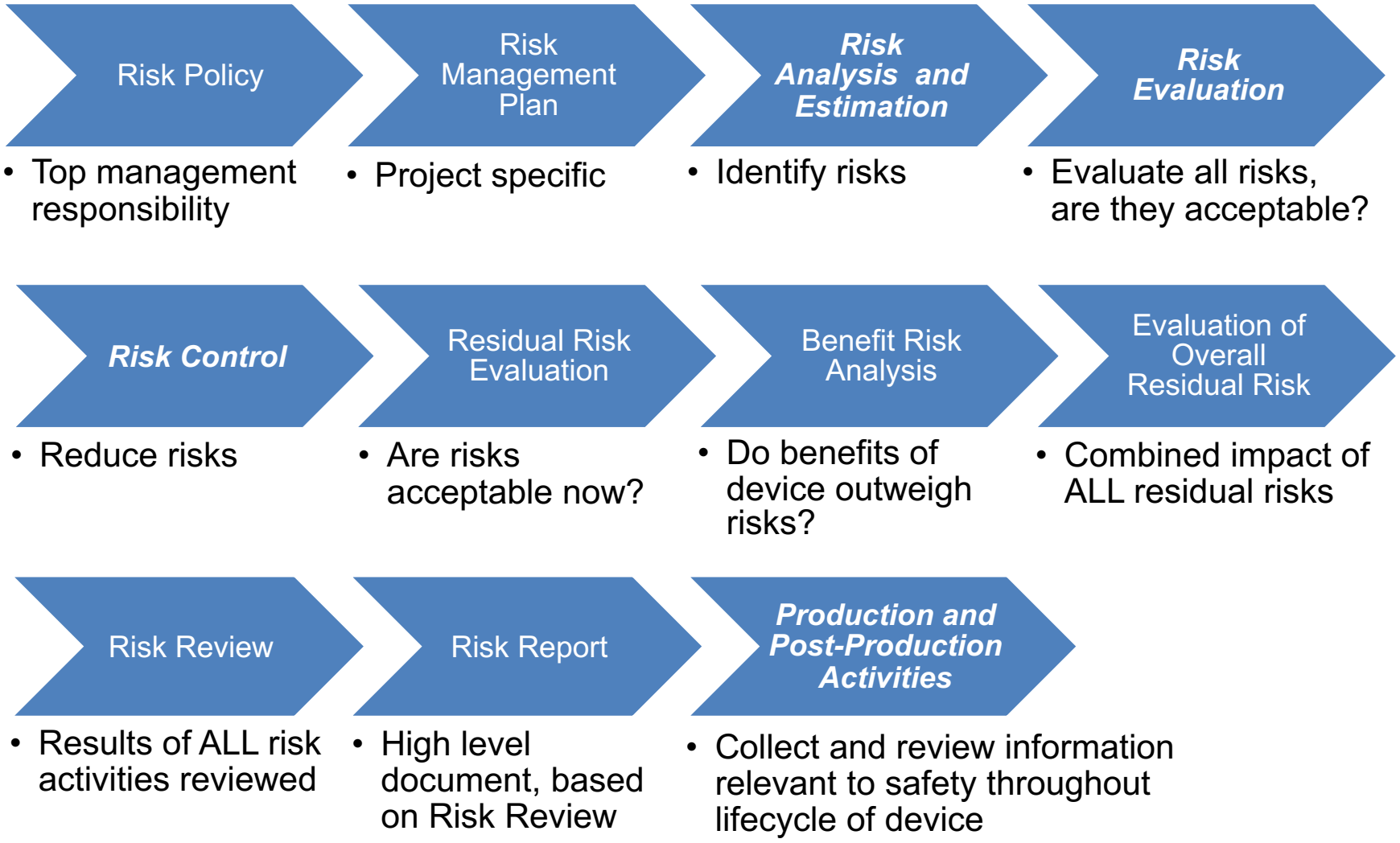
Where You May Consider "Risk"

Throughout Total Product Life Cycle

Key Components of Risk

RISK: The combination of the probability of occurrence of HARM, and the severity of that HARM.

Overview of the Risk Management Process



Key Components of the Risk Management Process

- *Risk management* includes the following processes:
  - Risk Analysis
  - Risk Evaluation
  - Risk Control
  - Production and Post-Production Information

- FDA expects *risk management* activities to begin early in the design and development process and be integrated throughout a manufacturer's Quality Management System.

Risk Analysis

Risk Analysis

The systematic use of available information to identify hazards and to estimate the risk.

Key Definitions

Intended Use

14971: “Use for which a product, process, or service is intended according to the specification, instructions, and information provided by the manufacturer.”

Hazard

Potential Source of Harm

Note: Sources are always there, somewhere.

Hazardous Situation

Exposure to a Hazard

Note: It is the bridge between a hazard and harm.

Harm

Physical injury or damage to health of people, property or environment.

Key Definitions

- **Severity**
  - Measure of possible consequences of a hazard
- **Probability of Occurrence**
  - Chance that given event will occur, the likelihood something will happen

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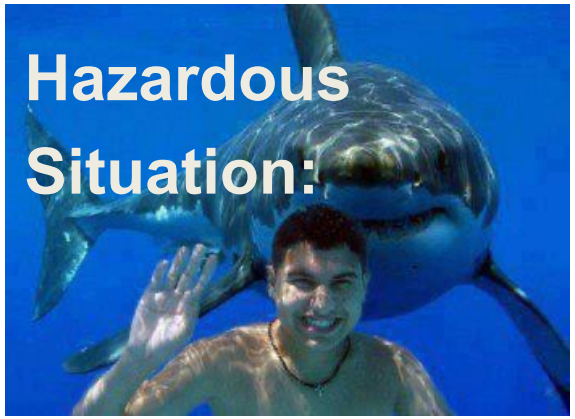
Example

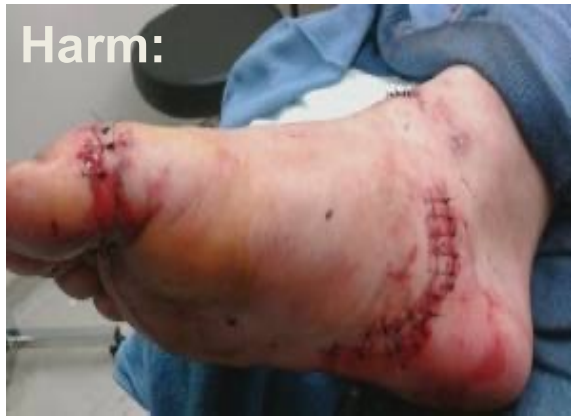
Potential Source of Harm.

