Clinical Evaluation Report Overview and the Literature Review Process

Hana Vegher, Ph.D., PMP

Manager, Clinical Evaluation Program

Worldwide Clinical Affairs, Abbott Vascular

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Outline

- Clinical Evaluation Definition
- Clinical Data
- Literature Review Process as a Critical Component of the Clinical Evaluation
- Risk Assessment
- Conclusion

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Clinical Evaluation

- The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer (MEDDEV 2.7.1. Rev.3)
- **Required by regulatory bodies (OUS) before the manufacturer places the device on the market**
- An ongoing and continuous process conducted throughout the life cycle of the devices

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Clinical Evaluation: Key Applicable Standards and Guidelines

Standard/Guidance	Title
EN ISO 14155:2011	Clinical Investigation of Medical Devices for Human Subjects Good Clinical Practice
NB-MED/2.7/Rec 3 (1999)	Notified Bodies' Recommendations on the Evaluation of Clinical Data
MEDDEV 2.7.1 Rev 3 (December 2009)	European Commissions Guidelines on Medical Devices: Evaluation of Clinical Data, A Guide for Manufacturers and Notified Bodies
MEDDEV 2.7.1 Appendix 1 (December 2008)	Evaluation of Clinical Data: A Guide for Manufacturers and Notified Bodies – Clinical Evaluation of Coronary Stents
MDD 93/42/EEC	Council Directive of the European Communities Concerning Medical Devices
EN ISO 14971: 2012, Medical Devices	British Standard: Application of Risk Management to Medical Devices
MEDDEV 2.12-1 Rev 8 (January 2013)	Guidelines on a Medical Devices Vigilance System
IMDRF GHTF SG5/N2R8 (May 2007)	Global Harmonization Task Force (Study Group 5) Clinical Evaluation
MEDDEV 2.12/2 Rev 2 (January 2012)	Guidelines on Medical Devices Post-Market Clinical Follow-Up Studies

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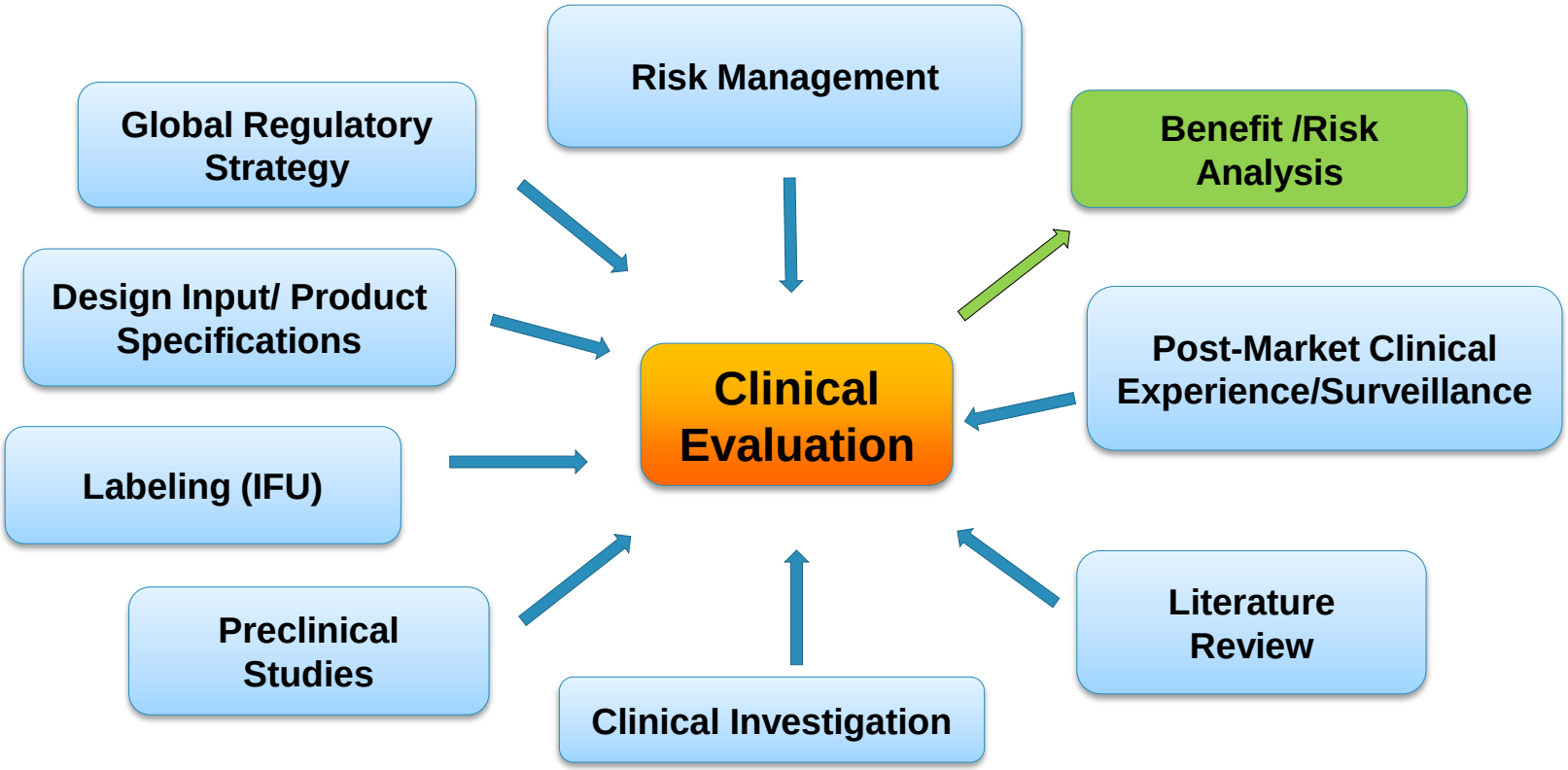
Clinical Evaluation Process

