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A leader in inhaled pharmaceuticals

IPAC-RS Device Working Group
Human factors and the design of inhalation devices

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team.

Topics

- Review of published research into the use of inhalation devices
  - approaches
  - findings
- Overview of human factors engineering (HFE) best practice in inhalation device development
  - introduction to analytical and empirical approaches
  - timing of HFE activities through development
- Review of practice
  - Published research
  - Approach to HFE during development within IPAC-RS members
- What next?

Review of Published Research on Devices *in Use* - what can this tell us?

- Approaches taken to human factors and assessing compliance
- Understand how devices are used in the 'real world'
- Tell us how well we're doing as device designers
- Give us benchmarks for real world error rates…
- … and guidance on study design
- Studies on marketed/established devices…
  - explore compliance issues
  - often include the inhalation manoeuvre
  - are usually performed by clinicians (sometimes sponsored)
  - can review use of patient's own device or experience with new device

Patients' own device

Dry Powder Inhalers: Factors Associated with Device Misuse
Siegfried Wieshammer and Jens Dreyhaupt, RDD 2009

- Evaluation of error rates in 4 marketed inhalers: Aerolizer®, Diskus®, HandiHaler®, Turbuhaler®
- Prospectively identified essential handling errors
- Subjects (224) were patients who used own devices

- **"Nearly one in three patients (30.9%) used DPIs ineffectively in study of 224 newly referred outpatients"**
- **"Error rate increased with age, … degree of airway obstruction, … and lack of prior training"**
  - **Probability of mis-use estimated to range from 10% to 83%**

Patients' own device

Handling of Inhaler Devices in Actual Pulmonary Practice: Metered-Dose Inhaler Versus Dry Powder Inhalers
Khassawneh et al; Respiratory Care, 2008

- Prospective observational study of patients using their prescribed device, using simple 3-4 'essential step' check list
- pMDI and three DPIs: Turbuhaler®, Diskus®, and Aerolizer®
- 300 asthma/COPD patients

- **"In actual pulmonary clinical practice the majority of patients were unable to use pMDI correctly" (75%)**
- **"Correct handling of DPI devices was variable" (7% - 43%)**

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Patients' own device

Inhalation technique and variables associated with misuse of conventional metered-dose inhalers and newer dry powder inhalers in experienced adults
Melani et al; Annals of allergy, asthma, and immunology., 2004

- Survey of inhalation technique in ~1,400 patients
- Patients' own device used, including inhalation
- Test Devices: pMDI (n= 1056), Aerolizer® (n= 230), Turbuhaler® (n=524) Diskus® (n=475)

- **"24% of patients … use pMDI poorly"**
- **"Failure to correctly perform essential steps for reliable lung delivery with the Aerolizer®, Turbohaler® and Diskus® was found in 17%, 23% and 24% of patients, respectively."**
- **"There was no difference in most variables correlated with poor inhalation between patients using pMDIs and those using DPIs"**

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New (to patient) device

Comparison of the Diskus® Inhaler and the Handihaler® Regarding Preference and Ease of Use
Van Der Palen at al; Journal of Aerosol Medicine, 2007

- Determined how many attempts were required for patients to correctly use the inhaler
- Also assessed acceptability of resistance using test pieces
- Subjects (60) were COPD patients with no experience of either device

- **"Ease of use was equally good with Diskus® and HandiHaler®"**
- **"One third (of subjects) inhaled perfectly after reading the instruction leaflet …"**
- **"… which increased to 85% after one instruction"**

New (to patient) device

Handling of and Preferences for Available Dry Powder Inhaler Systems by Patients with Asthma and COPD
Schulte et al; Journal of Aerosol Medicine & Pulmonary Drug Delivery, 2008

- Handling and preference assessed for 7 different DPIs
- Subjects (72) were asthma patients with no experience of any of the devices
- Empty devices used, inhalation checked by observation

- **% of patients with 'critical' handling errors after first use (reading leaflet) ranged from 25% to 72%**
- **% of patients with 'critical' handling errors after second use (instruction) ranged from 8% to 52%**
- **"Device handling and patient preference are closely correlated"**
- **"Reduced patients acceptance of a device, being dependent on device handling, may reduce … patients' compliance"**

Do these studies give us a 'benchmark'?