Always there… but just because it exists doesn't mean there will be Harm..



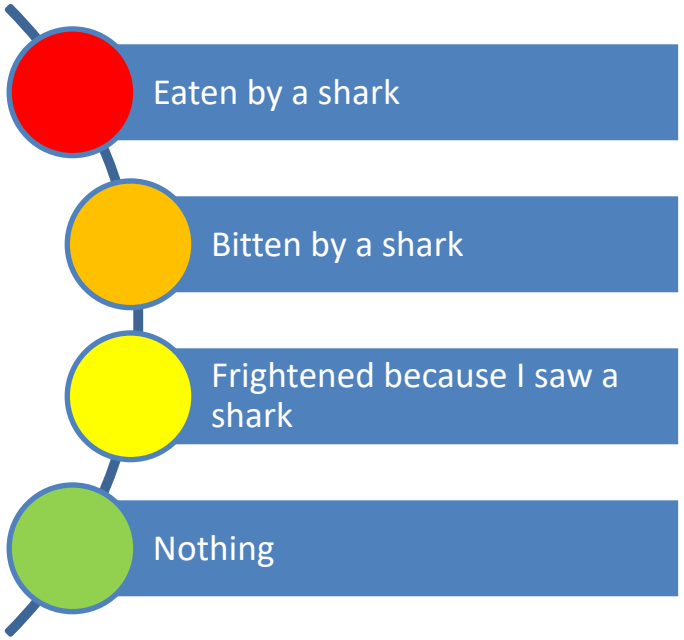
Exposure to a Hazard.

It's a situation where Harm could happen… It still hasn't happened though..



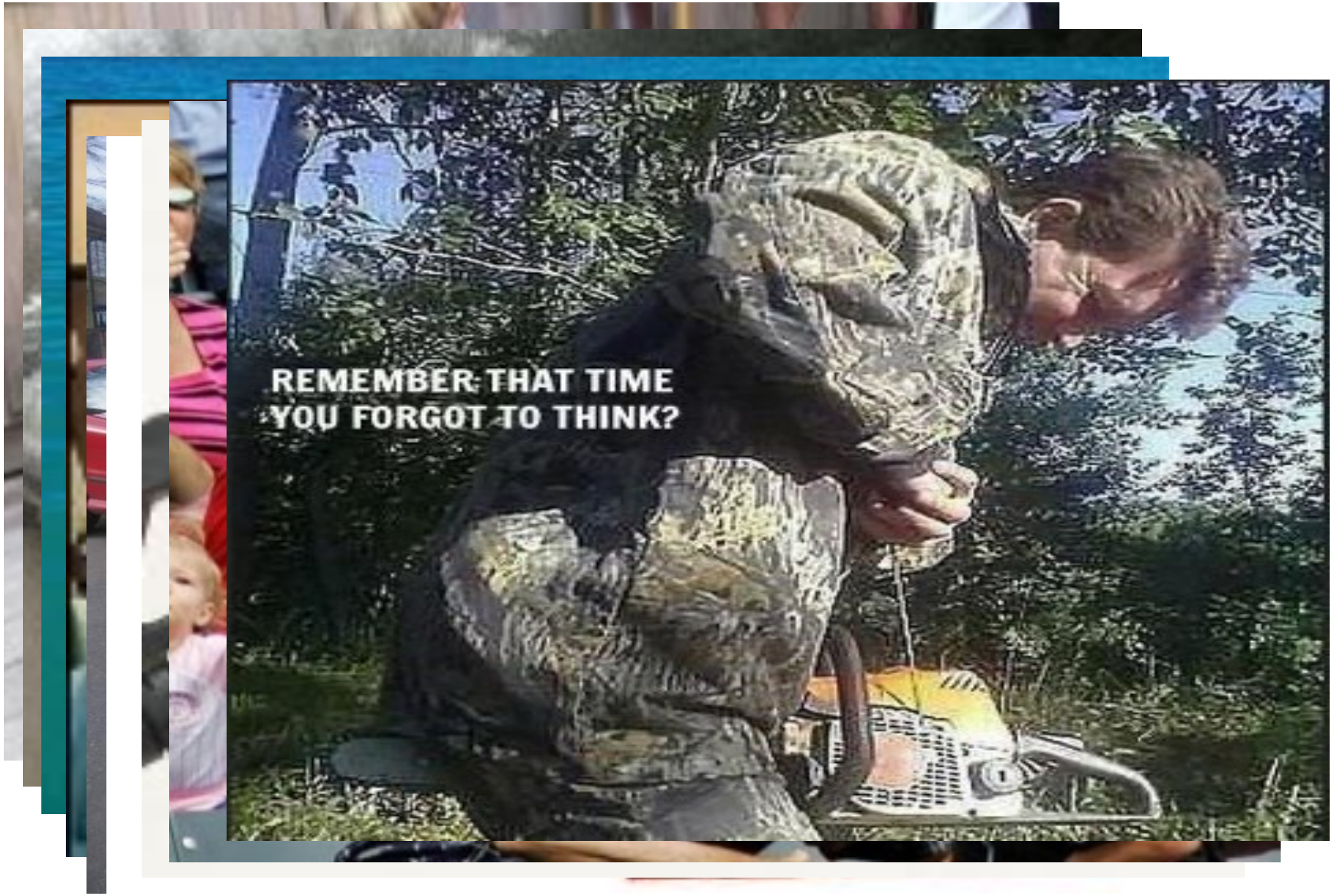
Physical injury or damage to health of people, property or environment.

