Content of Human Factors Information in Medical Device Marketing Submissions – Draft Guidance for Industry and Food and Drug Administration Staff, FDA-2015-D-4599-0008

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GENERAL COMMENTS ON THE DOCUMENT (optional)
We commend the Agency's leadership in proposing a risk-based approach to human factors engineering information in device marketing submissions and harmonizing with ISO 14971:2019, ANSI/AAMI HE75:2009/(R)2018, and IEC 62366-1:2015. We find the new tables and flowchart to be very helpful. The following comments provided were compiled by the ISPE Combination Product Community of Practice.
As this guidance was authored by CDRH, with consultation from OCP, we request additional clarity on how this guidance applies to drug-led or biologic-led combination products reviewed by CDER/CBER/DMEPA. Additionally, we request that the Agency clarifies whether the requirements in this guidance are applicable to Combination Products with Device constituents and how this guidance will need to be understood in relation to the "Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development" guidance. For example, we note certain definitions (e.g., critical task) and some parts (e.g., use of risk levels) in this draft guidance differ from the draft combination products human factors guidance[1]. We request this guidance includes references to the combination product human factors guidance, where differences exist, and provides clarity to sponsors of drug-/biologic-led combination products applications so that they adhere to the appropriate guidance.
Figure 1 and the accompanying text for HF Submission Category 1 under "Recommended Contents of Human Factor (HF) Information" suggest that an HF assessment is expected when there is no change to the user interface, intended users, uses, use environments, training, or labeling. We recommend more clarity be provided with an example of the level of information that would be expected (e.g., if a statement from the sponsor confirming the submission as HF Submission Category 1 would be considered sufficient).
ISPE recommends that consideration is given to aligning terminology in this guidance with ISO 14971:2019 – Medical devices – Risk management for medical devices, and potentially the recently revised ICH Guideline, Q9(R1), Quality Risk Management. Such alignment would be beneficial to sponsors developing medical devices and medical device constituents of combination products. For example, alignment on terms "risk analysis", and "risk control". As such, the title of Table 2 is "Use-Related Risk Analysis", however as the table does not include probability of occurrence column, Table 2 is

[1] United States Food and Drug Administration. Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development. https://www.fda.gov/files/about%20fda/published/Human-Factors-Studies-and-Related-Clinical-Study-Considerations-in-Combination-Product-Design-and-Development.pdf. Accessed 07 February 2023.

GENERAL COMMENTS ON THE DOCUMENT (optional)
not a risk analysis, but “use-related hazard analysis”. This terminology is also in accordance with AAMI/ANCI/IEC 62366-1’s use of the terminology, “hazard-related use scenario”.

Specific Comments on the Text

ISPE indicates text proposed for deletion with ~~strikethrough~~ and text proposed for addition with **bold and underlining**.

Section or Line Number	Current Text	Proposed Change	Rationale or Comment
Lines 16-17	“A unique aspect of medical devices is the critical role of device-user interface interactions for their safe use.”	“A unique aspect of medical devices is the critical ~~role~~ **impact the** device user-interface **design** ~~for their~~ **has on the** safe **and effective use of the device**.”	For additional clarity, we recommend amending this phrase to enable consistency across FDA guidance documents regarding human factors, which should simplify the interpretation of terms, and improve efficiency in execution of human factors studies.
Lines 28, 289, 368	“The main factors to consider in a risk-based approach to human factors assessment, as described in this draft guidance, include the identification of (i.e., presence of or modification to) critical tasks and the elimination or reduction of use-related hazards.”	We recommend using the terminology “use-related hazards” and “use-related hazard analysis,” where appropriate, and removing the term “use-related risks” and “use-related risk analysis”. Additionally, please add the new “use-related hazards” in the glossary.	The draft guidance interchanges the terms “use-related hazards” and “use-related risks” throughout the document. Refer to “use-related risks” on lines 36-37 and 308. However, the draft guidance does not provide a definition for the new use of the term “use-related hazards.” We believe that interchanging “risk” and “hazards” will cause confusion in the industry regarding what is a hazard, harm, hazardous situation, and risk.
Lines 40-41 (additional examples on	“The marketing submission should, where appropriate, demonstrate that the needs of the intended users were considered in the device design and that the device is safe and effective	We recommend consistently using one term for “device user-interface design” throughout the guidance and avoid interchanging the terms device, product, design, user-interface,	Kindly consider that the current guidance, *Applying Human Factors and Usability Engineering to Medical Devices*[2], provides industry with a simple foundation to build their HF processes. Ensuring

