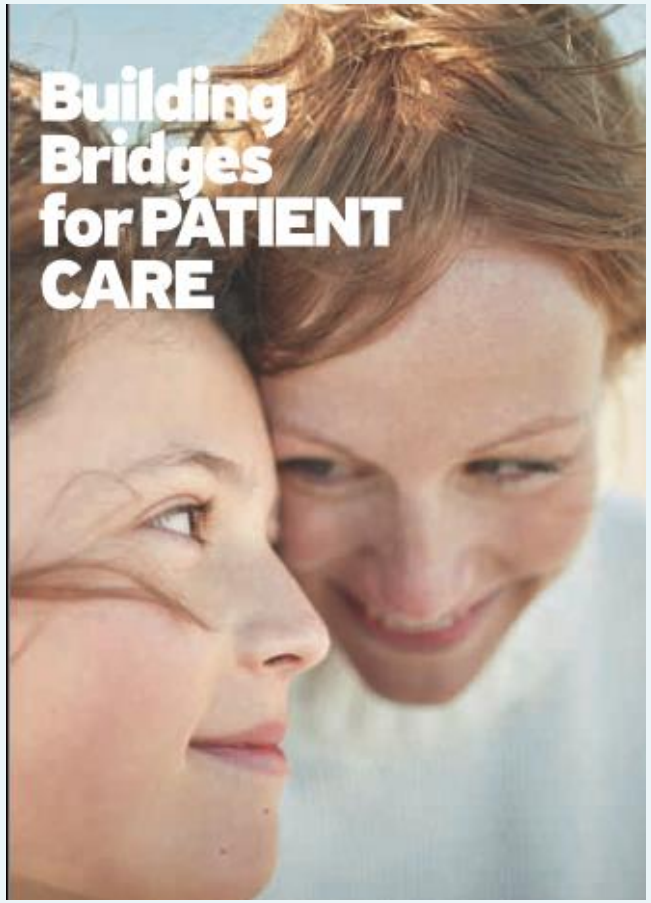
10th Global Drug Delivery
& Formulation Summit
March 12, 2019 - BERLIN



Human Factors Engineering for Medical Device Development

R. Vomscheid, PhD

Director, Devices Development & Technologies - IPSEN

PRESENTATION AGENDA

- Human Factors Engineering: overview & regulatory framework
- Patient-centricity in Device Design and Development
- Case study: Development of a New Delivery System for Somatuline® Autogel®
- Conclusion

DISCLOSURE

- I am currently employed by Ipsen
- This study was sponsored by Ipsen

Human Factors Engineering: overview & regulatory framework

Usability Engineering Process Objectives

"The aims of a usability engineering process are to deliver **products that are easy to use and safe in the intended context of use, and by intended users (whether by carers or patients themselves).** Users should not have to read, understand and remember complex instructions for use and adapt to the requirements of the device, or use it in an uncomfortable, incorrect and possibly dangerous way: a well-designed product will be easy to use, and will have a user interface that is consistent with user experiences and expectations.

In addition to safety considerations, products designed with human factors principles are more pleasing to use, and are therefore **likely to lead to better adherence to correct use**, at the required frequency. Human factors principles are therefore employed by many companies in design for customer loyalty and marketing purposes."*

* MHRA Human Factors and Usability Engineering – Guidance for Medical Devices Including Drug-device Combination Products, v1.0, p.13 (2017)
MHRA: Medicines and Healthcare products Regulatory Agency (UK)

Regulatory Landscape Medical Device Development / Human Factor Studies

EUROPE	USA
Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EE	21CFR820 Medical Device Quality System Regulation (and 21CFR part 4 cGMP for combination products)
ISO 13485:2016 requirements for a quality management system specific to the medical devices industry	
	AAMI/ANSI HE75:2009 Human factors engineering - Design of medical devices
ANSI/AAMI/IEC 62366-1:2015 Medical devices – Part 1: Application of usability engineering to medical devices	
IEC/TR 62366-2:2016 Medical devices - Part 2: Guidance on the application of usability engineering to medical devices	
ANSI/AAMI/ISO 14971:2007/(R)2016 Medical devices – Application of risk management to medical devices	

