MassBio
MASSACHUSETTS BIOTECHNOLOGY COUNCIL

Factoring in Human Factors: What You Don't Know *Can* Hurt You

Thursday, October 12, 2017

Factoring in Human Factors: What You Don't Know Can Hurt You

Speakers:

- **Rachel Aronchick,** Managing Human Factors Specialist, UL-Wiklund
- **Magali Hickey**, PhD, Director Formulation Development, Alkermes
- **Evan Sherr,** Vice President of Operations, Windgap Medical, Inc.
- **Melanie Turieo,** Director, Human Factors & Industrial Design, Global MedTech Division, Cambridge Consultants

Moderator:

- **Örn Almarsson**, PhD, Head of Formulation, Moderna Therapeutics

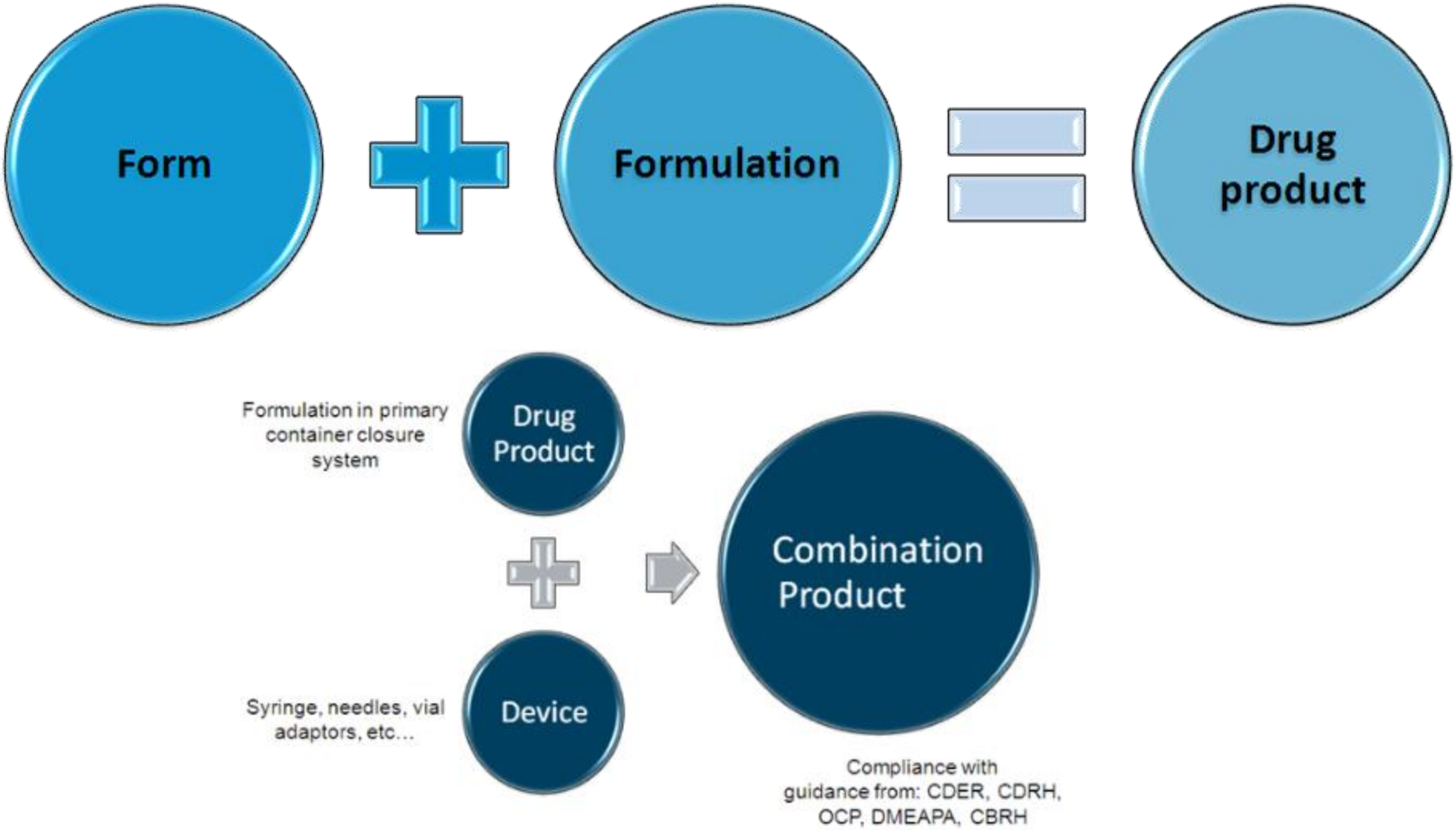
Factoring in Human Factors: What You Don't Know *Can* Hurt You

