IPAC-RS

International Pharmaceutical Aerosol Consortium on Regulation and Science

1500 K Street NW • Suite 1100 • Washington DC • 20005
Telephone +1 202 230 5607 • Fax +1 202 842 8465
Email info@ipacrs.com • Web www.ipacrs.com

IPAC-RS Comments on the Draft Guidance for Industry and Food and Drug Administration Staff on "Applying Human Factors and Usability Engineering to Optimize Medical Device Design" (FDA-2011-D-0469)

To Whom It May Concern:

On behalf of the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS), please find enclosed comments on the FDA Draft Guidance "Applying Human Factors and Usability Engineering to Optimize Medical Device Design" (FDA-2011-D-0469).

The International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS) is international association of innovator and generic companies that develop, manufacture or market orally inhaled and nasal drug products for local and systemic treatment of a variety of debilitating diseases such as asthma, chronic obstructive pulmonary disease and diabetes. We are committed to advancing consensus-based, scientifically driven standards and regulations for these products, with the purpose of facilitating the availability of high-quality, safe, and efficacious drug products to patients. Our member companies are primarily involved in the development of "Combination Drug Products", so are very interested in medical device design guidance and the impact upon "Combination Drug Products". The current members of IPAC-RS are: 3M, AstraZeneca, Boehringer Ingelheim, Catalent, Chiesi, GlaxoSmithKline, MannKind Corporation, Merck & Co., Inc., Novartis, Pfizer, Teva and Vectura Ltd.

We commend the U.S. Food and Drug Administration (or "the Agency") for drafting a guidance document to assist industry in conducting appropriate human factors testing and identifying device features that manufacturers should optimize throughout the total product life cycle. We appreciate your consideration of these comments, and should the Agency wish, would be willing to discuss any of them with the Agency as appropriate.

Regards,

Jacqueline Schumacher
Chair, IPAC-RS Board of Directors

IPAC-RS Comments on the Draft Guidance for Industry and Food and Drug Administration Staff on "Applying Human Factors and Usability Engineering to Optimize Medical Device Design" (FDA-2011-D-0469)

GENERAL COMMENTS

IPAC-RS commends the U.S. Food and Drug Administration (or "the Agency") for drafting a guidance document to assist industry in conducting appropriate human factors testing and identifying device features that manufacturers should optimize throughout the total product life cycle. IPAC-RS believes the provisions in this guidance will be helpful to industry by clarifying the Agency's current thinking on the topic. In particular, IPAC-RS strongly supports the Agency's intent to improve usability of devices to reduce use errors, injuries, and product recalls.

To increase the utility of this guidance, IPAC-RS recommends clarifying its scope. Many different types of medical devices exist, including devices that are part of combination products, and recognizing this diversity in the Guidance will increase its relevance and focus. Medical devices range from Intensive Care Unit (ICU) equipment to spoons, and corresponding recommendations for human factors and usability may vary. Consideration must also be given to the disease state for which devices are used (e.g., acute or prophylactic, chronic or episodic), as well as to the context in which they are used (e.g., clinical or non-clinical setting) and to the target user group (i.e. Healthcare Professional, pediatric patients, geriatric patients, etc.). Given this multiplicity of contexts and of device types, an extended discussion of scope would be welcome.

The review process for combination products incorporating devices should also be addressed. In particular, in situations where the device and the medicinal product form a single integral unit which is intended exclusively for use in the given combination and which is not reusable, that combination product would be reviewed and approved for use by CDER or CBER with a potential consult from CDRH. The principles outlined in this guidance should be considered in developing such combination products, and it would be helpful if the guidance acknowledged and outlined the inter-center coordination that would enable such consideration.