Key guidances for Human Factor Studies

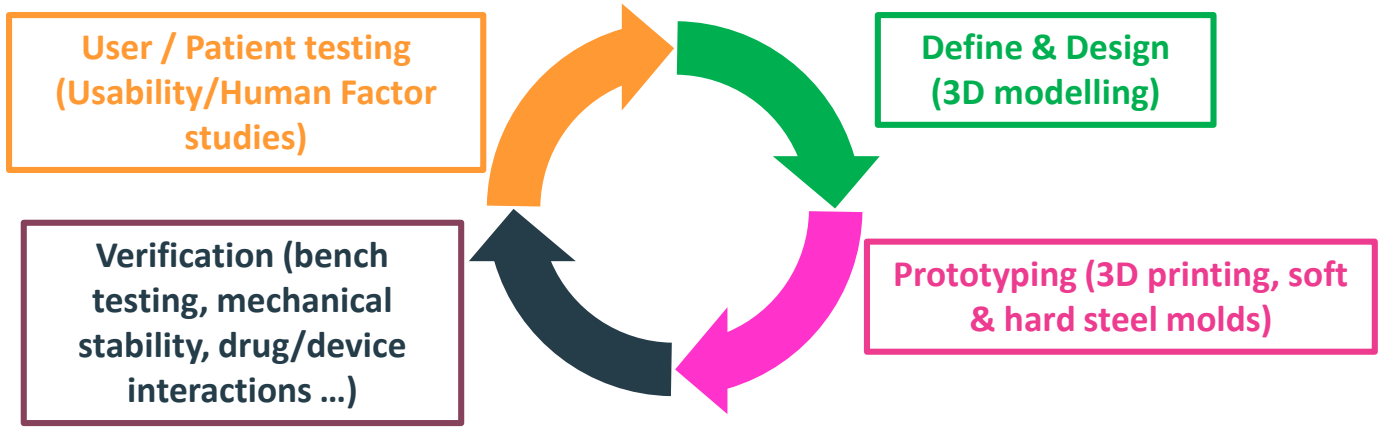
EUROPE	USA
MHRA Human Factors and Usability Engineering – Guidance for Medical Devices Including Drug-device Combination Products, v1.0 (2017)	**FDA Applying Human Factors and Usability Engineering to Medical Devices (2016)**
EMA PRAC* Good practice guide on risk minimisation and prevention of medication errors (2015)	FDA Safety Considerations for Product Design to Minimize Medication Errors (2016)
EC Guideline on the readability of the labelling and package leaflet of medicinal products for human use (2009)	FDA Human Factors Studies and Related Clinical Study Considerations in Combination Product Design and Development (Draft, 2016)
	FDA Design Considerations for Devices Intended for Home Use (2014)

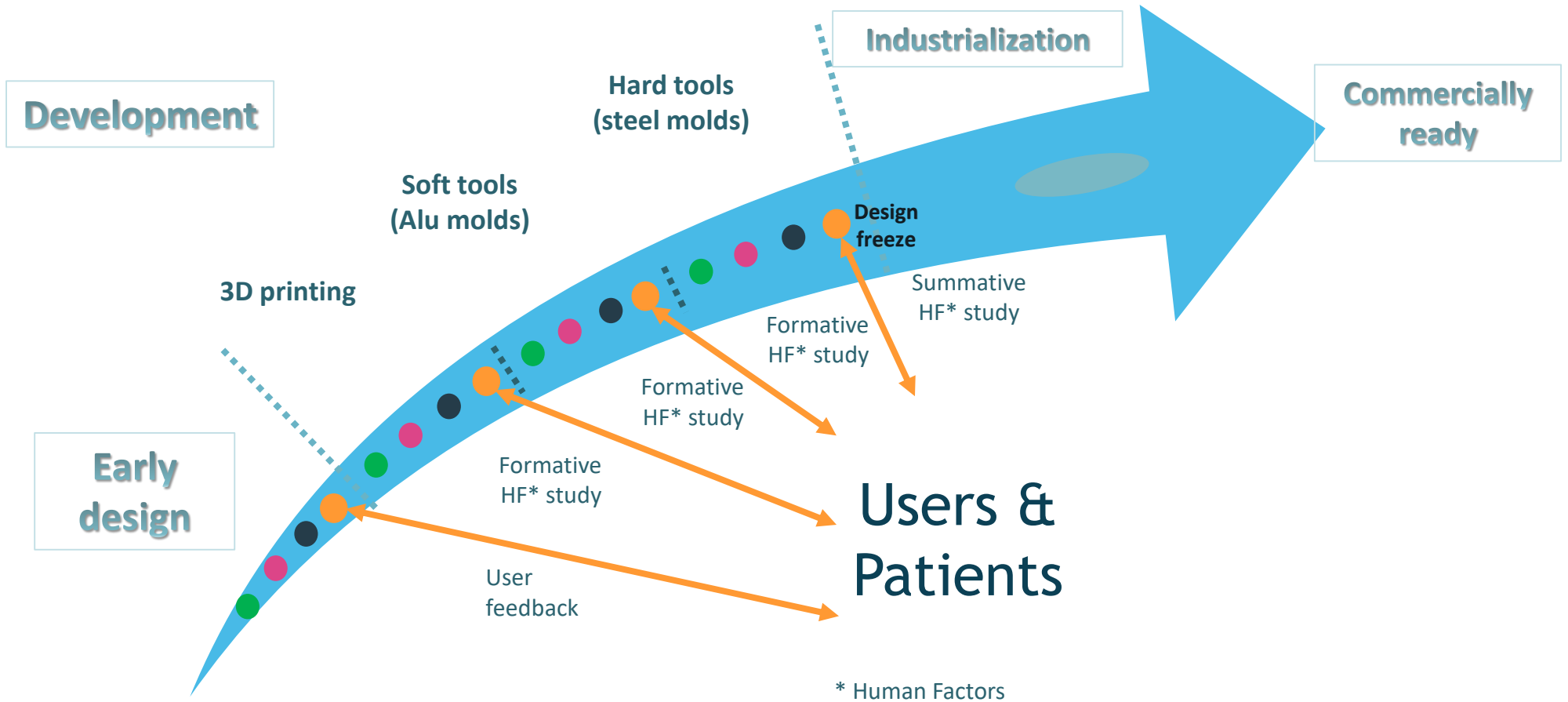
* The Pharmacovigilance Risk Assessment Committee (PRAC) is the European Medicines Agency's (EMA) committee responsible for assessing and monitoring the safety of human medicines
https://www.ema.europa.eu/en/committees/pharmacovigilance-risk-assessment-committee-prac