Ouch.

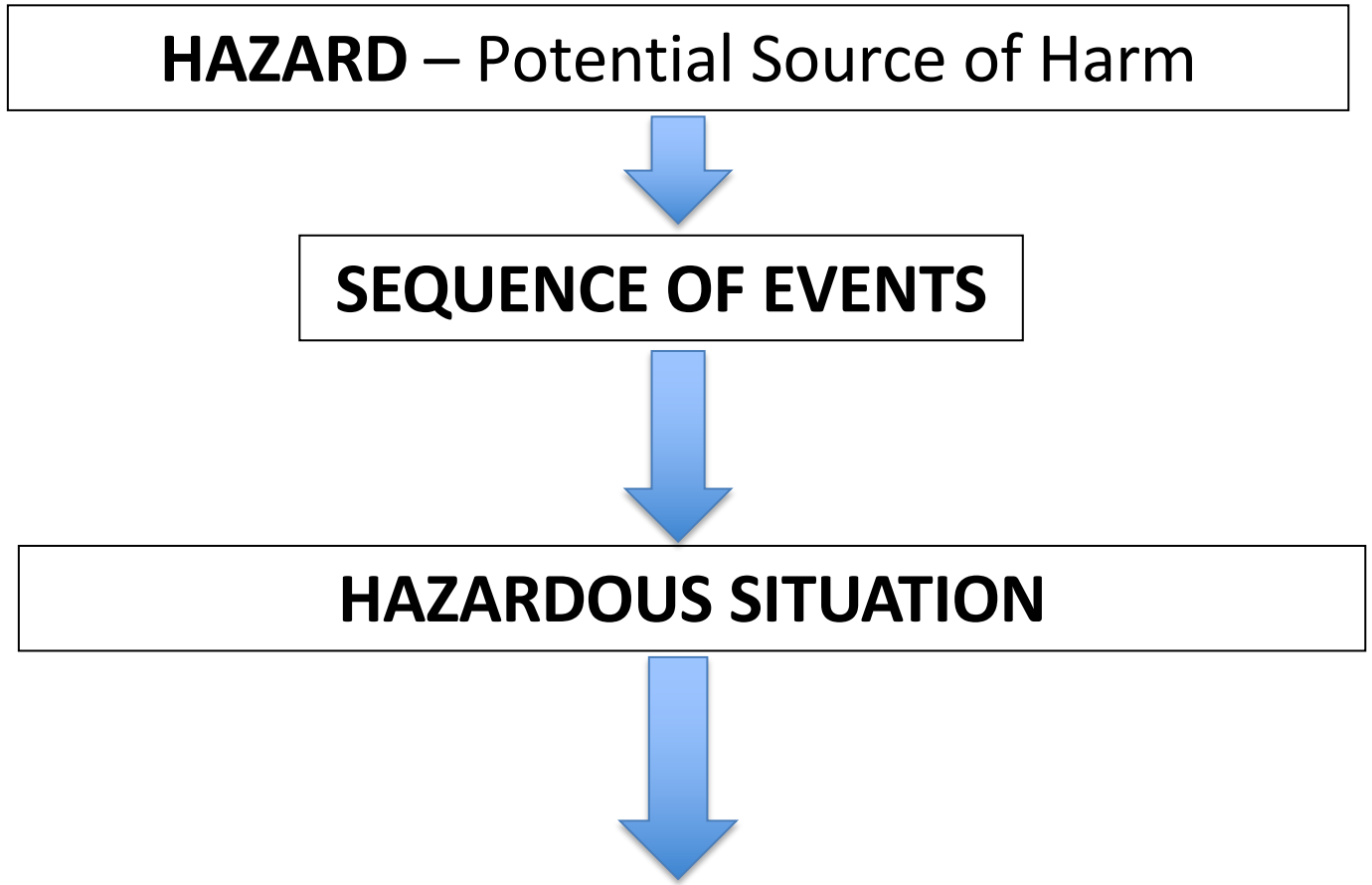


Harm and associated severity

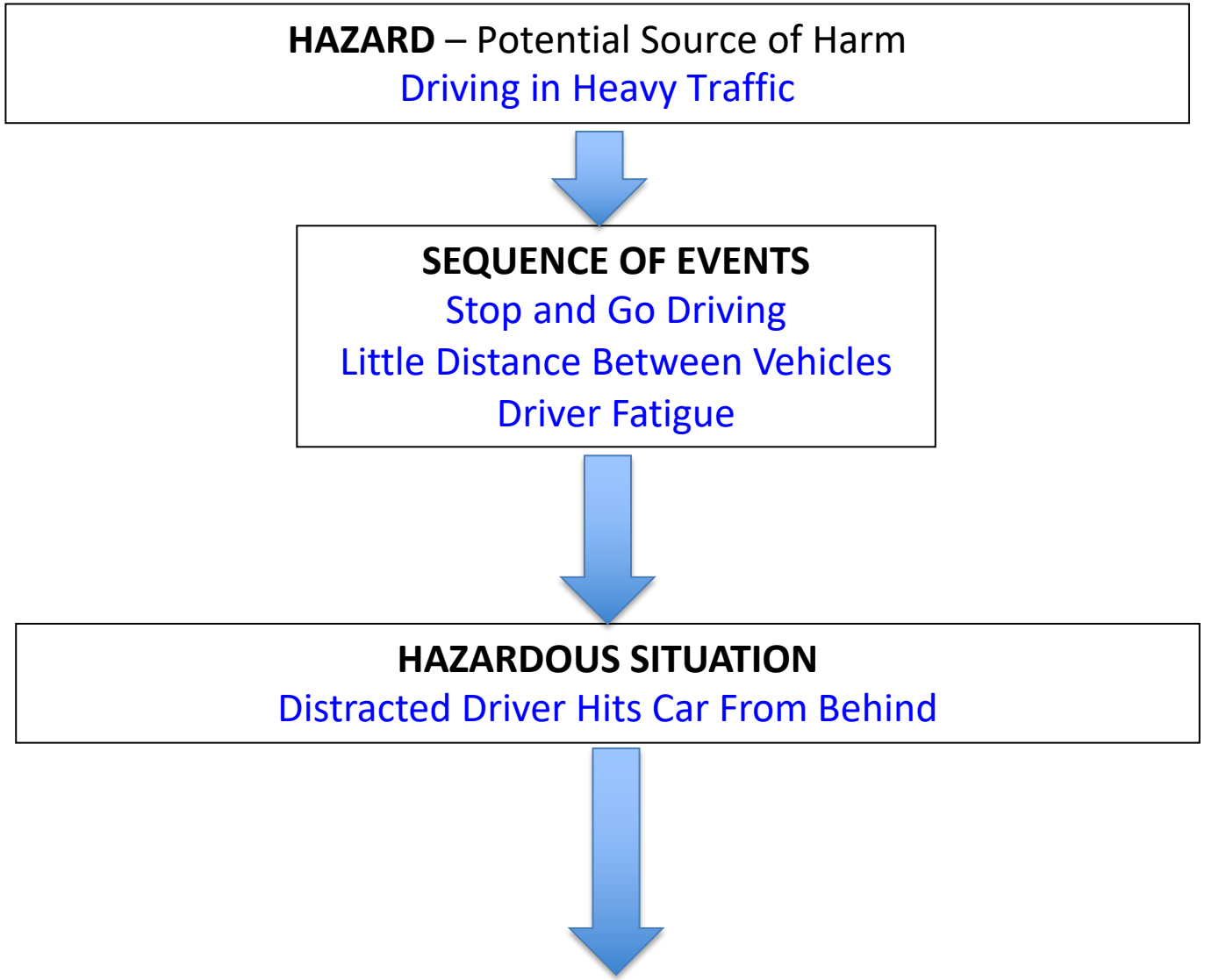
Quiz: Hazard, Hazardous Situation, or Harm ?