"Use error" should be sub-divided into critical and non-critical "use errors." While potential for both types of error may be discovered during development, this distinction is significant because the impact of and methods for eliminating or mitigating each type differ: a critical use error has the potential to result in a clinically significant event (i.e. no dose or more than double the dose being delivered) but a non-critical error does not have the potential to result in a clinically significant event (i.e. a sub-optimal dose). This classification should also be related to the overall clinical risk profile of the product as defined in the product risk management file and could be refined in the context of the disease state and the target user group. For example, while it may be appropriate to place greater reliance upon instructions for use (a user Manual/Patient Instruction Leaflet) for a simple medical device used in a chronic disease state for which HCP training is provided, it would be inappropriate to rely on a user manual/Patient Instruction Leaflet for a complex medical device used in an acute clinical situation.

It is concerning that "use error" as described in the Guidance is to be reviewed and studied by the sponsor without a relative reference point or control. In cases where a marketed product exists, the purpose of the validation testing should be to ensure that the candidate device imposes no critical "use errors" and must be non inferior in regards of non critical "use errors" with reference to the marketed device. The Guidance as written may inhibit innovation and progress by not discriminating between critical and non critical "use errors", requiring sponsors to show absence of use error. The Guidance could adopt language consistent with the 510K pre-market approval pathway where substantial equivalence to a marketed device must be established prior to approval. Human factor elements including use error should reside here as part of the larger review process. Having human factor principles included in the design control process is fundamental and evidence that such considerations were made by the sponsor should be required.

This Guidance should moreover encourage applicants to leverage all supportive data such as risk analyses, formative studies, *in-vitro* studies, etc. to reach a more comprehensive risk/benefit conclusion. The Guidance as currently written seems to frame human factors testing as the primary basis for risk-benefit assessments, yet we believe that a more holistic evidence-based perspective would be appropriate. In particular, for many combination products and orally inhaled and nasal combination products specifically, clinical trials are typically used to acquire a vast amount of patient usage data for target populations; this provides a tremendous opportunity for the program sponsors and CDRH to gain the insight they desire should be given appropriate weight in the guidance. Correspondingly, evaluations that could be performed during a clinical study such as patient questionnaires and site personnel interviews that would allow the sponsor to acquire the desired usability data should be outlined in more detail.

The implications of minor device changes must be clarified. For "Combination Drug Products", the interconnection between the Phase 3 clinical studies and the simulated use testing is complicated. The Agency has repeatedly stated that the final device must be used in the Phase 3 clinical studies; this Guidance states that device modifications must be made to address observed minor residual risks. How does industry strike a balance between these two requirements when implementing minor changes? Can the agency agree that any minor changes that did not impact the Drug Product Critical Quality Attributes could be verified on the basis on in-vitro data only.

It is reasonable that the Guidance reemphasize the need for applicants to seek clarification with the Agency on human factors at a pre-IND meeting and the EOP2 meeting (per CDER/CBER *Guidance for Industry IND Meetings for Human Drugs and Biologics Chemistry, Manufacturing, and Controls Information, May 2001*) with appropriate reference to the 2001 CDER/CBER Guidance that states:

Pre-IND

- *Drug-device delivery systems (e.g., demonstration of device and its characteristics, potential for overly rapid release of dose, particle size distribution considerations, where applicable)*

EOP2

- *Although the EOP2 meeting is important for all drugs, it is particularly important for new drug-device delivery systems. Specific considerations for container/closure system components for specialized delivery systems such as metered dose inhalers (MDIs), dry powder inhalers (DPIs), disposable pen injectors, transdermal patches, or other novel dosage forms*

- *Devices (e.g., pumps, valves, cartridge injectors, actuators), where applicable*

IPAC-RS is grateful for the opportunity to provide these comments and would be willing to discuss any of these issues with the Agency as appropriate. More specific comments on the text follow.