[2] United States Food and Drug Administration. Applying Human Factors and Usability Engineering to Medical Devices. https://www.fda.gov/media/80481/download. Accessed 07 February 2023.

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lines 157, 212, 271)	for the intended users, uses, and use environments."	device-user interface, final finished device, etc. For example, we recommend the following revision: "The marketing submission should, where appropriate, demonstrate that the needs of the intended users were considered in the device **user-interface** design and that the device is safe and effective for the intended users, uses, and use environments."	this new draft guidance document complements the final version of the Applying Human Factors guidance will be critical in value to industry. If this draft guidance is to complement that final guidance, kindly consider consistency in terms and accuracy of their use to minimize opportunities for confusion and variable interpretation, where possible.
42, 58, Line 179 (Figure 1 – HF Submission Category 3), 252, 262 (Table 1), 264 (Table 2), 306, 408	"validation testing"	Consider replacing "validation testing" throughout the document with "HF Validation Testing" when the intent is HF validation testing. Further, please clarify the distinction between HF validation and design validation.	HF validation and design validation are not equivalent terms; human factors validation testing represents one portion of design validation. Different objectives and methodologies and distinction are required to prevent confusion amongst device developers.
Line 43, (additional references to lines 308, 310, 418, 422)	"[…] and a description of residual risks."	We recommend updating descriptions and the definition of "residual risks" with "use-related residual risks".	We recommend clarity and consistency in terminology and consideration of ISO 14971:2019 emphasis on use-related residual risks.
Lines 100-152	See list of definitions.	**Risk** Combination of the probability of occurrence of harm and the severity of that harm [ISO 14 971:2019] **Risk Analysis** Systematic use of available information to identify hazards and to estimate the risk [ISO 14971:2019] **Risk Assessment** Overall process comprising a risk analysis and a risk evaluation [ISO 14971:2019]	We recommend considering the inclusion of the terminology and definitions in alignment with consensus standards. For example, in IEC 62366-1 the discussion is around use-related hazards, the term used is: **Hazard-related use scenario/Use-related hazards*** Use scenario that could lead to a hazardous situation or harm. *Note, the assessment of use-errors and potential harms, within 62366-1 is referred to as an assessment of hazard-related use scenarios: 5.2 Identify and describe hazard-related use scenarios and 5.3 Select the

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		Risk Control Process in which decisions are made and measures implemented by which risks are reduced to, or maintained within, specified levels [ISO 14971:2019] **Risk Evaluation** Process of comparing the estimated risk against given risk criteria to determine the acceptability of the risk [ISO 14971:2019] **Risk Management** Systematic application of management policies, procedures and practices to the tasks of analyzing, evaluating, controlling and monitoring risk [ISO 14971:2019] **Use Error** User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the use [ISO 14971:2019] **Use Safety** Freedom from unacceptable use-related risk [Applying Human Factors Guidance[2]] **Use Scenario** Specific sequence of tasks performed by a specific user in a specific use environment and any resulting response of the medical device [IEC 62366-1:2015-02+AMD1:2020]	hazard-related use scenarios for summative evaluation. [IEC 62366-1:2015-02+AMD1:2020] This terminology aligns with the established definitions of hazard, hazardous situation and harm.
Lines 105-107	"Critical task: a user task which, if performed incorrectly or not performed at all, would or could cause serious harm to the patient or user,	The definition of a "critical task" in this document differs from the *Human Factors Studies and Related Clinical Study*	Such alignment or reference would be beneficial to sponsors developing combination products that may include already approved/cleared medical devices.