Reported error rates for patients using their own device:

- **Nearly *one in three* patients (30.9%) used DPIs ineffectively in study of 224 newly referred outpatients**

- **Failure to correctly perform essential steps for reliable lung delivery with the Aerolizer®, Turbohaler® and Diskus® was found in *17%, 23% and 24%* of patients, respectively.**

Reported error rates for patients using a new device:

- **% of patients with 'critical' handling errors after first use (reading leaflet) ranged from 25% to 72%**
- **% of patients with 'critical' handling errors after second use (instruction) ranged from 8% to 52%**

- **One third of subjects inhaled correctly after reading instruction leaflet**
- **85% inhaled correctly after instruction**

Published papers give us valuable insights into device use and the complexities of conducting handling studies

- There is a lot of evidence that current devices fall short
  - Although impact of 'errors' isn't always clear – may not affect therapy

- Assessment of inhalation manoeuvre can be problematic …
  - Often assessed through observation
  - Again, clinical significance of 'poor technique' not always apparent

- Benchmark seems to be that 1/4 - 1/3 of DPI users use their inhalers 'incorrectly' (or not according to the instructions)

- Interesting correlations between acceptance and compliance, age and (non) compliance
  - User acceptance influences compliance

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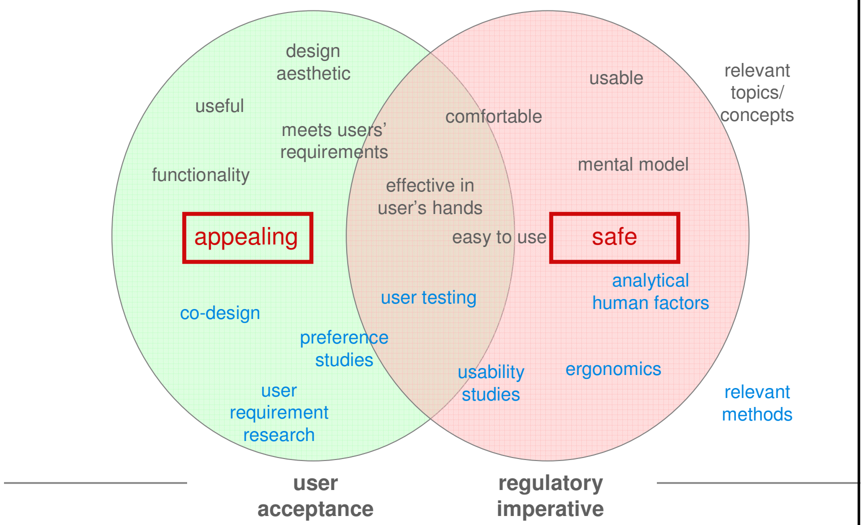
Why are user research and human factors important?



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Meeting the challenge – guidance and theory

- FDA guidance
  - Do it by Design
  - Human Factors Input to Risk Management
- key standards
  - ISO/IEC 62366
  - ANSI/AAMI HE74 and HE75:2009

HE75: HFE – Design of Medical Devices

- a useful methodology handbook
- provides guidance on key HFE issues for OINDP:
  - managing risk of use error
  - suggested HFE techniques through development
  - how to test usability of devices
- also a valuable source of information on
  - human abilities and anthropometry
  - documentation and packaging
  - broad range of HFE principles for certain user-interface attributes (controls, displays, alarms etc)