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Document Section	**Comment and Rationale**	**Proposed Change**
2. Scope	This section should be revised to distinguish between normal and abnormal use, to align FDA more closely with ISO 62336, which includes the clause, where the upper case terms are defined in the standard. "While the USABILITY ENGINEERING PROCESS can be used to identify ABNORMAL USE, this International Standard does not require the USABILITY ENGINEERING PROCESS to be used to assess or mitigate RISKS associated with ABNORMAL USE."	"This guidance provides recommendations for medical device design optimization through human factors analysis, testing and validation. The intent is to improve the quality of the device user interface such that errors that occur during normal use of the device are either eliminated or reduced. The recommendations in this document apply whenever a manufacturer performs human factors testing for a device."
3. Overview	The diversity of device types that exist should be recognized.	Add: "Medical devices range from ICU equipment to spoons and consideration must be given to the disease state for which they are being used, acute or prophylactic, chronic or episodic, the context in which they are used clinical or non-clinical setting and the target user group (i.e. Healthcare Professional, pediatric, geriatric, etc.)"
	The word "use error" is used extensively in this draft guidance, but it is not defined.	A definition of "use error" should be incorporated into the document and furthermore sub-divided into critical and non-critical "use errors": a critical use error has the potential to result in a clinically significant event (i.e. no dose or more than double the dose being delivered) but a non-critical error does not have the potential to result in a clinically significant event (i.e. a sub-optimal dose). This classification should also be related to the overall clinical risk profile of the product as defined in the product risk management file and could be refined in the context of the disease state and the

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		target user group. For example, while it may be appropriate to place greater reliance upon a user Manual/Patient Instruction Leaflet for a simple medical device used in a chronic disease state for which HCP training is provided, it would be inappropriate to rely on a user manual/Patient Instruction Leaflet for a complex medical device used in an acute clinical situation.
	Classification of use-related hazards should be recommended.	Following "Hazards caused specifically by how a device is used are referred to in this document as *use-related hazards* (Figure 2)," add the sentence "The use-related hazards should be further classified as critical or non-critical based on the rules stated above."
	For consistency with the above comment on scope, the final bullet about why use-related hazards occur should be removed.	Delete the bullet: "Devices are used in ways that were anticipated but inappropriate and for which adequate controls were not applied."
	Recognize the distinction between critical and non-critical errors in the list of steps about performing a successful HFE/UE analysis.	"Develop and apply strategies to mitigate or control use-related hazards (see Section 8) in consideration as to their potential impact upon patient safety as either critical or non critical; and…"
	Following the list of steps, add a sentence about evidence and rationale that the risk-based approach adopted was derived in the context of the disease state and target user population.	"It is incumbent upon the developers of medical devices to provide documentary evidence and supporting rationale that the risk based approach adopted with respect to critical and non critical use errors has been derived cognizant of the context of disease state and the target user population."
Figure 3	This figure should be revised such that the box that states "Risks Associated with Use –related Hazards Acceptable" should be revised to state "Risk Associated with Critical Use – related Hazards Acceptable" and subsequent box should state	Revise figure as described.

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	"New Critical Use-related Hazards introduced".	
4. Regulations, Guidance Documents, and Standards for HFE/UE	For consistency with ISO 62336 Figure B.1., recognition of use error resulting from abnormal use should be added.	"Validation testing (see Section 10) should be used to demonstrate that the potential for use error has been minimized, unless the use error resulted from abnormal use e.g., inadequate training, deliberate misuse, reckless use, sabotage, etc,"
4.3 National and International Standards	Under National and International Standards, the guidance document states: "For specific issues that are not consistent with any given recognized standard [on Table 1], this document takes precedence." This guidance provision seems quite prescriptive as it fails to acknowledge The Least Burdensome Approach the Agency stipulates in Section 11 of the current document as well as in its September 2007 CDRH *Guidance for Industry and FDA Staff - Recognition and Use of Consensus Standards*. Recognition of a standard is a process.	We recommend that the current draft guidance acknowledge The Least Burdensome Approach and appropriately reference the September 2007 CDRH Guidance.
5. Device Users, Use Environments and User Interfaces	*"The level of training users will have and/or receive"* does not indicate the user responsible for training.	Add: "and the identity of the probable end-use trainer (e.g. a respiratory nurse/ therapist in a clinical consulting room.)"
5. Figure 4	The term "Information Processing" is currently used. To help align terminology with that in HE 75 2009 (e.g. 5.6.3d) this should be changed to "Information Processing (Cognition)"	Change "Information Processing" to "Information Processing (Cognition)"