ISO 14971:2019 Annex C Figure C.1

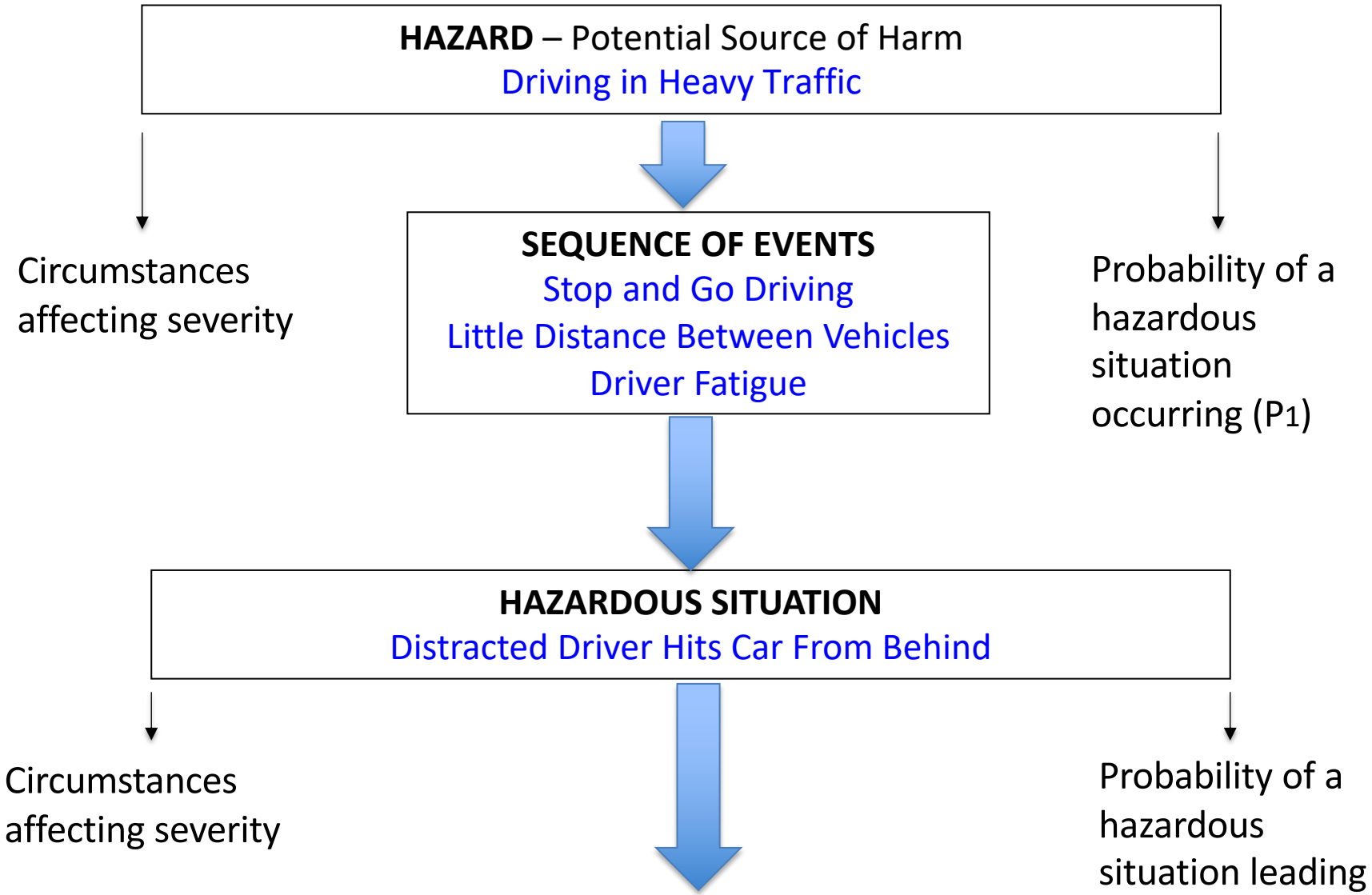


Example: Driving



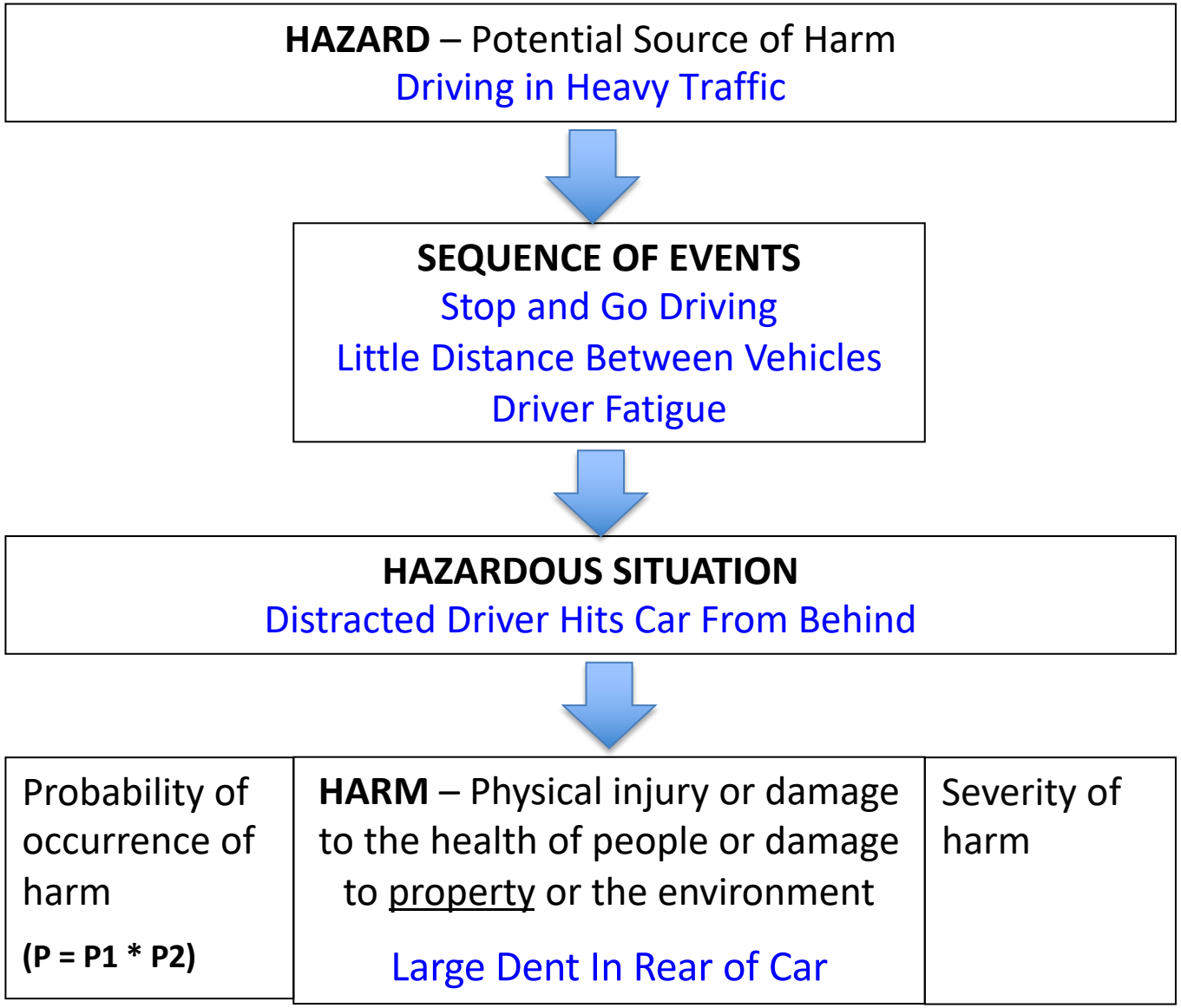
ISO 14971:2019 Annex C Figure C.1

Example: Driving



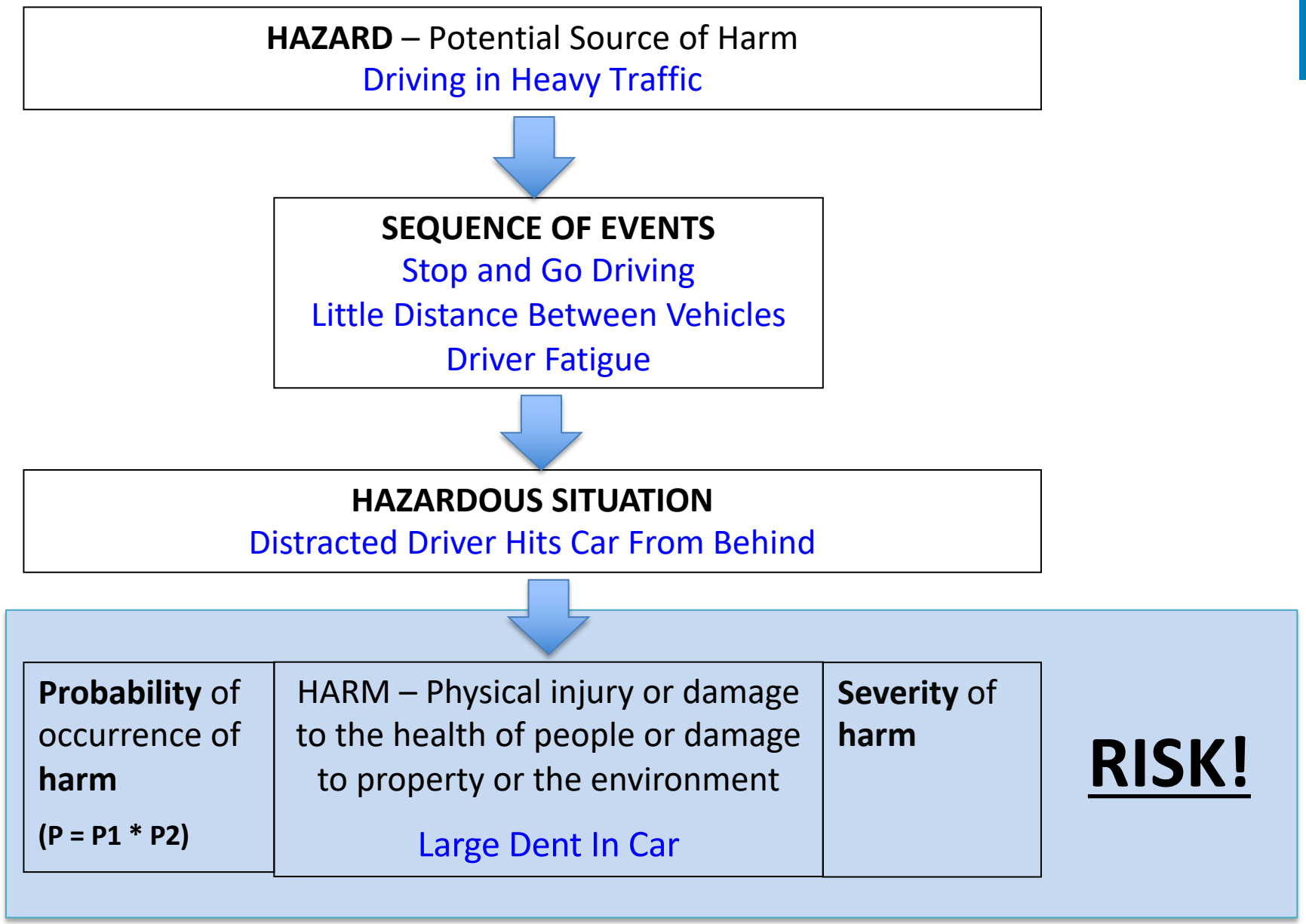
ISO 14971:2019 Annex C Figure C.1

Example: Driving



ISO 14971:2019 Annex C Figure C.1

Example: Driving



ISO 14971:2019 Annex C Figure C.1

Risk Evaluation

Risk Evaluation

Process of comparing the estimated risk (relative risk) against **given** (**predetermined**) **risk criteria** to determine acceptability of risk

Severity

Table D.3 — Example of five qualitative severity levels

Common terms	Possible description
Catastrophic	Results in patient death
Critical	Results in permanent impairment or life-threatening injury
Serious	Results in injury or impairment requiring professional medical intervention
Minor	Results in temporary injury or impairment not requiring professional medical intervention
Negligible	Inconvenience or temporary discomfort

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Probability / Likelihood

Table D.4 — Example of semi-quantitative probability levels

Common terms	Examples of probability range
Frequent	$\geq 10^{-3}$
Probable	$< 10^{-3}$ and $\geq 10^{-4}$
Occasional	$< 10^{-4}$ and $\geq 10^{-5}$
Remote	$< 10^{-5}$ and $\geq 10^{-6}$
Improbable	$< 10^{-6}$

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Use the Severity and Probability rankings to determine what is acceptable, unacceptable, and needs investigation

	Severity of Harm				
Probability of Harm	**Negl. – 1**	**Minor – 2**	**Serious – 3**	**Critical - 4**	**Cat. – 5**
Frequent – 5					