Using ANSI/AAMI HE75:2009 as our methodology handbook

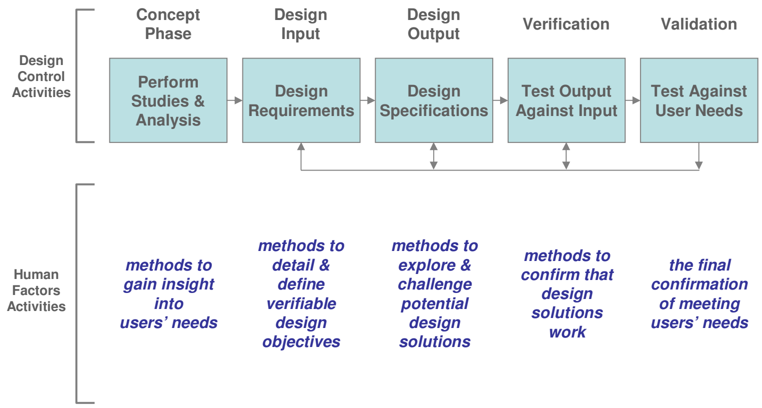

Figure adapted from AAMI HE75:2009

Some Core HFE Methodology

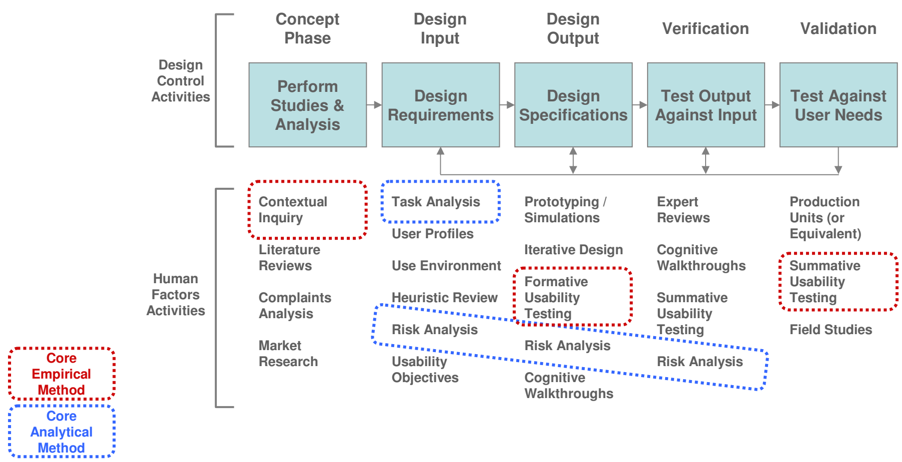

Figure taken from AAMI HE75:2009

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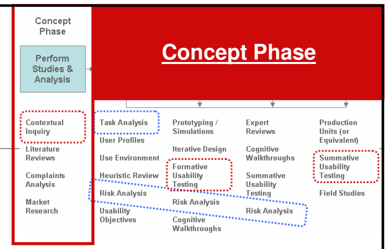
Concept Phase Activity

Defining User Requirement Metrics



example empirical method:

contextual enquiry

- focused research into the real world use of the intended device:
  - how used?
  - by who?
  - where?
  - when?
  - what current problems exist with similar devices?

purpose: to direct design and engineering from the outset regarding **fundamental user requirements**

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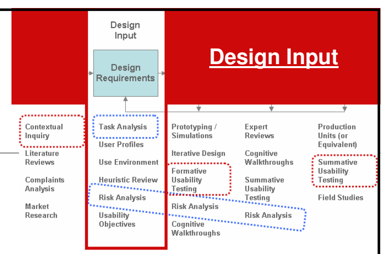
Design Input Activity

HFE as a fundamental Design Input

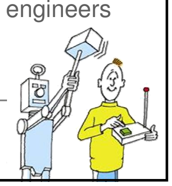


example analytical method:

task analysis

- analysis of the interaction between the user and the intended device
  - how the engineering and design of the device will fit, not conflict, with predictable user expectations
- initial use-related risk assessment
  - based on hazards defined in risk management plan
  - what will define a safe device?

purpose: on the basis of impact on the user, proactively establish **fundamental rules** for how the device should function, which engineers and designers must work within



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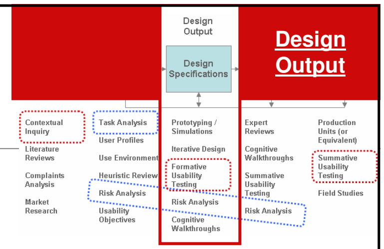
Design Output Activity

Usability testing within development



example empirical method:
formative usability testing

- observation of real, representative users using prototypes
- selection of competing design approaches
- development of training / instruction designs
- iterative
- provide "opportunities to fail" – it may be important to go back

purpose: to **challenge competing design approaches** and develop understanding of how users interact with device designs in practice

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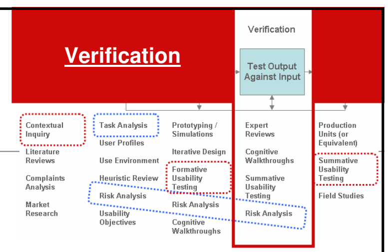
Verification Activity