Integrated into the quality system as an ongoing and continuous process conducted throughout the life cycle of the device



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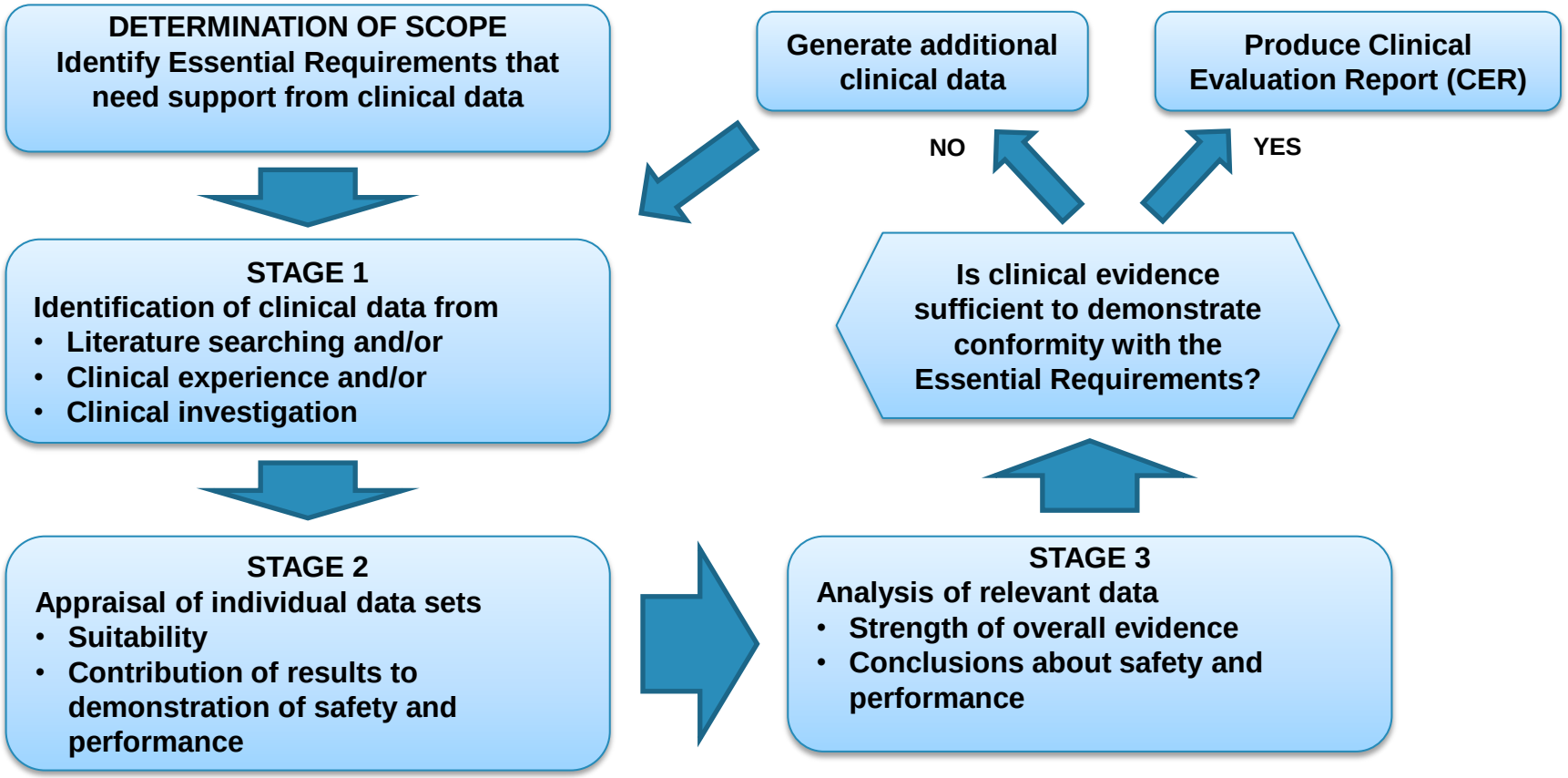
Clinical Evaluation Stages (MEDDEV 2.7.1 Rev. 3)