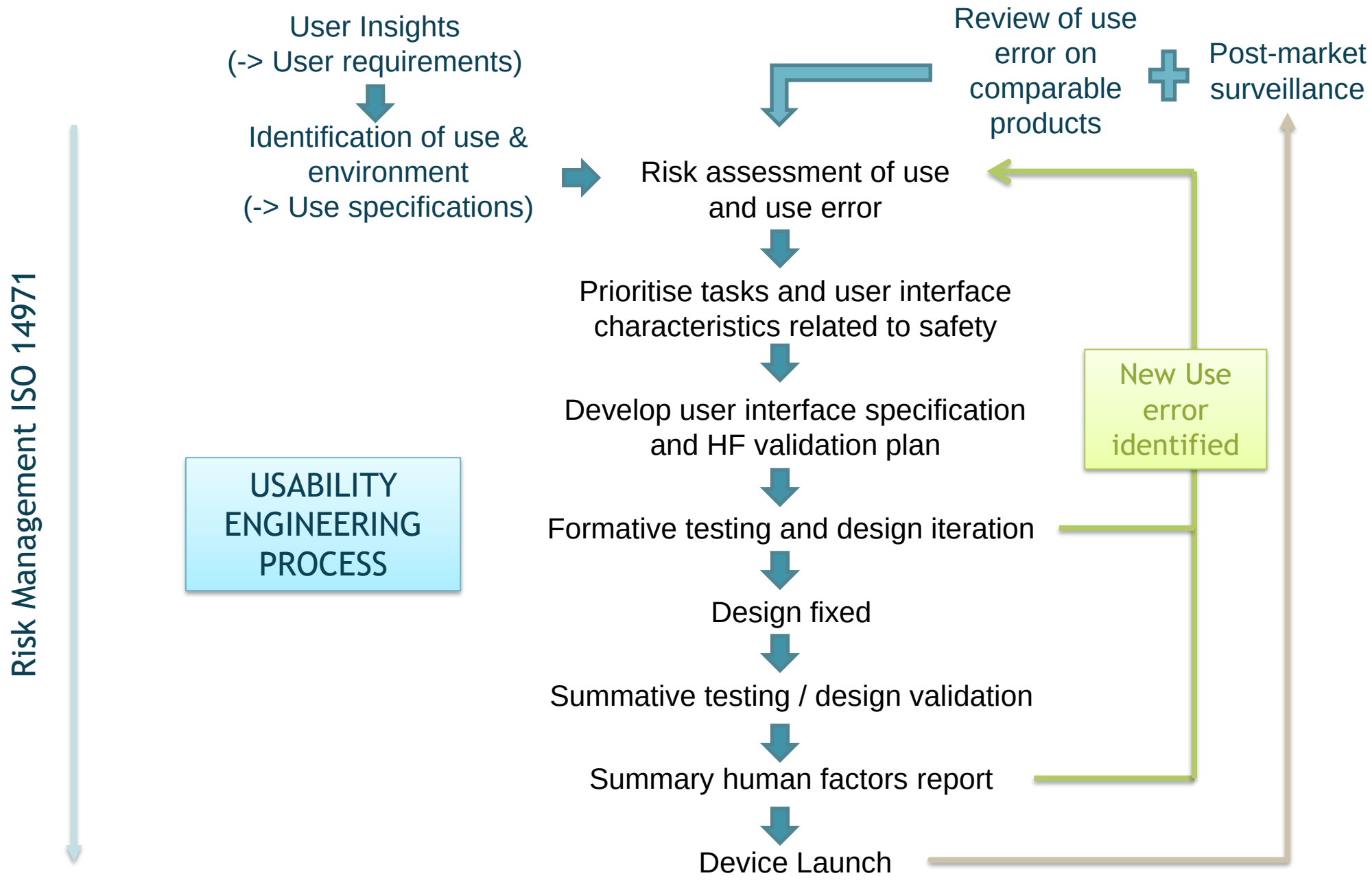
Patient-centricity in Device Design and Development