Probable – 4					
Occ. – 3					
Remote – 2					
Improb. – 1					

Risk Acceptance – Three Views

What the plan says

	Negl.	Minor	Serious	Critical	Cat.
Frequent					
Probable					
Occ.					
Remote					
Improb.					

What the manufacturer sees

	Negl.	Minor	Serious	Critical	Cat.
Frequent					
Probable					
Occ.					
Remote					
Improb.					

What a Regulator sees

	Negl.	Minor	Serious	Critical	Cat.
Frequent					
Probable					
Occ.					
Remote					
Improb.					

Risk Control

Risk Control

Process in which decisions are made and measures implemented by which risks are reduced to, or maintained within, specified levels.

Mitigations are called “risk controls”

There are different kinds of risk controls:

1. Inherent Safety – eliminate the problem
2. Protective measure – protect people from the problem
3. Information for Safety – tell someone about the problem

Example of Risk Controls

Inherent Safety
by design

Protective measures
(device or manufacturing)

Information for safety, and
user training

Examples of Protective Measures

Information for Safety

- If the hazardous situation cannot be removed by design, and if there are no protective measures, then and only then can you use information as a risk control.
- Need to demonstrate the information (e.g. labeling) is effective.

Production and Post-Production

Production and Post-Production Information

- Manufacturer has to establish, document, and maintain a system to collect and review information during production and post-production.
- The information is evaluated for safety
  - Are previously unrecognized hazards or hazardous situations present?