The clinical evaluation includes planning, assessment, and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device



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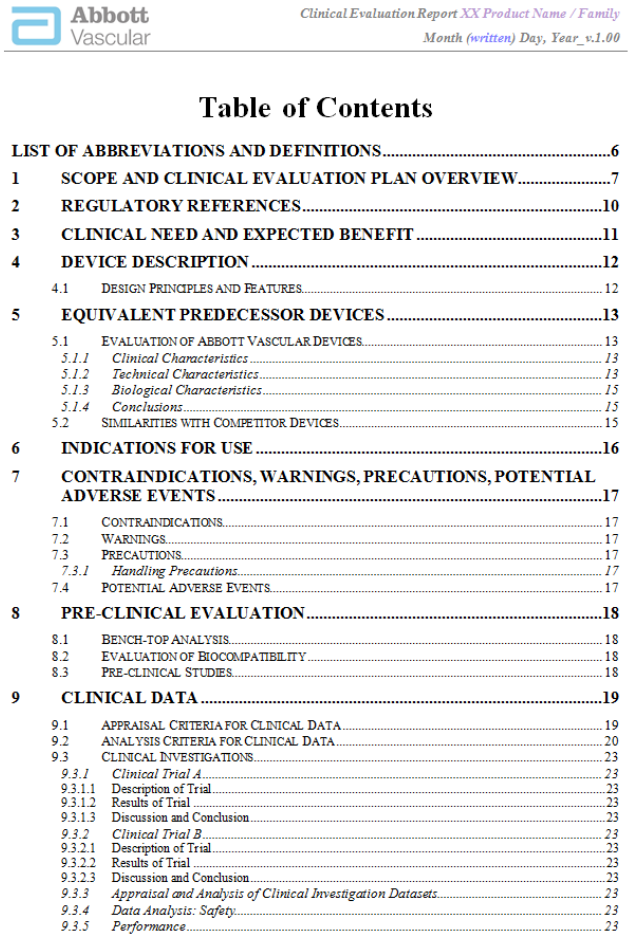
Clinical Evaluation: Planning and Preparation

Planning and Preparation

- Regulatory Standards, Guidelines
- Internal SOP/DOP for conducting Clinical Evaluation and Quality System related procedures
- Templates for Clinical Evaluation Plan (CEP) and Clinical Evaluation Report (CER)
  - CEP (pre-market)
  - Initial CER (pre-market)
  - Update to the CER (post-market)
- Training

CER Template Example



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Clinical Evaluation Report XX Product Name / Family
Month (written) Day, Year_v.1.00

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Clinical Evaluation: Planning and Preparation

Scoping the Clinical Evaluation (MEDDEV 2.7.1 Rev. 3)

- Before a clinical evaluation is undertaken, the manufacturer should define its scope based on the Essential Requirements that need to be addressed from a clinical perspective

- Considerations should include:
  - whether there are any design features of the device or target treatment populations that require specific attention
  - whether data from equivalent devices can be used to support the safety and/or performance of the device in question
  - the data source(s) and type(s) of data to be used in the clinical evaluation

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Clinical Evaluation: Clinical Data

Safety and performance of *device* is evaluated using weighted clinical data from *device* and/or equivalent predecessor devices

- Clinical Investigation Data
- Critically-Evaluated Scientific Literature for *device* and/or equivalent devices
- Post Market Clinical Experience data

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Clinical Evaluation: Defining the Criteria for Appraisal and Analysis of the Identified Clinical Data

Appraisal Criteria for Suitability

Table D1 Sample Appraisal Criteria for Suitability

Sutability Criteria	Description		Grading System
Appropriate device	Were the data generated from the device in question?	D1 D2 D3	Actual device Equivalent device Other device
Appropriate device application	Was the device used for the same intended use (e.g., methods of deployment, application, etc.)?	A1 A2 A3	Same use Minor deviation Major deviation
Appropriate patient group	Where the data generated from a patient group that is representative of the intended treatment population e.g., age, sex, etc.) and clinical condition (i.e., disease, including state and severity)?	P1 P2 P3	Applicable Limited Different population
Acceptable report/data collation	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	R1 R2 R3	High quality Minor deficiencies Insufficient information

MEDDEV 2.7.1 Rev. 3

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Clinical Evaluation: Defining the Criteria for Appraisal and Analysis of the Identified Clinical Data