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	'The user interface also includes the device labeling, which includes package labels, any instructions for use in user manuals, package inserts, instructions on the device itself, and any accompanying informational materials.' We believe that where materials such as promotional materials will be provided to the end user, such materials could be considered for use in human factors studies where such an approach is representative of the end use environment.	It would be helpful to clarify whether ODE considers informational materials that are not part of regulatory labeling, e.g. approved promotional materials, to be acceptable for use in human factors assessments.
5.1 Device Users	["*Individuals in the intended user populations should be able to use medical devices safely and* effectively and without unintentionally making errors *that could compromise positive outcomes".]*	"effectively with reasonable efficiency and ease and without unintentionally"…
5.1 Device Users (List of user characteristics)	["Sensory abilities (i.e., vision, hearing, tactile sensitivity)"]	Suggest addition of: "Color perception/ blindness".
	["Cognitive abilities, including memory,"]	Suggest addition of: "Education and training".
	["Mental and emotional state"]	Suggest addition of: "Potential for episodic variance in mental and emotional state and fatigue".
	["Knowledge of and experience with the particular device"]	Suggest addition of: "Experience with other or similar devices that may lead to positive or negative transfer effects".
	Add ethnicity and cultural customs to the list of bullets	Additional bullet: "Ethnicity and cultural customs, including native language."

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	Suggest addition of content to acknowledge the relationship between non-permanent user characteristics and the potential variability in the end use environment. For example operational procedures and pressures which may drive, control or limit behavior, as defined as a temporary user characteristic (e.g. an emergency room upon reception of multiple casualties).	Add the content described.
5.2 Device User Environments	An example that highlights the risk of interchangeability in the clinical environment (as a major cause of impatient mortality due to human error should be added to the phrase, "Examples of environmental hazards in the clinical setting include the following…"	"…Differentiation and interchangeability risks may be present: e.g. there may be multiple identical devices within the immediate vicinity of the user."
	The non-clinical environment potential characteristics list includes characteristics/ attributes which are not exclusive to non-clinical environments (e.g. not all clinical environments may control temperature, humidity, etc.), but which have been omitted from the list of hazards in the clinical setting.	These attributes should be recognized in the list of potential hazards in the clinical setting.
5.3 Device User Interfaces	The introduction to this section does not clearly link the considerations of a device user interface and its end users and the end use environment(s)/ scenario(s), as previously covered in sections 5.2 and 5.3.	It should be clear that the user interface is determined as design inputs to meet the user requirements.

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	There is no definition or guidance on 'critical steps'. This is mentioned as required later in the document in section 6.2.3 Function and Task Analysis, as 'critical use steps'. Previously the terminology used to classify 'critical use steps' was: "Primary operating functions".	A definition of critical use steps should be added to the document. ISO-62366:2007 section 3.21, defines "primary operating functions" as: The MANUFACTURER shall determine the PRIMARY OPERATING FUNCTIONS and record them in the USABILITY ENGINEERING FILE. The inputs to the PRIMARY OPERATING FUNCTIONS shall include the following: - frequently used functions (see 5.2) and; - functions related to SAFETY of the MEDICAL DEVICE.
6.1 Identification of Known Problems	The sentence which begins "Other sources of information on known use-related hazards are current device users, journal articles, proceedings of professional meetings, newsletters, and relevant internet sites..." does not include previous human factors studies and/or market research conducted by the manufacturer as competitive assessment and investigates user requirements, which should provide input to beginning the assessment process. (This may include pre-design control "concept documents" from the origin of the device development project which serves to define user requirements).	"Other sources of information on known use-related hazards are current device users, journal articles, previous human factors studies and/or market research conducted by the manufacturer, proceedings of professional meetings, newsletters, and relevant internet sites."
	"Known use error" is a key term to the requirements of this guidance document, but is not defined.	Add the following definition of a known use error: "A use error which is known to have occurred previously with the medical device or similar medical devices, and, foreseeable use errors which are likely to occur based on available information to date".