DEVICES

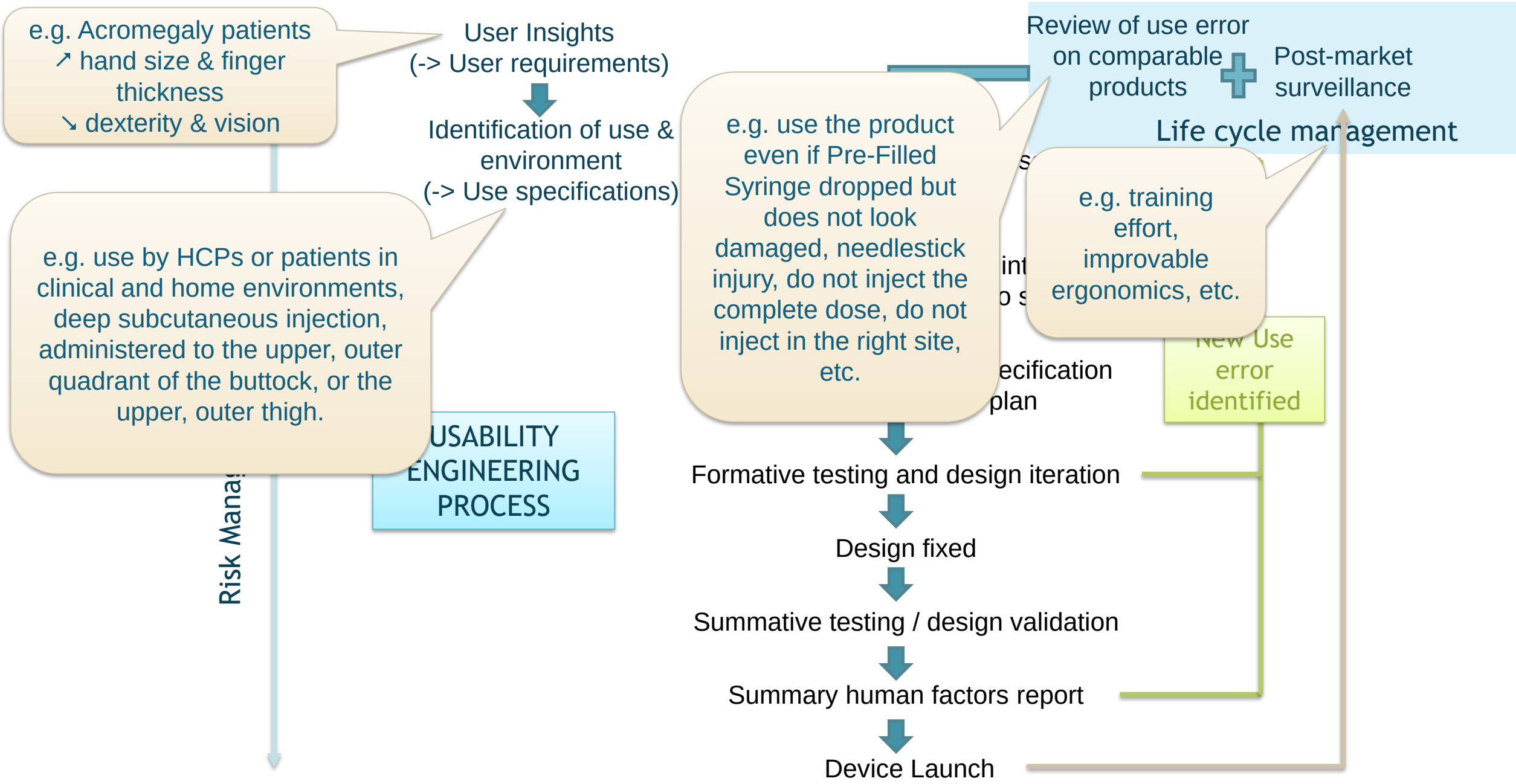
PATIENT-CENTRIC DEVELOPMENT PROCESS

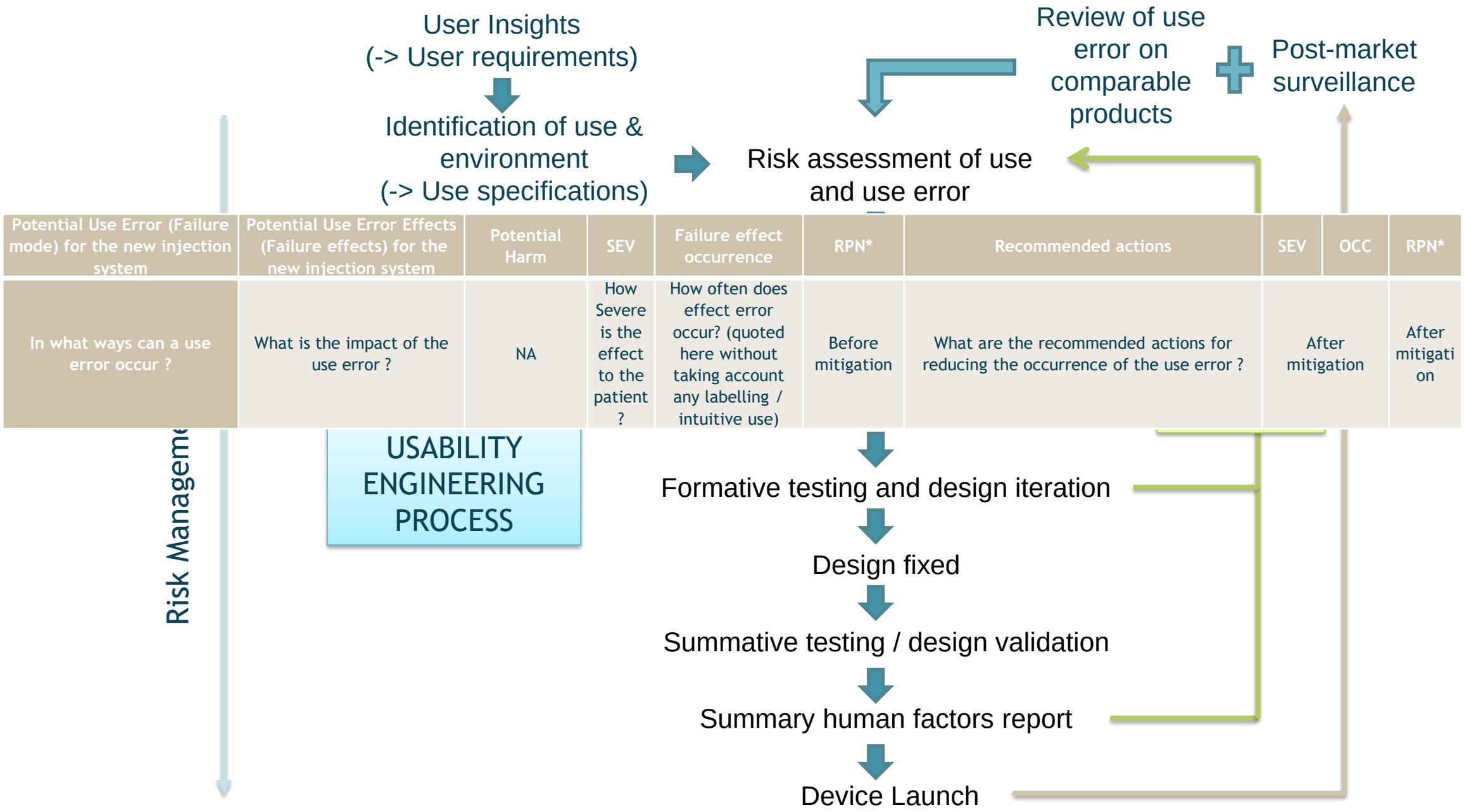




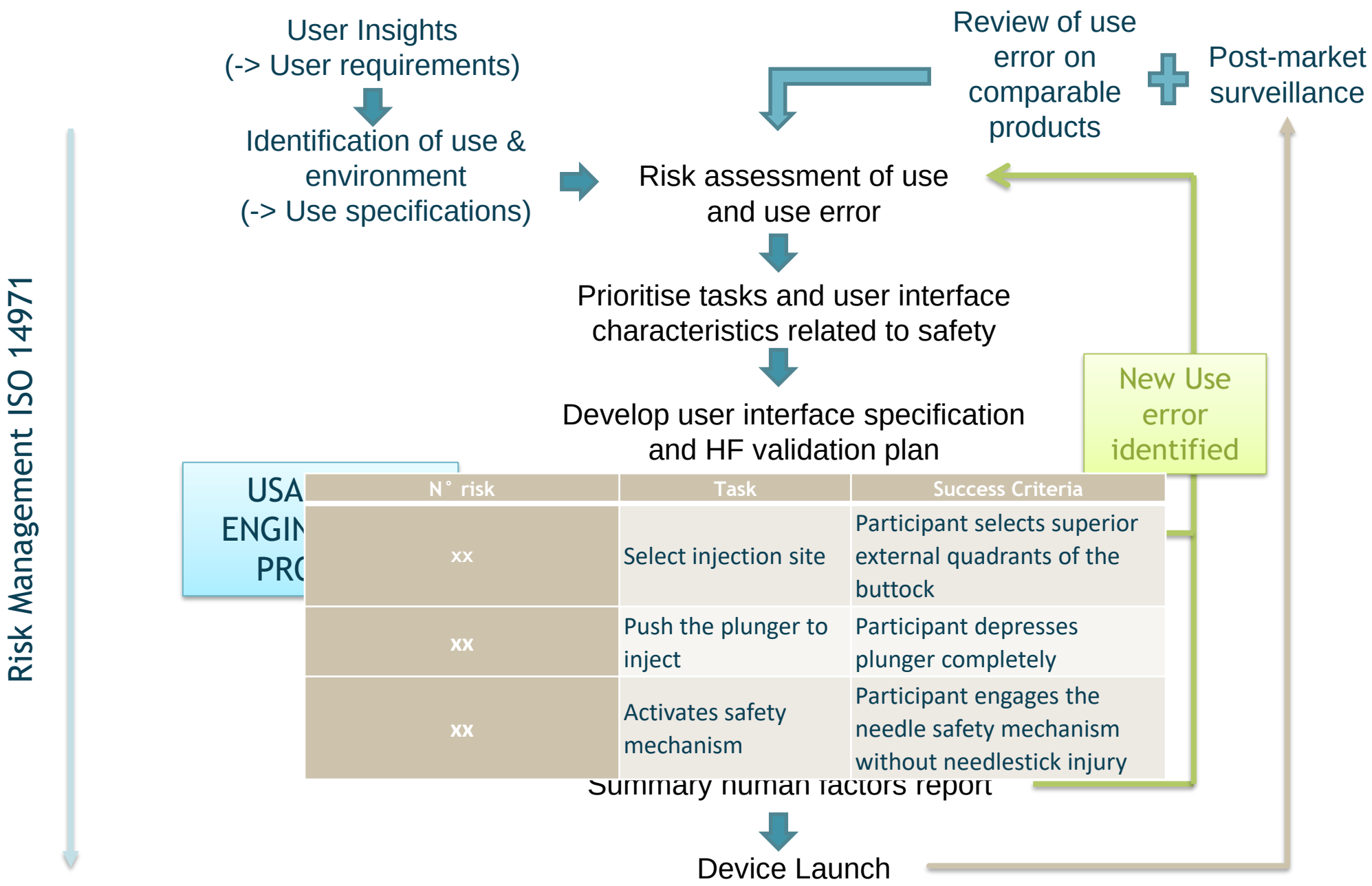


Adapted from MHRA Human Factors and Usability Engineering – Guidance for Medical Devices Including Drug-device Combination Products, v1.0, p.14 (2017)


e.g. Acromegaly patients
↗ hand size & finger thickness
↘ dexterity & vision
User Insights
(-> User requirements)
Identification of use & environment
(-> Use specifications)
e.g. use by HCPs or patients in clinical and home environments, deep subcutaneous injection, administered to the upper, outer quadrant of the buttock, or the upper, outer thigh.
USABILITY ENGINEERING PROCESS
Risk Manag
Review of use error on comparable products
Post-market surveillance
Life cycle management
e.g. use the product even if Pre-Filled Syringe dropped but does not look damaged, needlestick injury, do not inject the complete dose, do not inject in the right site, etc.
e.g. training effort, improvable ergonomics, etc.
ecification
plan
New Use error identified
Formative testing and design iteration
Design fixed
Summative testing / design validation
Summary human factors report
Device Launch