Appraisal Criteria for Data Contribution

Table D2 Sample Appraisal Criteria for Data Contribution

Data Contribution Criteria	Description		Grading System
Data source type	Was the design of the study appropriate?	T1 T2	Yes No
Outcome measures	Do the outcome measures reported reflect the intended performance of the device?	O1 O2	Yes No
Follow up	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1 F2	Yes No
Statistical significance	Has a statistical analysis of the data been provided and is it appropriate?	S1 S2	Yes No
Clinical significance	Was the magnitude of the treatment effect observed clinically significant?	C1 C2	Yes No

MEDDEV 2.7.1 Rev. 3

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Clinical Evaluation: Analysis Criteria and Clinical Data Weighting

The clinical data appraised for Suitability and Data Contribution will be further assessed to evaluate its relative contribution towards safety and performance

- A Weighting Level is assigned to data based on the equivalence criteria to evaluate its relative contribution to the safety and performance assessment

EXAMPLE:

- **Weight Level 1** will be given to data which reports on the actual device
- **Weight Level 2** will be given to data which reports on an equivalent predecessor device
- **Weight Level 3** will be given to data which reports on other similar device
- Overall Weighting: **Level 1> Level 2> Level 3**

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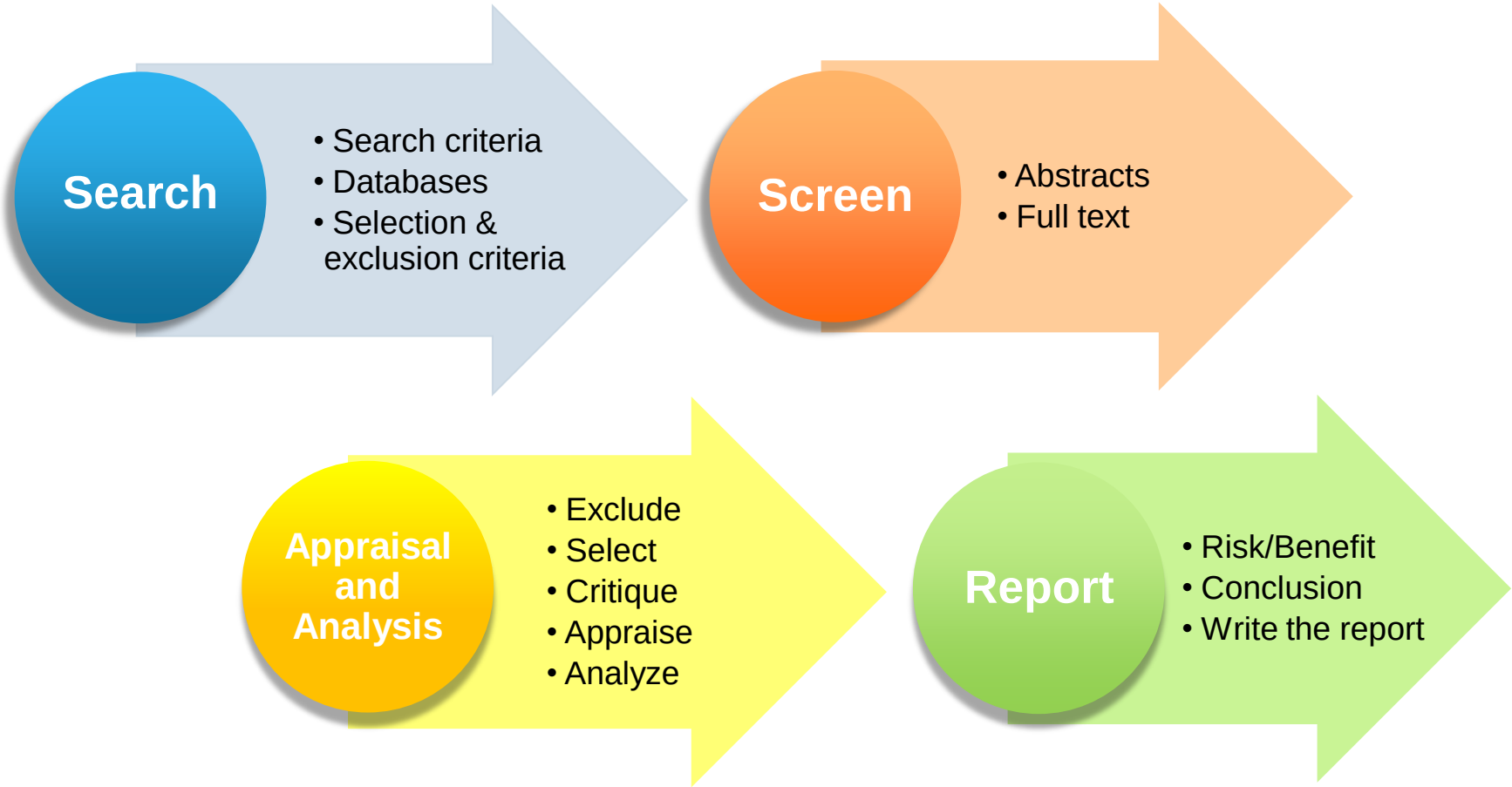
Clinical Evaluation: Literature Review Process as a Critical Component of the Clinical Evaluation