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6.2.1 Contextual Inquiry	The description of contextual inquiry presumes the inclusion of an investigative device/ prototype. However, testing devices is not the only relevant application of the contextual inquiry method to medical device human factors. Contextual inquiry is a frequently used tool to understand user requirements, prior to testing of an investigational device/ prototype. The role of contextual inquiry as a means of investigating end user requirements is not described under this section.	The role of contextual inquiry as a means of investigating user end requirements should be described.
6.2.2 Interviews and Focus Groups	The distinctions between section 6.2.1 on contextual inquiry, which also refers to the use of user interviews, and this section should be more clear. In the context of this section the interview is not ethnographic/ contextual, meaning it is not conducted in the actual environment of end use. Commonly, interviews and focus groups are conducted in specific testing facilities where anonymous viewing and recording facilities are available.	The section on interviews should highlight that an interview or focus group often forms the setting for the conduct of a simulated use trial.

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	The independence and impartiality of the interviewer conducting both interviews and focus groups is important factor in the conduct of reliable interviews or focus groups. (This links with guidance included in this document that members of the design team should not participate in user research unless necessary, which has been included in this document). AAMI/ANSI-HE:75:2009 section Section 5.3.2 General considerations for managing risk: f). States: Members of the design team should not participate in evaluations of use, especially validation (summative usability) studies. Other employees of the manufacturing company are generally not good test candidates either, because they are likely to be biased toward positive assessments.	The independence and impartiality of the interviewer conducting both interviews and focus groups should be mentioned as an important factor in the conduct of reliable interviews or focus groups.
6.2.3 Function and Task Analysis	This section does not specifically highlight the need to consider 'foreseeable worst case scenarios', as had been previously stressed in previous guidance. (See section: 4.7.2. Consider worst-case scenarios, AAMI/ANSI-HE-75:2009).	Recommend consideration of foreseeable worst-case scenarios.
	Although the key areas for investigation discussed in this section are detailed, they do not align strongly the inputs required to the risk management process or with the typical terminology used. Human factors studies can be used as a basis for determining estimates for: occurrence (how frequently did a use error occur?) and severity (what happened as a result/ what would a user have done, etc.) as well as detectability (did the users recognize a use error or failure had occurred/ was the user able to self-recover?).	Align this section with the input required for the risk management process as described.

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	[*"How might they occur?"*] This bullet does not highlight the need for investigation of the difference between, 'how a failure occurred' and 'what the cause of the use error (failure) was'?	Include a top-level classification of causes. Further, classify use error by the recognized "Categories of foreseeable USER action" (IEC 1782/07) and included in ISO 62366:2008, Figure B1. "Where typical use error mode is classified by either a: Slip, lapse or mistake."
	"Abnormal use", which may apply in context of analyzing human factors findings and should not be confused with use error, should be defined.	Define abnormal use. ISO 62366:2008 Section 3.1 defines ABNORMAL USE, as: Intentional act or intentional omission of an act by the RESPONSIBLE ORGANIZATION or USER of a MEDICAL DEVICE as a result of conduct that is beyond any further reasonable means of RISK control by the MANUFACTURER.
	For the phrase "Will certain user interactions with the device degrade the accuracy, safety and effectiveness of the devices' subsequent operations (and if so, what are these interactions and how are device operations affected)?" it would be helpful to refer to Perception, Cognition, Action breakdown of task analysis and align with HE75:2009 e.g. 5.6.3 d).	"Will certain user interactions with the device degrade the accuracy, safety and effectiveness of the devices' subsequent operations (and if so, what are these interactions and how are device operations affected)?"