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	where harm is defined to include compromised medical care."	*Considerations in Combination Product Design and Development Draft Guidance*.[1] Please consider harmonizing the definition of "critical task", such as a reference be added to the combination product guidance definition.	
Lines 118-123	"Human factors validation testing: Testing conducted at the end of the device development process to assess user interactions with a device user interface to identify use errors that would or could result in serious harm to the patient or user. Human factors validation testing is also used to assess the effectiveness of risk management measures. Human factors validation testing represents one portion of design validation."	We recommend the following revision: "Human factors validation testing: Testing conducted at the end of the device development process to assess user interactions with a device user interface to identify use errors that would or could result in serious harm to the patient or user **and support demonstration of safe and effective use**. Human factors validation testing is also used to assess the effectiveness of risk ~~management~~ **control** measures**.** Human factors validation testing represents one portion of design validation."	We recommend the following clarification and replacing the term "risk management measures" with "risk control measures" as given in ISO 14971:2019 (and ICH Q9(R1)).
Line 128	"Serious harm: Includes both serious injury and death."	See Rationale or Comment column.	For clarity, ISPE recommends that a full definition is given for "Serious Harm" rather than indicating only what may be included. A suggestion would be the same as a serious adverse event: https://www.fda.gov/safety/reporting-serious-problems-fda/what-serious-adverse-event)
Line 148-151	"Use-related risk: Combined probability, occurrence, and severity of harm for a given aspect of device use or for the overall use of a device. Use-related risk analysis: Systematic use of available information to identify use related hazards and to estimate the use-related risk."	We recommend if keeping the "risk" term, rephrasing the definition to match the use within the established FDA guidances and ISO 14971:2019 and ICH Q9(R1). Please consider a more appropriate term to be used, aligned with FDA-recognized consensus standards, such as Use-Related Hazards/ Hazard related Use Scenarios, and Use-related Hazard Analysis.	The definitions around *Hazard, Hazardous Situation, Harm, Risk Assessment, Risk Analysis and Risk Control* are clearly defined in ISO 14971:2019 (and ICH Q9(R1)). The language in this and other human factors guidance is not consistent with these definitions. This is causing significant confusion in industry.

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		We request additional clarity be provided for probability in the use-related risks analysis term, as in past communications, the Agency has provided guidance to consider severity of harm independent of probability of occurrence.	Kindly consider that "Risk" terminology be used consistently within this and other human factors guidance.
155-157	"The purpose of including human factors engineering information in a marketing submission is to help the manufacturer meet the applicable legal standard by demonstrating that the user interface of the device is appropriate for the intended users, uses, and use environments."	We recommend removing these lines. They are confusing, conflict with other sections and do not set the tone for a risk-based approach. **Or replace with:** The purpose of including human factors engineering information in a marketing submission is to ~~confirm manufacturers meet the applicable legal standard by demonstrating that the user interface of the device is appropriate~~ **provide data to support the conclusion that the user interface supports safe and effective use via conducting the appropriate human factors analyses**.	The term "legal standard" is unclear. This section directly conflicts with lines 84-88. In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.
Lines 209-211	"The use-related risk analysis incorporating risk analysis approaches such as Failure Mode and Effects Analysis (FMEA), analysis of known use problems, and formative evaluation should be referenced to answer this question."	See Rationale or Comment column.	In alignment with our General comment and on line 148 to 151, we request additional clarity as 1) Table 2 does not contain a "probability" column which is a key component of FMEAs, and 2) the Agency has repeatedly stated probability is not applicable to human factors, therefore not appropriate in a Use-Related Hazard Analysis.
Lines 217-220	"[…], we recommend considering if those changes influence the cognitive and/or visual perception or the physical interaction between the user and the device."	We recommend the following revision: "[…], we recommend considering if those changes influence the ~~cognitive and/or visual perception or the physical interaction~~ **cognitive or sensory perception or cognition in the interaction** between the user and the ~~user and the~~ device **user-interface design**."	Critical perception senses may not only include sight, but also sound, touch, etc. Further, stating that this is between the user and the device implies that only the device is in scope, rather than the entirety of the user interface.