Objective and Strategy of the Literature Review



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Clinical Evaluation: Literature Search Protocol

Example of Literature Search Protocol

- Search 1
  - Device Name
  - Equivalent Predecessor Device Name
  - Period Covered by Search
  - Name of the Person Undertaking the Search
  - Literature sources used to identify data: list databases (details can be included in an appendix)
  - Boolean Search Terminology: list specific terms
  - Selection Criteria
  - Unedited Search Algorithm

Clinical Evaluation: Literature Dataset Appraisal and Analysis

The clinical data appraised for Suitability and Data Contribution is further assessed within each level to evaluate its relative contribution towards safety and performance

Example of Appraisal and Analysis

Article		Appraisal Criteria for Suitability				Appraisal Criteria for Data Contribution					Overall Weighting
Article No.	Author & Date										
[Actual Device]											
1		D1	A1	P1	R1	T1	O1	F1	S1	C1	Level 1
4		D1	A1	P1	R1	T2	O1	F1	S1	C1	
5		D1	A1	P1	R2	T2	O2	F2	S2	C2	
6		D1	A1	P1	R2	T2	O1	F1	S2	C1	
11		D1	A1	P1	R3	T2	O1	F2	S3	C1	
[Equivalent Predecessor Device]											
2		D2	A1	P1	R1	T2	O1	F1	S2	C1	Level 2
3		D2	A1	P1	R2	T2	O1	F1	S2	C1	
7		D2	A2	P2	R3	T2	O1	F1	S3	C1	
[Other Similar Devices]											
8		D3	A1	P1	R3	T3	O1	F2	S2	C1	Level 3
9		D3	A1	P1	R1	T2	O1	F1	S2	C1	
10		D3	A1	P1	R1	T2	O1	F1	S1	C1	
12		D3	A1	P1	R3	T2	O1	F1	S3	C1	
13		D3	A1	P1	R3	T2	O1	F1	S3	C1	
14		D3	A1	P1	R3	T2	O1	F1	S3	C1	
15		D3	A1	P1	R1	T1	O1	F1	S1	C1	
16		D3	A1	P1	R1	T2	O1	F1	S1	C1	
17		D3	A1	P1	R3	T2	O1	F1	S3	C1	

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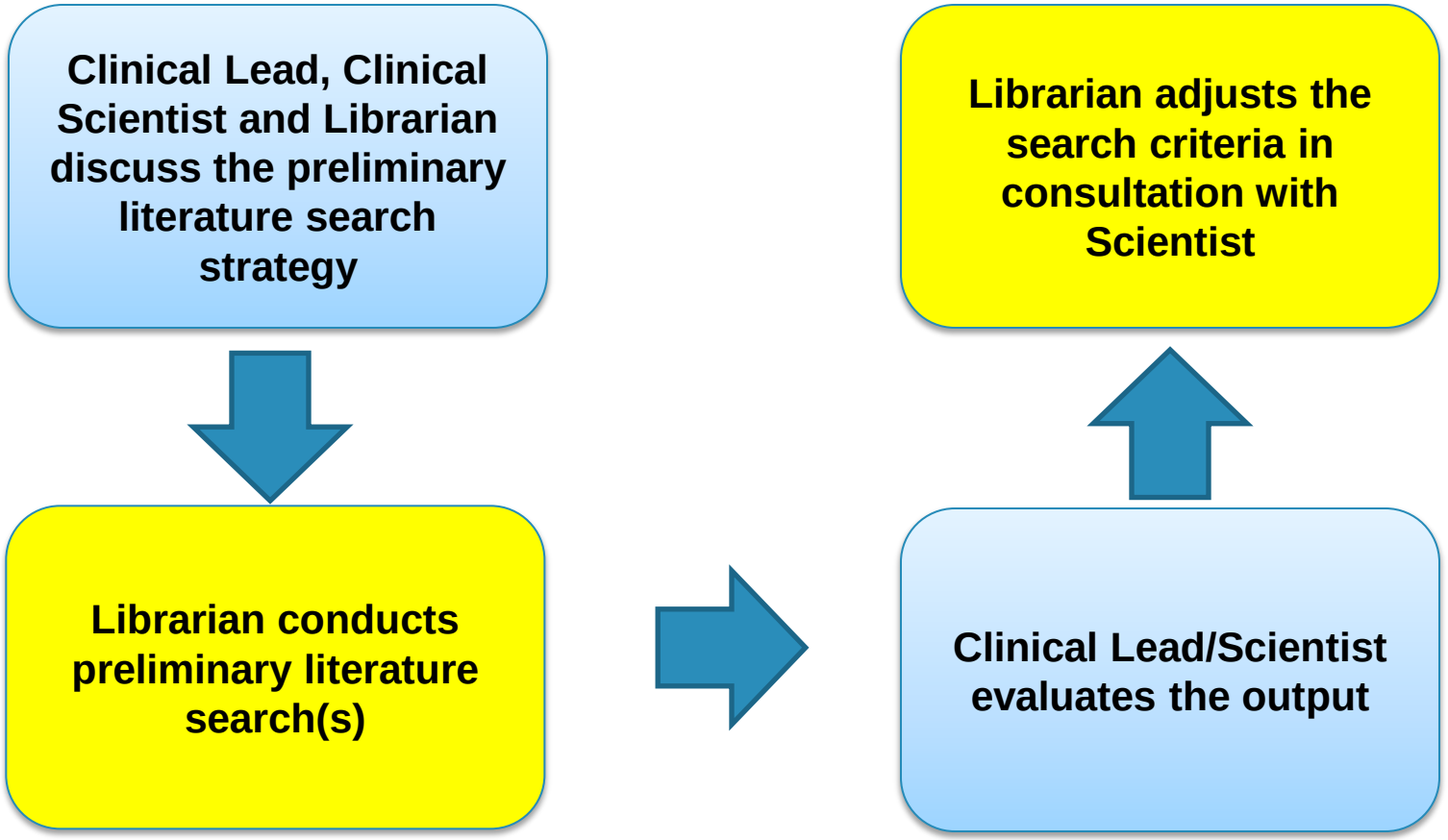
Clinical Evaluation: Literature Review Conclusion