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6.2.4 Heuristic Analysis	'For medical devices, general de-facto standards are applicable at times while others are unique for certain kinds or types of medical devices.' A key element of any design process by a Medical Device Manufacturer will include a review of the surrounding IP landscape and an understanding of the commercial Freedom-to-Operate for a given medical device. It is important that ODE appreciate such considerations in their review and assessment of any apparent 'de-facto' standards in the assessment of a device's user interface. Whilst de-facto standards should be considered in the first instance, there will be times when such approaches are not accessible to medical device manufacturers for use in their medical device design for IP reasons. No matter what the medical device design, the end device must be proven to be acceptable from a usability and human factors perspective.	Acknowledge the considerations described regarding 'de-facto' standards.
6.2.5 Expert Reviews	No caution is provided on over-reliance on "thought leaders", which presents risks due to potential bias or limit's in knowledge. (Reference: AAMI/ANSI-HE-75:2009 section 4.5.2 Do not rely exclusively on "thought leaders")	"…predict actual device use. However, caution should be used to identify potential bias or limits in knowledge of experts."
7. Formative Evaluations	There are no top-level requirements for the documentation of formative evaluations mentioned in this section.	Suggest that formative evaluations, even with small numbers of test subjects, should at a minimum include: • Definition of aims, goals and study objectives. • Clear definition of applicability of study population as appropriately representative of the intended end user population (for the stage of the study). • Definition of the procedure to be used for assessment, data collection and reporting. • A clear record of outcomes and subsequent user interface changes.

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	AAMI/ANSI-HE-75:2009 section 3.39 defines a "Formative study" as: "formative usability testing": Usability testing that is performed early with simulations and the earliest working prototypes and that explores whether usability objectives are attainable, but without strict acceptance criteria.	On the assumption that the intended meaning has not changed in this applicability to this guidance, clarify the following: • Formative usability assessments are used to establish usability goals. • Formative usability assessments do not have strict acceptance criteria. Additionally the following points may apply: • Formative usability assessments can form an early opportunity to 'stress test' the prototype user interface in user groups which pose a greater challenge, such as those groups with impairments.
	The bulleted list beginning *"Formative human factors assessments serve the following HFE/UE goals:"* does not include several attributes which may apply as formative assessment HFE/ UE goals.	Add the following points to the list: • Comparative assessment versus competitor/ predicate device(s) (benchmarking) • Test of intuitiveness, effectiveness of applied heuristics • Test ergonomic suitability for purpose and end use populations • Assessment of device appeal and user satisfaction (may be assessed in context of an interview following use)

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8. Mitigation and Control of Use-Related Hazards	The text should be revised so that it reflects the distinction between critical and non-critical errors, the disease state and care setting, and elaborates on the strategies to control or mitigate risk.	Use related hazards that are identified through analytical approaches or formative evaluations should be classified as either being critical or non-critical. This designation should be assigned in the context of the disease state, acute or prophylactic, episodic or chronic, administration in a clinical or non clinical setting clinical setting and the target user group population (i.e. pediatric, geriatric, carer and/or Healthcare Professional). Critical and non-critical user error should be designed out or controlled prior to submitting the device for HFE/UE validation testing. Use-related hazards often require a combination of mitigation and control strategies. The following list presents the order of overall priority for applying strategies to control or mitigate risks of use-related hazards : • Modify the device design to remove a hazard or reduce its consequences: For example, making the user interface intuitive and ensuring that critical information is effectively communicated to the user can reduce the likelihood of or eliminate certain use-related hazards. If hazards cannot be eliminated, the design should, to the extent possible, reduce their likelihood and the severity of any consequences. • Make the user interface, including its operating logic, error tolerant: When errors occur during device use, such as users pressing an adjacent key on a keypad, the device should act to preclude a hazardous outcome. Safety mechanisms such as physical safety guards, shielded controls, or software or hardware interlocks will make the design more tolerant of errors that users might make. • Alert users to the hazard: When neither design nor safety features will eliminate a use-related hazard or adequately mitigate the consequences, the device should