  - Is estimated risk(s) from a hazardous situation no longer acceptable?
  - Are there new or revised standards
- Results of the production and post-production evaluation feed back into to the risk management process

Risk Management from a Regulatory Perspective

Benefit and Benefit-Risk Analysis

Benefit: Positive impact or desirable outcome of the use of a *medical device* on the health of an individual, or a positive impact on patient management or public health

Benefits can include positive impact on clinical outcome, the patient's quality of life, outcomes related to diagnosis, positive impact from diagnostic devices on clinical outcomes, or positive impact on public health.

Benefit-risk analysis is a part of the risk management process in ISO 14971 and is important from a regulatory perspective!

- The *benefit-risk* analysis is used to determine if the *residual risk* is outweighed by the expected *benefits* of the *intended use* of the *medical device*.
- *Benefit-risk* analyses cannot be used to weigh *residual risks* against business advantages or economic advantages (i.e. for business decision making).

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Scenario

ABC Diagnostics has received an out of specification trend of complaints that their COVID-19 diagnostic product is generating incorrect negative results. Complaints indicate that the product is performing at a sensitivity of 95% and the product label claim is a sensitivity (i.e. not miss a negative result) of 99%. As a result, some patients are being misdiagnosed as not having COVID-19. These patients are not being treated appropriately and risk further spread of the contagious disease.