- Conclusion of the Literature Review
  - Provide conclusions for clinical evidence categorized into weight levels based on their relevance towards addressing the safety and performance of the device
    - Level 1 Evidence: Actual Device
    - Level 2 Evidence: Equivalent Predecessor Device
    - Level 3 Evidence: Other Similar Device
  - Provide conclusions about any new risks and evaluate their impact on the product literature, risk assessment, product design, etc.

Example of Literature Review Process



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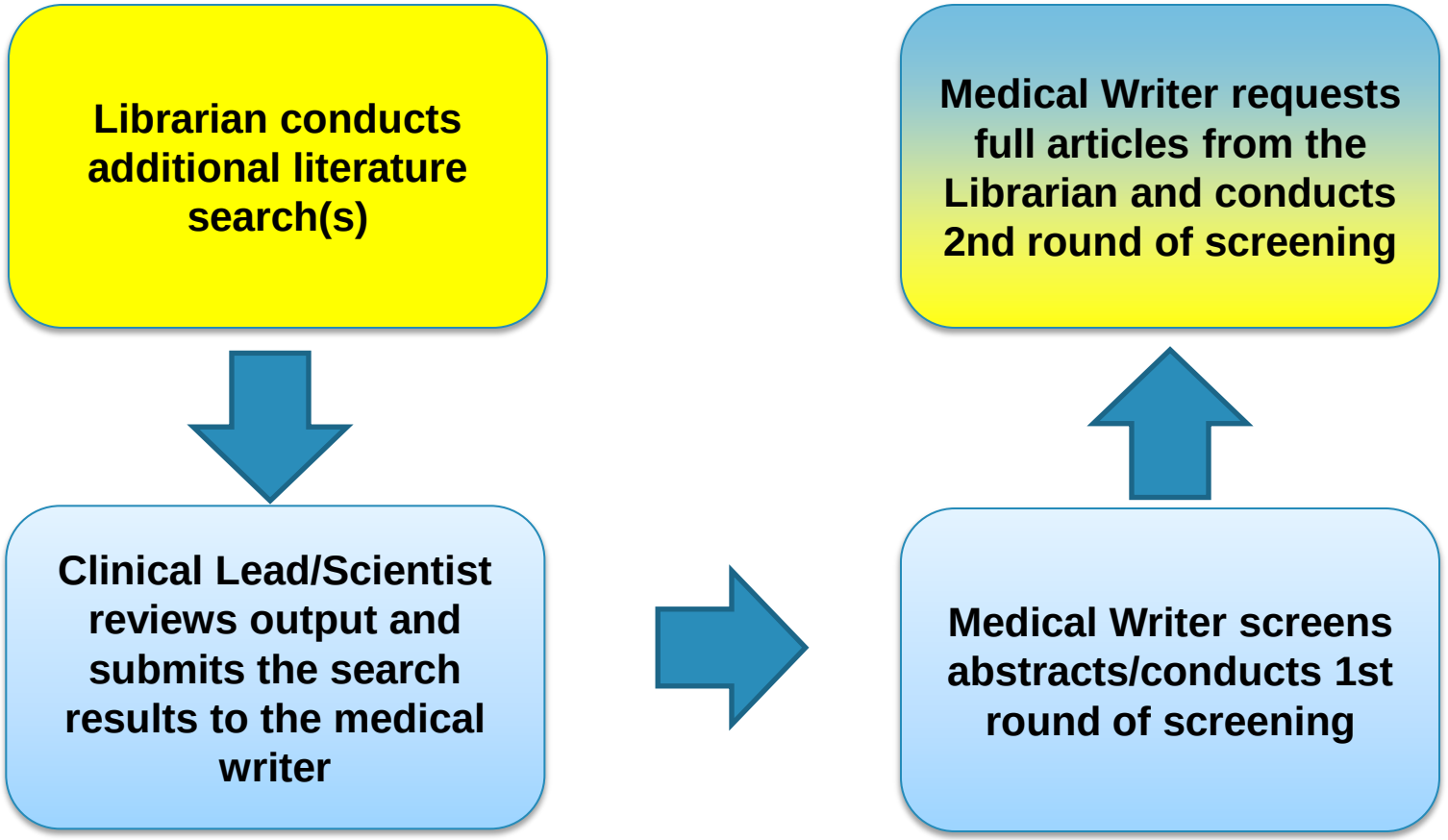
Example of Literature Review Process Cont'd