Magali Hickey

MassBio Forum

October 2017

Classification as a Combination Product



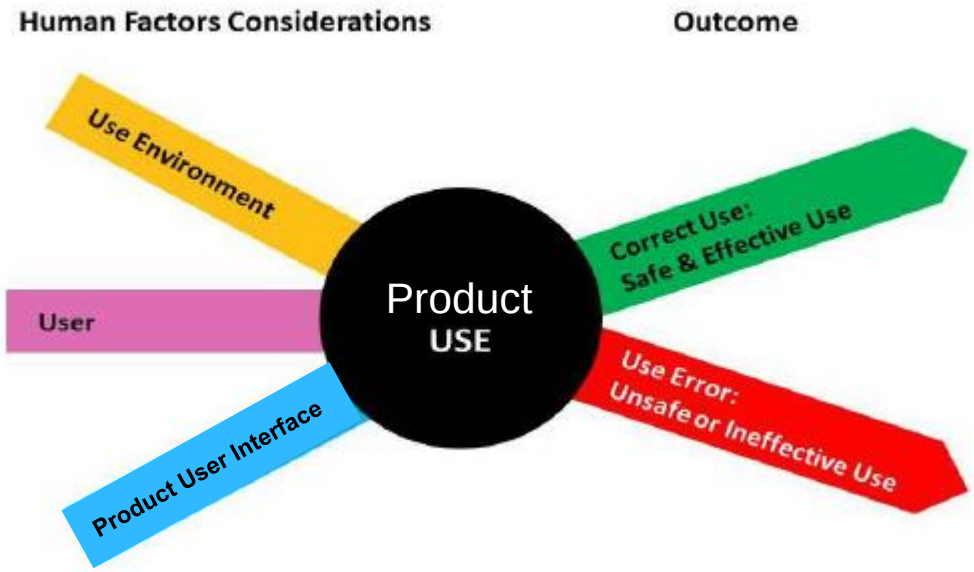
https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM258957.pdf

Guidance Documents to Support Development

Document Source	Final or Draft Guidance Document Titles
CDER	Guidance for Industry - Safety Consideration for Product Design to Minimize Medication Errors Guidance (Apr 2016) https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm331810.pdf
CDER	Draft Guidance - Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (Apr 2013) https://www.fda.gov/downloads/drugs/guidances/ucm349009.pdf
CDRH	Guidance for Industry and Food and Drug Administration Staff - Applying Human Factors and Usability Engineering to Medical Devices (Feb 2016) https://www.fda.gov/downloads/MedicalDevices/.../UCM259760.pdf
CDER, CDRH, CBER, and OCP	Guidance for Industry and Food and Drug Administration Staff - Technical considerations for Pen, Jet and Related Injectors Intended for Use with Drugs and Biological Products (Jun 2013) https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm147095.pdf
CDER, CDRH, CBER and OCP	Draft Guidance for Industry and FDA Staff - Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development (Feb 2016) https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm484345.pdf
OCP	Guidance for Industry and Food and Drug Administration Staff - Current GMP Practice Requirements for Combination Products (Jan 2017) https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm429304.pdf

What are Human Factors?