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Line 217	"Each identified critical task should be connected to the use-related risk analysis."	**For modified devices,** each identified critical task should be connected to the use-related risk analysis.	Text added to clarify that the content in lines 217-221 pertains to instances where devices are modified.
Lines 217-221	"When determining if a critical task has been affected by a change to the device-user interface, we recommend considering if those changes influence the cognitive and/or visual perception or the physical interaction between the user and the device. A reduction or increase in the steps to execute a critical task may be considered as affecting the critical task."	When determining if a critical task has been ~~affected~~**impacted** by a change to the device-user interface, we recommend considering if those changes influence the cognitive and/or ~~visual~~ **sensory** perception or the physical interaction between the user and the ~~device~~ **user interface**. A reduction or increase in the steps to execute a critical task may be considered as ~~affecting~~**impacting** the critical task.	Beginning in line 218, Section IV-A of the guidance shifts from the term **"impact"** to **"affect",** relative to critical tasks. Recommend replacing **"affected"** with **"impacted"** and **"affecting"** with **"impacting"** throughout the guidance, where appropriate, to clarify that all examples given in this section relate to assessing the second bullet point under Decision Point C and align with the wording, "*Based on the use-related risk analysis for the modified device, are there new critical tasks introduced or are existing critical tasks impacted*". This recommendation also applies to the current wording in lines **406, 409, and 624,** where "affected", "affected" and "affect" should be replaced with "**impacted", "impacted", and "impact"** respectively.
Lines 220-221	"A reduction or increase in the steps to execute a critical task may be considered as affecting the critical task."	A reduction or increase in the steps to execute a critical task may be considered as ~~affecting~~**impacting** the critical task. **Note that in cases where device modifications result in elimination of one or more critical tasks in their entirety, such an elimination is not considered an impact to the critical tasks for the purpose of answering the question posed in Decision Point C. These instances of elimination of critical tasks would not trigger HF Submission Category 3.**	Additional clarification in the guidance is needed regarding how modifications to an existing device impact critical tasks. The example given, "*A reduction or increase in the steps to execute a critical task may be considered as affecting the critical task*," is true. However, there could be instances where the impact to critical tasks due to a device modification leads to the elimination of one or more critical tasks (e.g., a device modification includes automation of a formerly manual task). Elimination of a critical task could, in some cases, accurately be described as "A reduction in steps to execute a critical task." Recommend including the additional text in the guidance to clarify that complete elimination of a critical task would not be considered an "impact" for the purposes of answering the question in Decision Point C.