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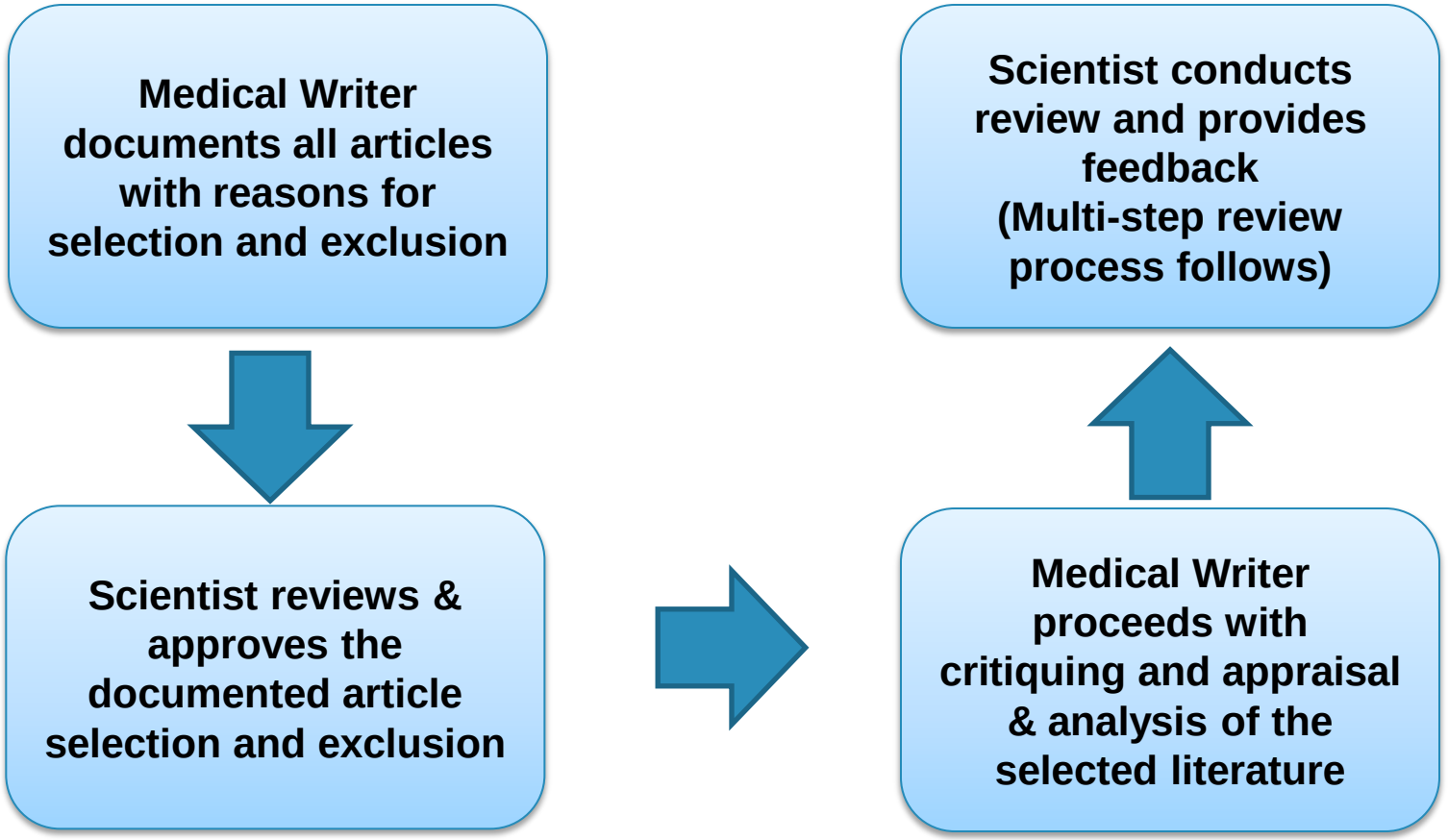
Example of Literature Review Process Cont'd