* Risk Priority Number


User Insights
(-> User requirements)
Identification of use & environment
(-> Use specifications)
Review of use error on comparable products
Post-market surveillance
Risk assessment of use and use error
Prioritise tasks and user interface characteristics related to safety
Develop user interface specification and HF validation plan
New Use error identified
N° risk
Task
Success Criteria
xx
Select injection site
Participant selects superior external quadrants of the buttock
xx
Push the plunger to inject
Participant depresses plunger completely
xx
Activates safety mechanism
Participant engages the needle safety mechanism without needlestick injury
Summary human factors report
Device Launch
Risk Management ISO 14971

Case study:Development of a New Delivery System for Somatuline® Autogel®

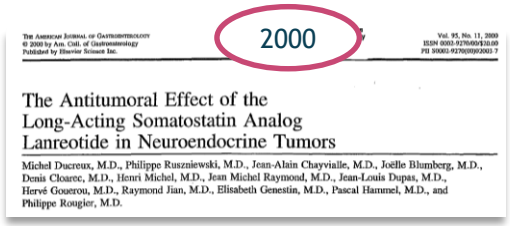
Ipsen vision & commitment in Acromegaly & NET*

1995

Somatuline Long-Acting 30 mg;

(1/ 15 days)

2000



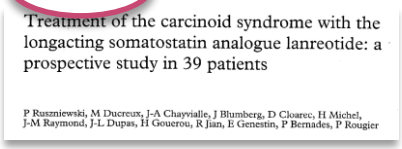
The Antitumoral Effect of the Long-Acting Somatostatin Analog Lanreotide in Neuroendocrine Tumors

Michel Ducreux, M.D., Philippe Ruszniewski, M.D., Jean-Alain Chayvialle, M.D., Joëlle Blumberg, M.D., Denis Cloarec, M.D., Henri Michel, M.D., Jean Michel Raymond, M.D., Jean-Louis Dupas, M.D., Hervé Gouerou, M.D., Raymond Jian, M.D., Elisabeth Genestin, M.D., Pascal Hammel, M.D., and Philippe Rougier, M.D.

2001

Somatuline autogel 60, 90, 120 mg, ready-to-use (1/ 28 days)

1996



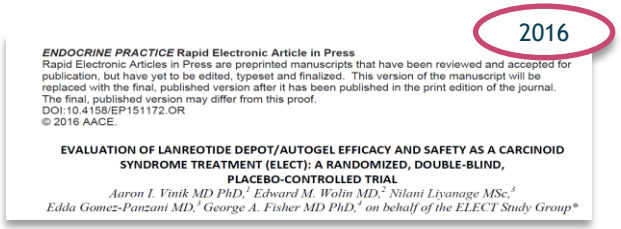
Treatment of the carcinoid syndrome with the longacting somatostatin analogue lanreotide: a prospective study in 39 patients

P Ruszniewski, M Ducreux, J-A Chayvialle, J Blumberg, D Cloarec, H Michel, J-M Raymond, J-L Dupas, H Gouerou, R Jian, E Genestin, P Bernades, P Rougier

2010

Somatuline autogel ready-to-use + with safety system (1/28 days)

2016



ENDOCRINE PRACTICE Rapid Electronic Article in Press

Rapid Electronic Articles in Press are preprinted manuscripts that have been reviewed and accepted for publication, but have yet to be edited, typeset and finalized. This version of the manuscript will be replaced with the final, published version after it has been published in the print edition of the journal. The final, published version may differ from this proof.

DOI:10.4158/EP151172.OR

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EVALUATION OF LANREOTIDE DEPOT/AUTOGEL EFFICACY AND SAFETY AS A CARCINOID SYNDROME TREATMENT (ELECT): A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

*Aaron I. Vinik MD PhD,[1] Edward M. Wolin MD,[2] Nilani Liyanage MSc,[3] Edda Gomez-Panzani MD,[3] George A. Fisher MD PhD,[4] on behalf of the ELECT Study Group**

2014

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

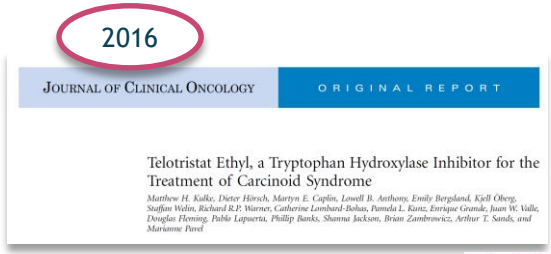
Lanreotide in Metastatic Enteropancreatic Neuroendocrine Tumors