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		detect the condition and provide an adequate warning signal to users. • Develop written procedures and training for safe operation: If it is impossible to eliminate hazards through any of the previous strategies, or to enhance other control or mitigation strategies, then written procedures, labeling enhancements, and training for safe operation are the remaining options. For critical user errors, by first intent, the design should either be modified or the operating logic should be such that the failure cannot occur. For non-critical failure modes it may be appropriate to alert the user and/or develop written procedures and training for safe operation. Instructions, labeling, and training can influence users to use devices safely and effectively and are critical HFE/UE considerations for safe device use. However, because they rely on the user to remember or refer back to the information, these approaches are less effective than modifications to the design of the user interface. In addition, training may be inconsistent or unavailable. Therefore, mitigation of critical and non critical use errors should not, by first intent, focus on instruction, labeling, or training fixes in isolation, since these "patches" might not be adequate. A combination of these strategies might be your best approach. Regardless of the strategy used, subsequent testing should be done to ensure that you have successfully controlled the critical use errors and that your risk mitigation efforts have not introduced new critical use risks.

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10 Human Factors Validation Testing	Rewrite the second paragraph to address critical vs. non-critical errors.	"For the device to be considered to be optimized with respect to safety and effectiveness of use, validation testing should be designed such that it is sufficiently sensitive to capture critical and non critical user errors that exist whether the users are aware of critical and non critical user errors or not. Further, the test results should show no patterns of critical and non critical use errors or difficulties that could be eliminated or reduced using the strategies defined in Section 8. We recommend…"
	A paragraph should be added at the end regarding the purpose of validation testing where a marketed product exists.	"In cases where a marketed product exists, the purpose of the validation testing should be to ensure that the candidate device imposes no critical "use errors" and must be non inferior in regards of non critical "use errors" with reference to the marketed device."
10.1 Simulated Use Validation Testing	This section should incorporate a recommendation to assess the effectiveness of the patient leaflet.	"Test participants should be given an opportunity to use the device independently, without training and/or access to the Patient Instruction Leaflet and -subsequently after having accessed the Patient Instruction Leaflet, in as natural a manner as possible, without guidance, coaching, praise or critique from the test facilitator or moderator. This is key to assessing the criticality of the Patient Instruction Leaflet in the successful use of -the -medical device. Users should not…"

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10.1.1 Task and Scenarios	This section should address critical and non-critical errors.	"Tasks or use scenarios with a low frequency of occurrence that are associated with critical use errors require… …process and the risk mitigation hierarchy described in Section 8 for critical and non critical use errors."
10.1.2 Test Participants	Under Test Participants (Subjects), the guidance document states: "…it may be advisable to test the maximum number of participants that your budgets and schedules allow." This leaves much to the reader's interpretation.	Encourage companies to seek the Agency's input in situations where resource may be a constraint.
	In regard to the statement, 'To adequately represent users in the United States population, the participants in the validation test should reside in the United States,' further clarification on why the subjects should reside in the United States would be appreciated. In some cases, human factors validation tests performed in countries other than the United States could represent the United States population, specifically where the patient/end user profile, prescription practice, training/instruction process and end use of a medical device in the country where the validation test is run is the same as that in the United States.	Provide clarification on geographic demographics for test participants; replace critical tasks with critical and non critical use errors; and capture critical and noncritical use errors.
10.1.3 Participant Training	This should address the use of patient leaflets and the practicability of allowing time to pass.	"…untrained users. Alternatively, the study should be designed that such that all patients ability use the medical device as intended should be assessed prior and post training and review of the Patient instruction Leaflet. This is key to assessing the criticality of the Patient Instruction Leaflet in the successful use of the medical device."