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Clinical Evaluation: Risk Assessment

- The current Risk Assessment Report
- Evaluation of Clinical Data (e.g. literature review) for any new risks not discussed/considered in the Risk Assessment Report and IFU
  - Consider whether Risk Assessment Report or IFU needs to be updated
- Clinical Risk to Benefit Assessment
  - Summarize the benefits
  - Summarize the risks
  - Summarize the mitigation of the risks
- Conclude whether the over-all benefits outweigh the risks

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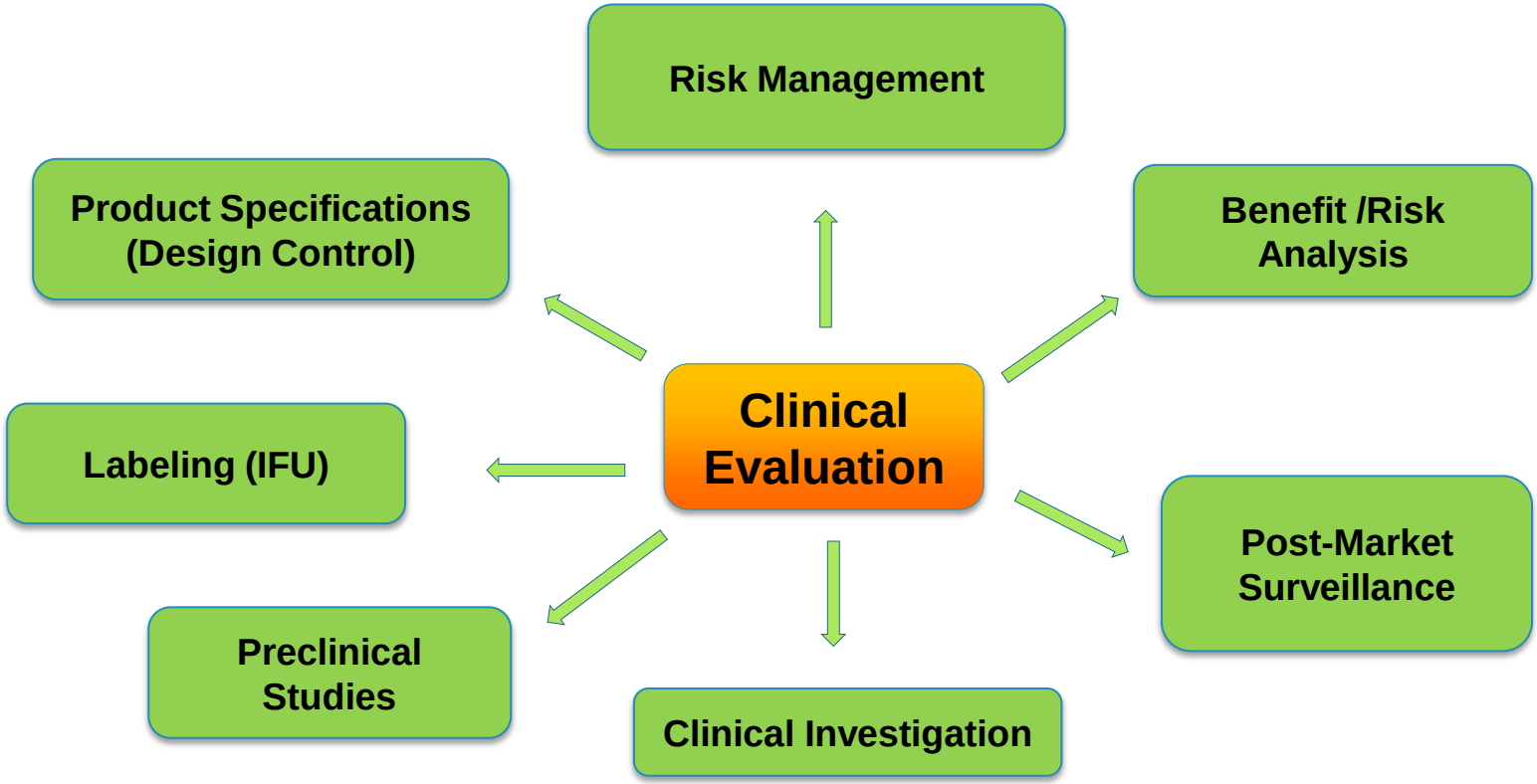
Clinical Evaluation: Conclusion

- Outline clearly the conclusions reached about the safety and performance of the device from the evaluation, with respect to the intended use of the device
- State whether:
  - clinical evidence demonstrates conformity with relevant Essential Requirements
  - performance and safety of the device as claimed have been established
  - risks associated with the use of the device are acceptable when weighed against the benefits to the patient

Clinical Evaluation Process

Integrated into the quality system as an ongoing and continuous process conducted throughout the life cycle of the device



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THANK YOU

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