Martyn E. Caplin, D.M., Marianne Pavel, M.D., Jarosław B. Ćwikła, M.D., Ph.D., Alexandria T. Phan, M.D., Markus Raderer, M.D., Eva Sedláčková, M.D., Guillaume Cadiot, M.D., Ph.D., Edward M. Wolin, M.D., Jaume Capdevila, M.D., Lucy Wall, M.D., Guido Rindi, M.D., Ph.D., Alison Langley, M.Sc., Séverine Martinez, B.Sc., Joëlle Blumberg, M.D., and Philippe Ruszniewski, M.D., Ph.D., for the CLARINET Investigators*

2017

Xermelo

2016



JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Telotristat Ethyl, a Tryptophan Hydroxylase Inhibitor for the Treatment of Carcinoid Syndrome

Matthew H. Kulke, Dieter Hörsch, Martyn E. Caplin, Lowell B. Anthony, Emily Bergsland, Kjell Öberg, Staffan Welin, Richard R.P. Warner, Catherine Lombard-Bohas, Pamela L. Kunz, Enrique Grande, Juan W. Valle, Douglas Fleming, Pablo Lapuerta, Phillip Banks, Shanna Jackson, Brian Zambrowicz, Arthur T. Sands, and Marianne Pavel

2018

Endocrine-Related Cancer | M Pavel et al. | Telotristat ethyl for carcinoid syndrome | 25:3 | 309–322

RESEARCH

Telotristat ethyl in carcinoid syndrome: safety and efficacy in the TELECAST phase 3 trial

Marianne Pavel[1,*], David J Gross[2], Marta Benavent[3,4], Petros Perros[5], Raj Srirajaskanthan[6], Richard R P Warner[7], Matthew H Kulke[8], Lowell B Anthony[9], Pamela L Kunz[10], Dieter Hörsch[11], Martin O Weickert[12], Pablo Lapuerta[13], Wenjun Jiang[13], Kenneth Kassler-Taub[13], Suman Wason[13], Rosanna Fleming[13], Douglas Fleming[14,*] and Rocio Garcia-Carbonero[15]

2019

Somatuline autogel ready-to-use, + with safety system, new syringe (1/28 days)

Ruszniewski, Gut 1996; Ducreux, AMGastroenterology 2000; Caplin, NEJM 2014; Vinik Endoc Practice 2016; Kulke, JCO 2016; Pavel et al. Endocrine-Related Cancer 2018

*NeuroendocrineTumors

Somatuline® Autogel® indications

(1) Treatment of acromegaly when circulating levels of growth hormone and/or IGF-1 remain abnormal after surgery and/or radiotherapy or in patients who otherwise require medical treatment.

(2) Treatment of G1 and a subset of G2 (Ki67<10%) gastroenteropancreatic neuroendocrine tumours (GEP-NETs) of midgut, pancreatic or unknown origin (where hindgut sites have been excluded) in adults with unresectable locally advanced or metastatic disease.

(3) Treatment of symptoms associated with neuroendocrine (particularly carcinoid) tumours.

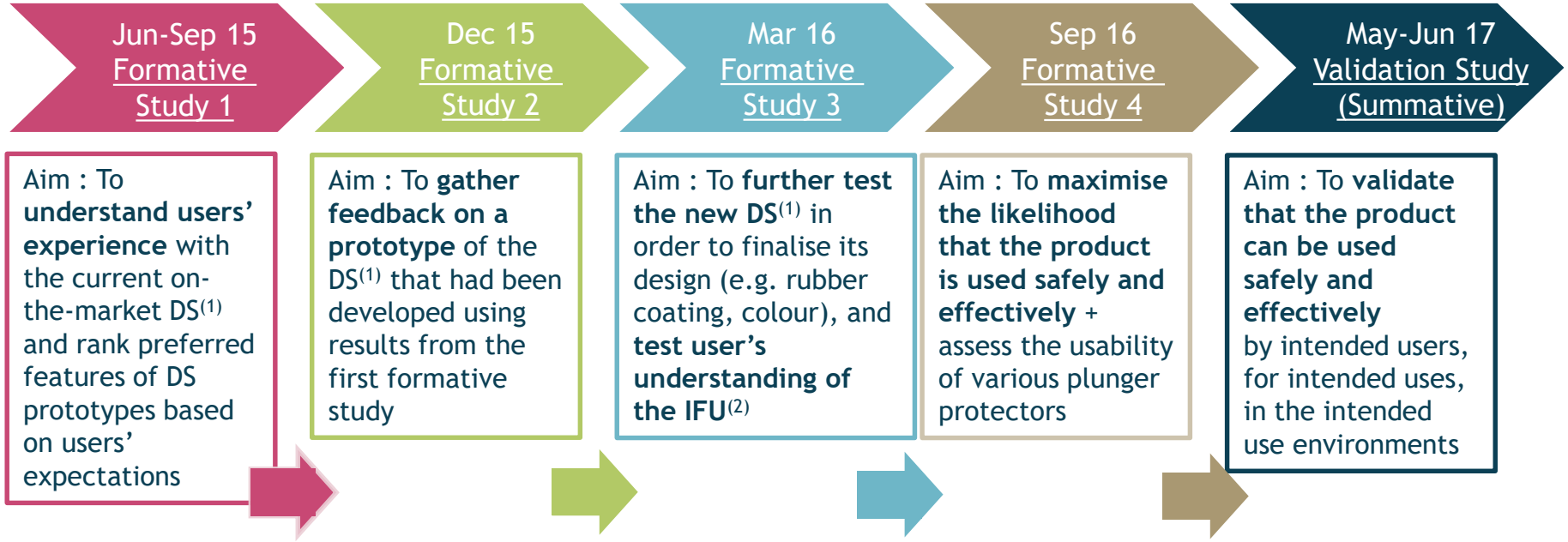
Source: https://www.hpra.ie/img/uploaded/swedocuments/08c164f3-f344-4821-b9a7-3750eb2a0c60.pdf