HFE as part of Risk Management



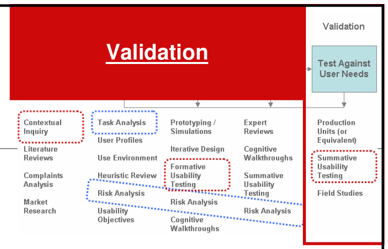
example analytical method:
use-related risk analysis

- the use-related risk equivalent of FMEA – a detailed and exhaustive assessment of the risk associated with use of the device as designed
  - built on the hazard definitions and risk acceptance criteria defined in the project risk management plan
  - e.g. based on a state-space map
  - e.g. including sequences of use-errors that can lead to hazards
  - ideally, including lab-based practical exploration of device performance under variation of user input

purpose: to confirm – **by analysis** - that a **safe device design** has been delivered

Validation Activity

Usability Validation

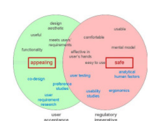


example empirical method:
summative usability testing

- evidence of the usability of your device, achieved through 'simulated use' validation study with the final device / instructions for use designs

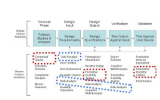
purpose: to provide a single study that confirms **acceptable usability of the final design** as submitted for approval

Summary



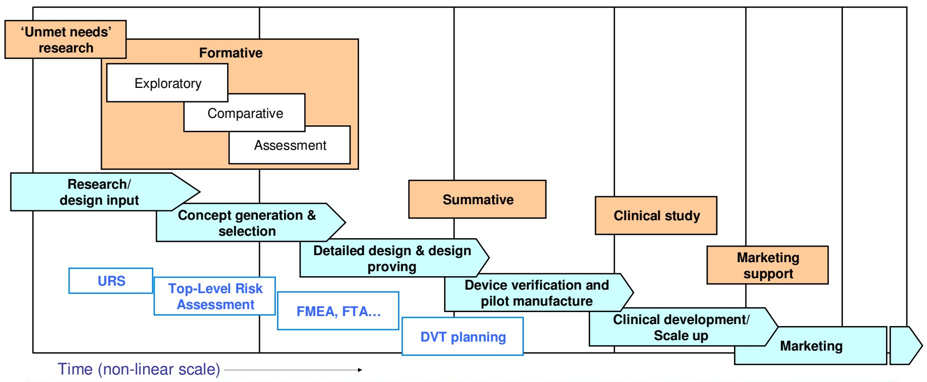
- Our objective is safe *and* appealing devices
- Human Factors Engineering (HFE) is the relevant discipline
  - HFE a key part of risk management as well as design activities

- HE75 is a good guide
- Best practice will incorporate both analytical and empirical methods



Review of 'actual' practice

- Studies on devices in development/pre-launch…
  - aim to inform the design and design process
  - help to produce attractive, easy-to-use devices
  - help to manage design risk/safety



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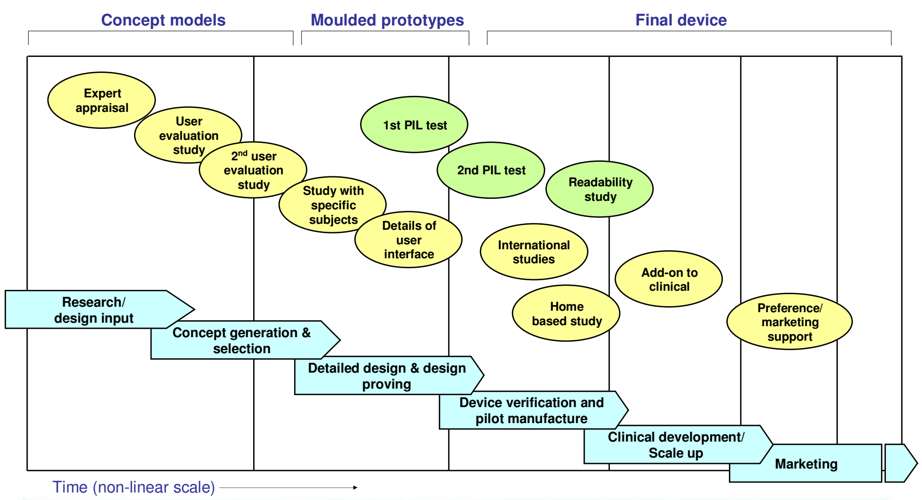
Vectura example: GyroHaler® user handling studies – actual and planned



