



# Factory CRO

*First in Man*  
***Now you know what, but do you know how?***

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*Factory CRO 14 juni 2017*



# First in Man - Do you know how?

**A First in Man;  
Do you know how?**





# First in Man

**How to do it?**

**Study Design Considerations**

**Process overview NL, GER, UK**

**Research Landscape**



# First in Man -Design of your Clinical Investigation

## Design your Clinical Investigation



# First in Man -Design of your Clinical Investigation

## Selection of your Investigators

**Required Qualifications**

**The key opinion leader who is never in OR, or the less known investigator with experience ?**

**Skill set of the Investigator  
(eg. the expert vs the novice)**

**Are you measuring the learning capacity of the investigator?**

**Location  
(eg. does location matter?)**

**Are there local procedures that will impact your endpoints?  
eg. insurance policies**

**Is there already a standard of care?**

**SOC can differ per hospital  
What is the impact of the new procedure on the SOC**



# First in Man - Design of your Clinical Investigation

## Training of your Investigational sites

Learning Curve

New devices, new procedure require training

Procedure Training (eg. roll-in patients)

Are you measuring the learning capacity of the investigator?

Include all relevant dept.

Often not only one dept involved



# First in Man - Design of your Clinical Investigation

## Identification and enrollment of Subjects

Selection of subjects

Eg. Sportsmen vs Elderly

Expectation enrollment rate

Safety first  
(you don't know what will happen)

Expectations Subjects

What can they expect?



# First in Man - Design of your Clinical Investigation

## Monitoring

Monitoring

Monitoring of data vs monitoring of procedures

Frequency

What are you looking for?



# First in Man - Design of your Clinical Investigation

## Safety

Definitions

Reporting

DSMB

Progress of diseases?

Monitoring of subjects

Understand what to report

Who reports to whom? What to expect?

Independent review

What are you looking at?

Visit schedule



# First in Man - Design of your Clinical Investigation

## Expectations

**Sponsor**

**What do they expect from the Investigators?**

**Investigator**

**What can they expect from the device etc?**

**Subject**

**Time to relieve? Potential Side effects?**



# First in Man - Design of your Clinical Investigation

## External Challenges

**Funding**

**New resources when certain milestones are accomplished**

**Insurance Companies**

**SIIC versus Coverage versus METC**

**Competing studies**

**Will my product make it to the market on time?**



# First in Man - Design of your Clinical Investigation

## Common Mistakes

Data is biased

Poor design

Subject bias

Select correct outcome measures

Does my investigation answer my questions?  
etc?

Wrong population selected?  
Time to relieve? Potential Side effects?



# First in Man - Ethics Committee

**Expected from ECs for first in Man in NL**

**Medical Device Expertise**

**It is not just a box that needs to be checked**

**Don't hesitate to consult external experts**

**National + International standards & regulations**

**What is your referenced standard?  
ISO 14155 - GCP?**



# First in Man - Process overview

NL

EC Approval

CA notification

GER

EC Approval

CA notification

UK

EC Approval

CA notification

Separate submission to local EC  
Standard Pharmaceutical CTA -  
not applicable to device studies.

Local ECs give their consolidated  
feedback via DIMDI  
Requirement for Investigators to  
have MPG training

Medical device studies will be  
reviewed by specialized medical  
devices RECs



# First in Man - EC & CA

## CA and EC

Is there overlap?

Application Form

Data allowing  
identification of the  
device

Clinical Investigation  
Plan

Investigator's Brochure

Confirmation of  
Insurance of Subjects

Documents used to  
obtain informed  
consent

a Positive Vote of the  
Ethics Committee

Approval Board of  
Directors ( if applicable)

Name of the Medical  
Practitioner responsible  
for the Investigation

The place, starting date  
and the estimated  
duration of the  
Investigation

a statement that the  
device in question  
conforms to the  
essential requirements

Statements  
\* Human Blood  
\* Animal Origin

WHAT SHOULD YOU SUBMIT



# First in Man - Review by EC and CA

**CA: Review for compliance with  
*Wet op medische hulpmiddelen***

**EC: Review for compliance with  
*WMO (Wet Medisch Wetenschappelijk Onderzoek  
met mensen)***



# First in Man - Do you know how?

**A First in Man;  
Do you know how?**

**It is a team effort of  
multiple disciplines**

**Understand the role of the  
various key players and act  
accordingly**



# First in Man - the Key players

**EU  
Legislation**

**Manufacturer**

**Notified  
Bodies**

**Competent  
Authorities**

**Ethics  
Committee**

**International  
Standards**

**Investigator**

**Subjects**

**CRO**





# First in Man - Where to get your info

**EU  
Legislation**

**Competent  
Authorities**

**Notified  
Bodies**

**Manufacturer**

**Ethics  
Committees**

**International  
Standards**

**Investigator**

**Subjects**

**CRO**

## **Peter Ruys:**

Your Assistant: the Legislation for Medical Device Regulation

## **Erik Vollenbregt:**

Legal issues relating to clinical investigation of medical devices

## **Paul Riem Vis**

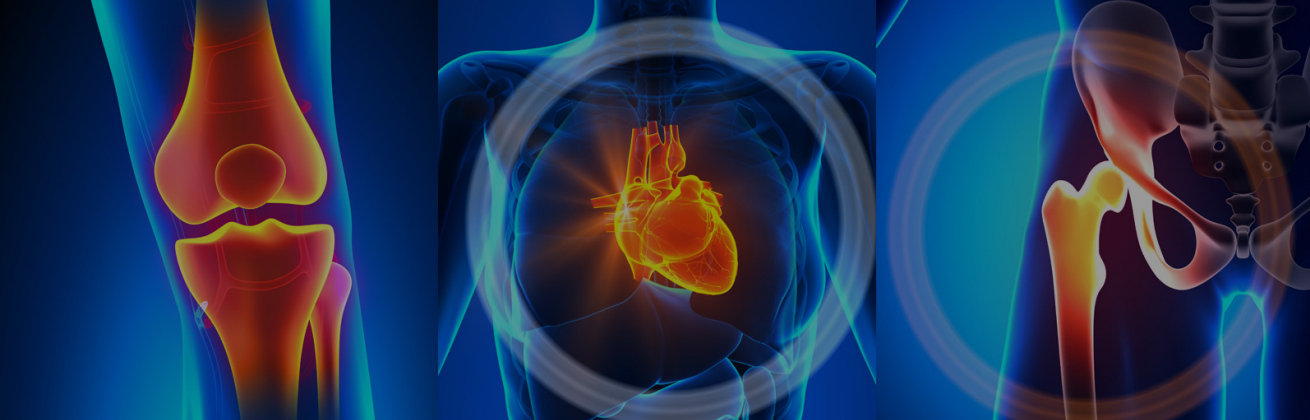
The IGZ and first in man medical device clinical studies

## **Jeannette van Loon:**

Biological safety evaluation of medical devices: a risk management process

## **Joris Bannenberg**

First in Man; Now you know what, but do you know how?



# First in Man - Things to consider