Scenario Poll

Based on the information given, what type of benefit-risk decision should ABC Diagnostics make?

1. Recall the product

2. Leave the product in the field

3. Not sure

Regulatory Risk-Based Decisions

- Risk-based decision making is essential to US FDA's approach:
  - Medical Device Classification
  - Medical Device Premarket Submissions – Determination of safety and effectiveness of a device
  - Scheduling of Inspections
  - Recalls
  - Enforcement Actions

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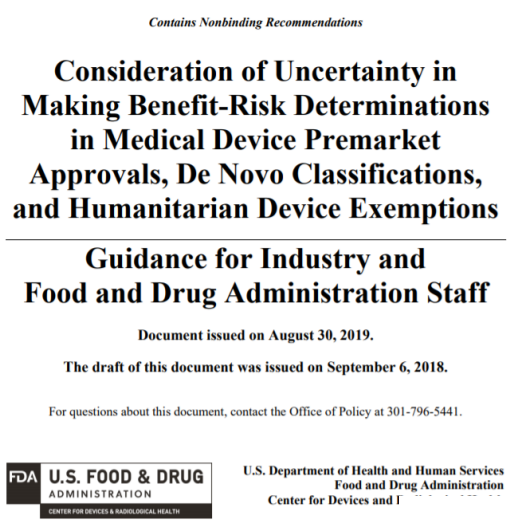
FDA Benefit-Risk Determinations

- Benefit-Risk Guidances (IDE, PMA/*de novo,* 510(k))
  - Identification of 'probable risks' and 'probable benefits' that are supported by valid scientific evidence.
- Assessment of Benefit
  - Type of benefit
  - Probability of patient experiencing benefit
  - Duration of effect
- Assessment of Risks
  - Severity, types, number and rates of harmful events
  - Probability of a harmful event
  - Duration of a harmful event
  - Risk from false-positive/false-negative (diagnostics)

FDA Benefit-Risk Guidances



Contains Nonbinding Recommendations

Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions

Guidance for Industry and Food and Drug Administration Staff

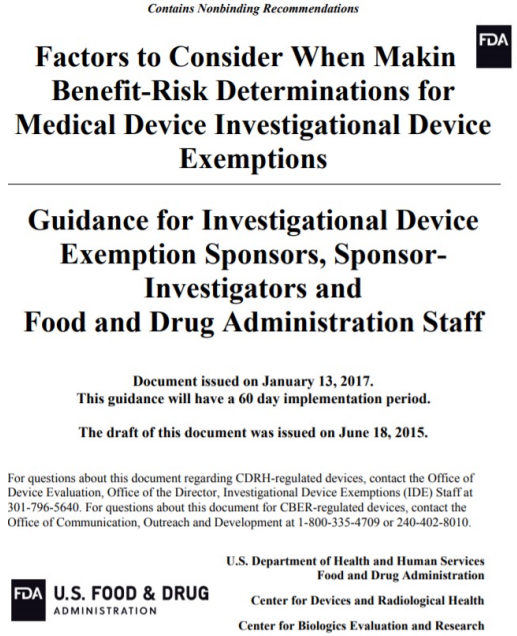
Document issued on August 30, 2019.

The draft of this document was issued on September 6, 2018.

For questions about this document, contact the Office of Policy at 301-796-5441.

U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and R



Contains Nonbinding Recommendations

Factors to Consider When Makin Benefit-Risk Determinations for Medical Device Investigational Device Exemptions

Guidance for Investigational Device Exemption Sponsors, Sponsor-Investigators and Food and Drug Administration Staff

Document issued on January 13, 2017.
This guidance will have a 60 day implementation period.

The draft of this document was issued on June 18, 2015.

For questions about this document regarding CDRH-regulated devices, contact the Office of Device Evaluation, Office of the Director, Investigational Device Exemptions (IDE) Staff at 301-796-5640. For questions about this document for CBER-regulated devices, contact the Office of Communication, Outreach and Development at 1-800-335-4709 or 240-402-8010.

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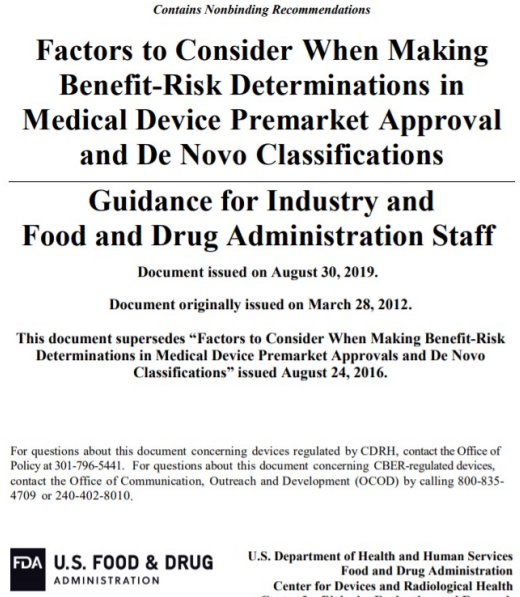
Center for Biologics Evaluation and Research



Contains Nonbinding Recommendations

Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications

Guidance for Industry and Food and Drug Administration Staff

Document issued on August 30, 2019.

Document originally issued on March 28, 2012.

This document supersedes "Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approvals and De Novo Classifications" issued August 24, 2016.

For questions about this document concerning devices regulated by CDRH, contact the Office of Policy at 301-796-5441. For questions about this document concerning CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD) by calling 800-835-4709 or 240-402-8010.