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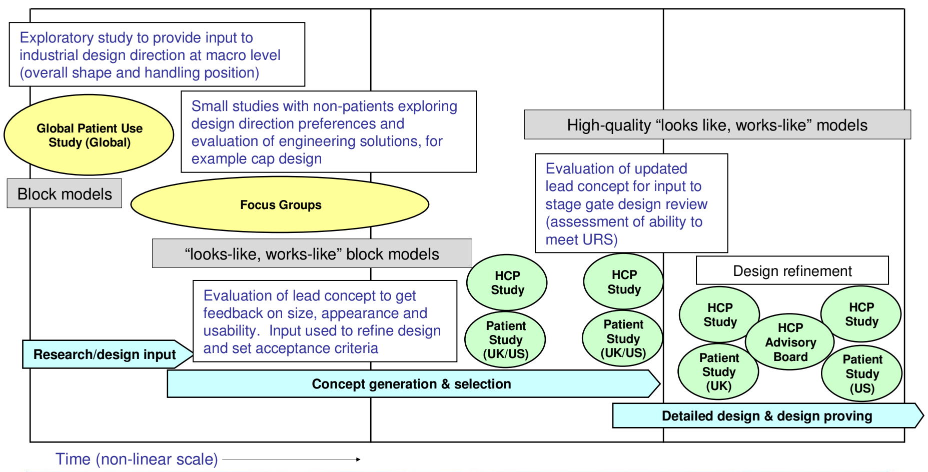
Novartis example, with focus on design phases
(with thanks to Novartis members of Device WG)



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Typical 'formative' study design (concept phase):

- 12-24 subjects:
  - usually patients (i.e. inhaler user)
  - sometimes selected by age/inhaler type etc
- Broad study objective to inform design process/selection
- Should however have specific aim to identify unanticipated use-related hazards as part of risk management process
- Stimulus/test material includes concept models, usually as representative of the 'user experience' as possible
- Specific areas of design can be explored with greater numbers of non-patients
  - E.g. interpretation of particular features, legibility, grip etc can be explored with larger numbers of non-patients more easily and quickly
- Inhalation manoeuvre not included
- Often includes preference aspect to address 'do they like it?' alongside 'can they use it?'

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Typical ‘summative’ study design (verification phase):

- 12++ subjects
- Explicitly part of the risk management/device verification process
- Focus on robustness and safe & effective use
- Will form part of an overall picture created from clinical studies, flow rates studies, lab-based device verification testing etc
- Legibility and comprehension of IFU also addressed
- ‘Worst case’ studies may be used to assess use and robustness in the absence of IFU and instruction
- Study materials likely to be final-form devices/IFU

Devices pre-launch – 2 published examples

A comparison of the efficacy, safety and device handling of Fluticasone Propionate 50μg BD via the Diskus®/AccuHaler® and Diskhaler® inhalers in asthmatic children
Cohen et al; RESPIR. CRIT. CARE MED. 1995

- 4 week safety and efficacy study incorporating device handling and preference
- 267 subjects
- Formed part of clinical development programme

- **77% of Diskus® patients and 71% of Diskhaler® patients were able to use the devices correctly after first instruction**
- **81% of Diskus® patients and 51% of Diskhaler® patients found the devices very easy to use**
- **70% of patients preferred Diskus®**

Characteristics of a capsule based dry powder inhaler, Breezhaler®
Pavkov et al; Current Medical Research & Opinion, 2010

- Brief report on performance characteristics and robustness, based on results from a number of studies
- Studies included PIF assessment, robustness, complaint rate (90,000 devices)

- **Patients can achieve the necessary flow rate**
- **Low number of complaints, no functional device failures**

Conclusions

- Standards / regulators are capturing best practice and setting expectations
  - Basic approaches are clear
  - But, regulations derive from multiple sources
  - Benchmarks aren't established
- OINDP industry is developing and implementing best practice:
  - As a key part of the risk management process
  - To develop better devices for patients
- But we are in the early stages of developing a consistent industry approach
  - Little shared experience so far
  - Situation is comparable to introduction of FMEA 15-20 years ago
  - Interesting comparison with 'mature' discussion and awareness of analytical methods
- Conferences/discussions such as this will help industry and regulators to move forward, building consistency and confidence

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