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		"For this reason, where practicable, a period of time…"
10.1.4: Data Collection: Performance Data	The Guidance should recognize that there are multiple methods for capturing user experiences, and that interviewing is one of these; it could also elaborate on the interviewing process.	"One method for capturing user experiences during validation testing is to do a post-test interview comprised of open-ended questions. It is important that this assessment is conducted in such a manner that the interviewee does not feel disinclined to offer a response for fear of offending or feels compelled to say something. The questions should first address the device overall and should then address each critical task or use scenario. Responses should be evaluated with the interviewee to determine whether they should be classified as critical or non-critical use errors. For example: • "Did you have any difficulty using this device? Was anything confusing?" • "What might make the device (or instructions) better?" • "Please tell me about this [error or problem observed]." The questions should address each critical aspect of use. The validation test should include essential "subjective" assessments by participants for all critical tasks."
	Performance data should focus on critical errors and high-priority tasks.	"The data should focus on high-priority tasks and on critical use errors that could result in harm to a patient or a user."

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10.1.5 Interpretation of Validation Test Results and Addressing Problems	This section should also be revised to reflect the distinction between critical and non-critical errors, and acknowledge the challenges of designing a completely risk-free system, due to a variety of factors.	"Problems with the design of the device, labeling, or training requirements should have been identified and addressed prior to validation testing. When critical use problems do occur during validation testing, this usually indicates that the previous HFE/UE steps were not performed adequately. The root causes of critical use errors identified during validation testing should be evaluated from the perspective of the test participants involved and direct performance data will support this determination. Data analysis should include subjective feedback regarding critical use errors, difficulties, "close calls," and any task failures by test participants. Depending on the extent of the risk mitigation strategies required as per the hierarchy defined in Section 8, revalidation may be necessary. You should address failures and difficulties associated with greater than minimal risk and attributable to the user interface by designing and implementing risk mitigation strategies, as per the hierarchy defined in Section 8,and, where appropriate, re-testing those elements to confirm their success at reducing critical use errors to acceptable levels without introducing any new critical use errors. *Residual Risk* It is important to recognize that irrespective of the diligence undertaken in the design of a medical device, the associated training and the provision of explicit instructions for use it is impossible to design any system that is error proof, risk free or cannot be misused or abused. For this reason, some amount of residual risk will always remain. The fact that risk was identified from the results of validation testing does not necessarily mean that it is residual. True residual risk must be resistant to elimination or mitigation through any potential

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		modifications to the user interface, accessories, labeling, or training. Failures or difficulties with use that have been determined to represent residual risk should be described and classified as either critical or non-critical use errors as per Section 8, as well as whether or not failures that occurred were associated with the design of the device, its labeling, or the content or proximity of training, and the extent of the association. The analysis of residual risk should determine if design modifications are indicated or if not, as per the hierarchy described in Section 8, the analysis should demonstrate that the residual risk is outweighed by the advantages offered by the device. If critical use errors that could have negative clinical impact on patients are identified, planning to address them in subsequent versions of the device is not acceptable."
10.2 Clinical Validation Testing	Under Clinical Validation Testing, the guidance document states: "Due to the nature of some types of device use or use environments that may be particularly challenging or poorly understood, it might be necessary to validate a device under conditions of actual use in a clinical study." A few concrete examples of such device use or use environments could be very helpful.	Add examples of such device use or use environments.

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Appendix A, Section 7	Under Conclusion, the guidance document states: "This section should discuss any residual risk that remained after analysis of validation test findings. If applicable, this section should provide a sound rationale that modifications to the user interface (including accessories, training, and labeling) would not further reduce risk, are not possible or practical, and are outweighed by the benefits that may be derived from use of the device, as designed." As with Section 10.1.5., demonstration of the impossible is not part of science or engineering.	This section should simply state: "This section should discuss any residual risk that remained after analysis of validation test findings. If applicable, this section should provide a sound rationale that the level of residual risk is outweighed by the benefits that may be derived from use of the device, as designed."