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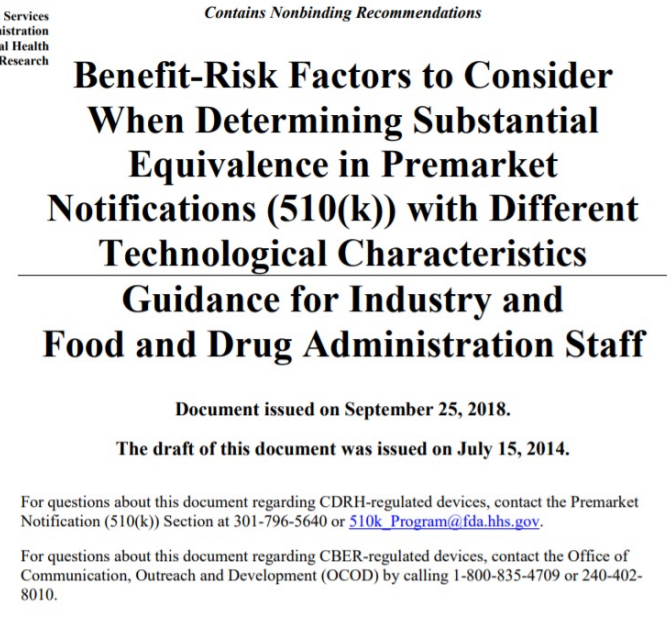


Contains Nonbinding Recommendations

Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications (510(k)) with Different Technological Characteristics

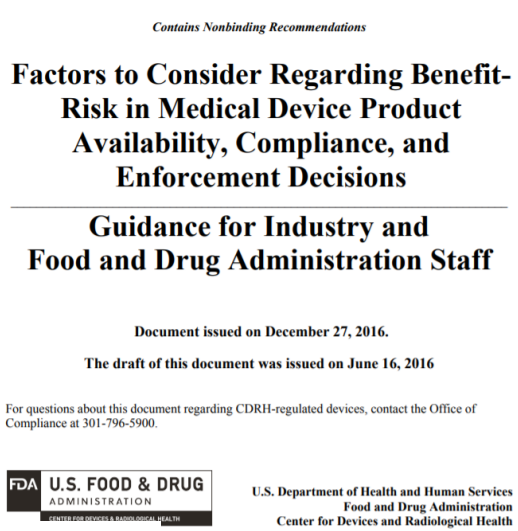
Guidance for Industry and Food and Drug Administration Staff

Document issued on September 25, 2018.

The draft of this document was issued on July 15, 2014.

For questions about this document regarding CDRH-regulated devices, contact the Premarket Notification (510(k)) Section at 301-796-5640 or 510k_Program@fda.hhs.gov.

For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD) by calling 1-800-835-4709 or 240-402-8010.



Contains Nonbinding Recommendations

Factors to Consider Regarding Benefit-Risk in Medical Device Product Availability, Compliance, and Enforcement Decisions

Guidance for Industry and Food and Drug Administration Staff

Document issued on December 27, 2016.

The draft of this document was issued on June 16, 2016

For questions about this document regarding CDRH-regulated devices, contact the Office of Compliance at 301-796-5900.

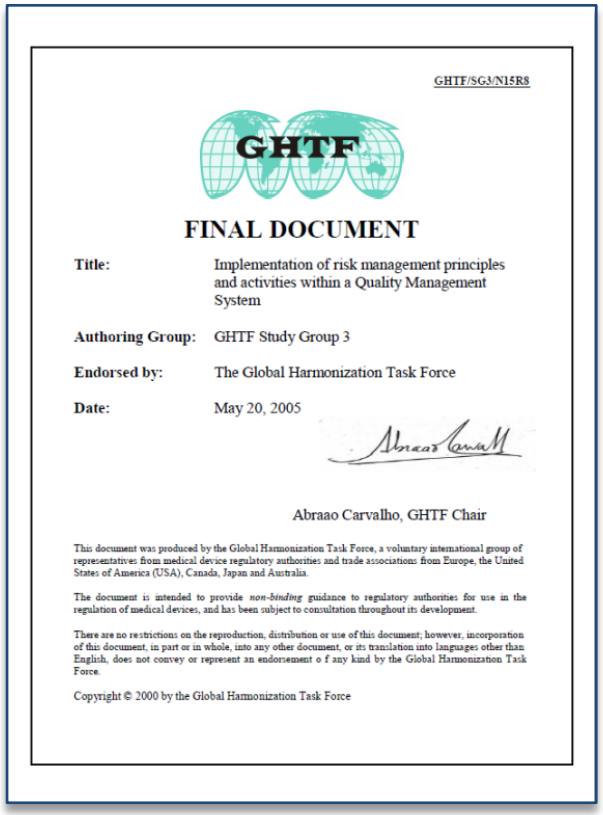
U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Risk Management
Global Harmonization Task Force (GHTF)
Guidance Document

Implementation of Risk Management Principles and Activities within a Quality Management System

- Key Principles:
  - Risk management activities should begin as early as possible in the design and development phase, when it is easier to prevent problems rather than correcting them later.
  - Relying on design and development processes to control risk is not sufficient.
  - After release of the device to market, risk management activities should be linked to quality management processes.



GHTF/SG3/N15R8

GHTF

FINAL DOCUMENT

Title: Implementation of risk management principles and activities within a Quality Management System

Authoring Group: GHTF Study Group 3

Endorsed by: The Global Harmonization Task Force

Date: May 20, 2005

Abraao Carvalho, GHTF Chair

This document was produced by the Global Harmonization Task Force, a voluntary international group of representatives from medical device regulatory authorities and trade associations from Europe, the United States of America (USA), Canada, Japan and Australia.

The document is intended to provide *non-binding* guidance to regulatory authorities for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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**Document will be revised by the IMDRF QMS Working Group*

Summary

- Risk management spans the full total product lifecycle of medical devices
- Risk management activities must be embedded throughout a manufacturer's Quality Management System
- Concepts of risk are included in regulatory requirements as well as international documents and standards

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Resources

Cited Resource	URL
ISO 14971:2019 Medical devices – Applications of risk management to medical devices	www.iso.org/standard/72704.html (for purchase from standards organization)
ISO/TR 24971:2020 Medical devices — Guidance on the application of ISO 14971	www.iso.org/standard/74437.html (for purchase from standards organization)


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