- Human Factors (HF): the study of how humans behave physically and psychologically in relation to particular environments, products, or services
- HF testing plays an important role in fulfilling design validation
  - Final product has to demonstrate safety and effectiveness in the hands of intended users



Applying Human Factors & Usability Engineering to Medical Devices (February 2016)

Typical Agency Feedback

- At this time, it appears you are proposing a kit
- Careful consideration should be given to determining a packaging configuration that best suits the ----------needs for safely and accurately administering the drug product
- If your proposed kit is similar to another currently marketed kit, you will want to research use errors and other problems that have occurred in the past with the currently marketed kit so they may be addressed in the design of your kit
- Perform a comprehensive risk analysis in order to be sure there are no unique risks associated with using this kit. This analysis will allow you to identify the use-related risks associated with your kit

Emphasis on Reduction of Medication Errors

- Draft guidance published in December 2012 from CDER:
  - Safety Considerations for Product Design to Minimize Medication Errors
  - Cited Institute of Medicine (IOM) report published in 2000: 44,000 to 98,000 deaths yearly due to medical errors → 8th leading cause of death in the U.S.
  - 7,000 deaths attributed to medication error

- IOM further published a report in 2006 indicating that 30% of medication errors can be related to packaging and labeling

- British Medical Journal publication in 2016 estimates that medication errors are the third leading cause of death in the US
  - Greater than 250,000 deaths each year may be attributed to medical errors

Kohn LT, Corrigan JM, Donaldson MS, eds. *To Err Is Human: Building a Safer Health System*. Institute of Medicine, National Academies Press: Washington DC, 2000.
Aspden P, Wolcott JA, Bootman JL, Cronenwett LR, eds. *Preventing Medication Errors*. Institute of Medicine, The National Academies Press: Washington, DC. 2006. Chapter 6, p. 275.
BMJ 2016; 353 doi: https://doi.org/10.1136/bmj.i2139 (Published 03 May 2016) *BMJ* 2016;353:i2139

Agency Feedback/Complete Response Letters Citing Human Factors Assessments

Drug product	NDA submission	Feedback/CRL Date	Approval date
Abaloparatide pre-filled pen (Radius)	March 2016	September 2016	April 2017 (HF results submitted December 2016)
Epinephrine pre-filled syringe (Adamis Pharmaceuticals)	May 2014	March 2015 June 2016	June 2017
Abilify tablet with ingestible sensor (Otsuka with Proteus Digital Health)	September 2015	April 2016	Application resubmitted May 2017
Probuphine – Buprenorphine subdermal implant (Titan Pharmaceuticals)	October 2012	April 2013	May 26, 2016 (Major amendment: February 2016)
Zalviso - Sufentanil sublingual tablet system (Acel Rx)	September 2013	July 2014	N/A Approved in EU September 2015

Is the Game Changing? Feedback on Immediate Release Solid Dosage Form

- There are currently no approved ---------- containing a ---------- and --------- dosing regimen for ----------
  - Depending on the complexity of the dosing regimen as well as the container closure system and its associated labels and labeling, there may be unique risks associated with using your product. Perform a comprehensive use-related risk analysis

- Note that we have published three draft guidance documents that while not yet finalized, might be useful in understanding our current thinking and our approach to human factors and product design. We refer you to the following Agency draft guidances:
  - Applying Human Factors and Usability Engineering to Optimize Medical Device Design
  - Safety Considerations for Product Design to Minimize Medication Errors
  - Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors

Learnings and Key Take-Aways

- Develop every product with the patient and end user in mind
  - Don’t focus on interpreting guidance document and whether they apply
  - If not developing a combination product, human factors still matter but that does not mean you have to create an entire department to manage the paperwork
- Incorporate human factors into your clinical trials
  - Validations are now submitted to clinical modules
  - What you do clinically should reflect intended use commercially
- Be prepared to keep making improvements post-approval
  - Product complaints should be fed back to your development teams
  - Don’t learn something new about your product post-launch or in late stages of development

http://raps.org/Regulatory-Focus/News/2017/09/19/28491/Real-World-Evidence-FDA-Commits-to-Advancing-its-Use/

http://www.raps.org/Regulatory-Focus/News/2017/08/30/28366/FDA-Finalizes-Guidance-on-Using-Real-World-Evidence-for-Medical-Device-Regulatory-Decisions/

Upcoming MassBio Forums

October 18: Corporate Social Responsibility: For-profit/Non-profit Partnership with Purpose;NP

October 31: Going Virtual with CROs: Accelerating Product Development While Minimizing Organizational Scale; CRO/CMO

November 9: Clinical Trial Optimization via Simulations; BSCMCT

November 15: The NIH is Open for Business - Leveraging the NIH for Technology Development and Commercial Success including one-on-one Meeting Opportunities; EU