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Line 255	Section IV	Section ~~IV~~**V**	The human factors engineering report is described in **Section V**, not Section IV.
Line 260-261	See Table 1.	Add check to Use-Related Risk Analysis (URRA) in Category 2.	The premise of Category 2 is to provide rationale for why there are no critical tasks or no new critical tasks. However, in order to draw this conclusion, the sponsor must sufficiently complete the URRA. These data would be necessary for the Agency to support a conclusion to agree with the sponsor.
Line 263 (Table 2)	See Table 2.	We recommend separating "potential hazards and clinical harm" into two columns, one for "potential hazards" and one for "potential clinical harm."	Table 2 notes to include "potential hazards and clinical harm" for each task in the one column. We believe that combining these concepts may create confusion. We also recommend that Table 2 states whether this applies for combination products. This would also comply with ISO 14971:2019 best practices.
Line 263 (Table 2)	Missing hazardous situation column	Add a "hazardous situation" column.	In order to align with ISO 14971:2019 best practices and the definition, which is included in Section 3, this column should be included.
Footnote 26	"For example, such validation methods could include human factors testing or simulated use scenario."	Delete or provide clarification.	The way the footnote is currently written is confusing for developers and may lead to sponsors misinterpreting what is expected to be provided.
Line 265 (Table 3)	Existing table gives a partial URRA for the existing device, but does not require this information on the modified device risk analysis other than risk mitigations.	Change the table to allow for a more direct comparison between the original and modified device.	We believe combining the tables only provides partial information and does not provide a full comparative use-related risk analysis or user interface (UI) comparison.
Lines 287-288	"The information should discuss the safety-related human factors engineering considerations, processes, issues, resolutions, and conclusions."	We recommend removing the term "safety-related human factors engineering considerations…" in order to not introduce another new term.	The term "safety-related human factors engineering considerations…" requires further clarity.
Lines 288-290	"The information should describe the identification, evaluation, and final assessment of all use-related hazards from using the device."	The information should describe the identification, evaluation, and final assessment of all use-related hazards from using the device. **Human factors information for Sections 1-8 below constitutes a human factors engineering report. For marketing submissions where content is not submitted for all 8 sections**	The guidance references a "human factors engineering report" in several instances: Figure 1 (ref. page 7), lines 254 and 255 (ref. page 9), and inferred in the table header row in Table 1 (ref. page 10). The term "human factors engineering report" roughly corresponds to the term "HFE/UE report" used in FDA Guidance "*Applying Human Factors and Usability Engineering to Medical*

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		(e.g., HF submission Categories 1 and 2), submitted information is referred to as human factors information.	*Devices; Guidance for Industry and Food and Drug Administration Staff*"[2]. However, beginning in Section V, the guidance begins using the term **"human factors information"** to describe the same content. Although for HF Submission Categories 1 and 2 a full human factors engineering report is not required, this shift in terminology is confusing. The additional recommended text is proposed to provide clarification on requirements and terminology used within the guidance.
Lines 382-410	See Section 7.	We recommend the important discussion in Section 7 on critical tasks and risk analysis be summarized earlier in the guidance.	We believe that the information and discussion on critical tasks and risk analysis in Section 7 is a critical section that should be highlighted more prominently in this guidance.
Line 359	Section 5: Summary of preliminary analyses and evaluations	See Rationale or Comment column.	The order of Sections 5 and 6 in this draft guidance is opposite from the order in which these sections appear in FDA Guidance "*Applying Human Factors and Usability Engineering to Medical Devices; Guidance for Industry and Food and Drug Administration Staff*"[2]. The order of these two sections as presented in this draft guidance is more logical, since *Section 6: Analysis of hazards and risks associated with the use of the device* and *Section 7: Identification and description of critical tasks* are inter-related activities, and without *Section 5: Summary of preliminary analyses and evaluations* appearing between the two. As part of FDA's planned revision to the 2016 guidance, we recommend the order of these two sections in the 2016 guidance be revised to match the order of Sections 5 and 6 in this draft guidance.
Line 378	If you determine that a device change resulting in a modification to any task, association harm,…	If you determine that a device change resulting in modification to any **critical** task, associated harm,…	This statement is based on the information in section IV-A, Decision Point C, which advises manufacturers to assess whether modified devices have any new critical tasks or impacted critical tasks as an outcome of the modification. As such, an impact on a formerly non-critical task that does

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			not change the associated harm or risk mitigation measure would, by definition, not become a critical task and therefore, would not need to be further evaluated through HF validation testing. A rationale for making such a change to a non-critical task without HF validation testing should not be required.
Line 630	Like 0,…	Like ~~0~~**in Example B.1**,…	Please Revise to correct the reference.

End of document.