Somatuline® Autogel®- Life cycle management

1 delivery system for 3 Somatuline® Autogel® doses
Addition of a passive safety system

Improved ergonomics & user-friendliness
(market user feedback)

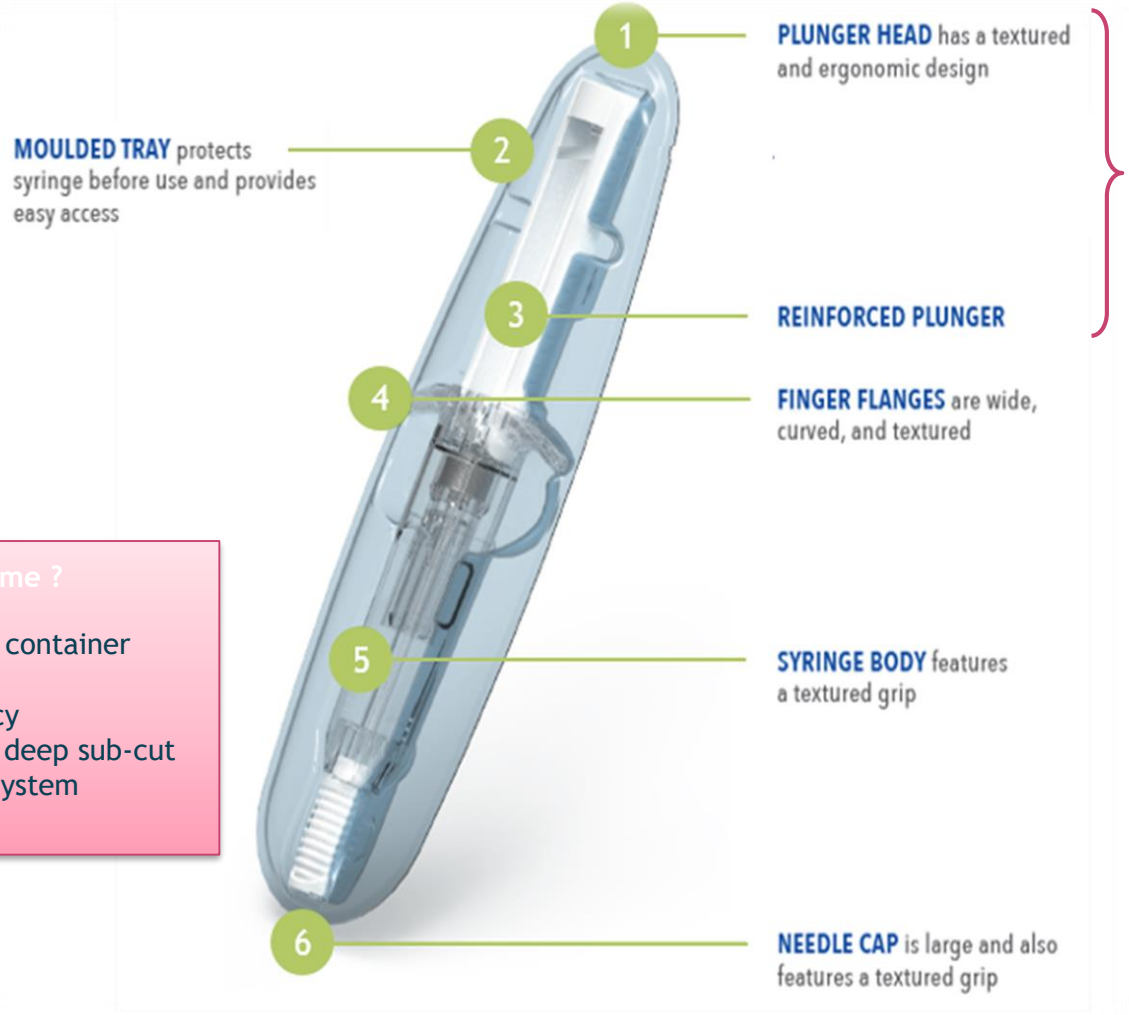
218 users gave their feedback to develop the new delivery system → 5 User studies for Regulatory submission in EU and US



(1) Delivery system
(2) Instruction for Use
(3) Acromegaly
(4) Neuroendocrine Tumors
(5) Healthcare Professionals

Somatuline® Autogel® – New Delivery System

Protective plastic tray to ensure no inadvertent depression of the plunger whilst within the packaging



A rigid plunger support with flat wide top to provide stability for depression with thumb

Wider & curved wings to aid those with limited dexterity (hand size, wearing gloves…)

Rigid, large and grippable syringe body to aid those with limited dexterity

Easy grip and removal of the cap to aid those with limited dexterity

What remains the same ?

- The formulation and primary container
- The low injection volume
- The syringe body transparency
- The needle size designed for deep sub-cut
- An automatic needle safety system
- Safety and effectiveness

CONCLUSION

Human Factors Engineering:

- Mandatory for device development. Detailed in US & UE regulations & guidance + international standards
- Patient-centric process by definition
- Essential for the development of a more ergonomic and user-friendly delivery system for Somatuline® Autogel®

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