EBF OPEN SYMPOSIUM

# Updating the organisational process and responsibility split for translational work with biomarkers and CoU – a pharma perspective

**Anna Laurén**
**Principal Scientist, PhD**
**Clinical Bioanalysis, Nonclinical and Clinical Assay Sciences**

# Non-clinical and clinical assay science (NCAS)

## 5 teams in NCAS

| BA - LC-MS (non-clinical + clinical) | BA-LBA (non-clinical) | BA-LBA (clinical) | IA (non-clinical + clinical) | IA (non-clinical + clinical) |
|---|---|---|---|---|

*One site in DK - Inhouse GLP/GCP laboratories for regulated work – outsourced case-by-case*

### Bioanalysis (BA)

Focus on PK assays according to Bioanalytical method validation (BMV) guidelines and delivery of data for TK/PK modelling

### Immunogenicity assay (IA)

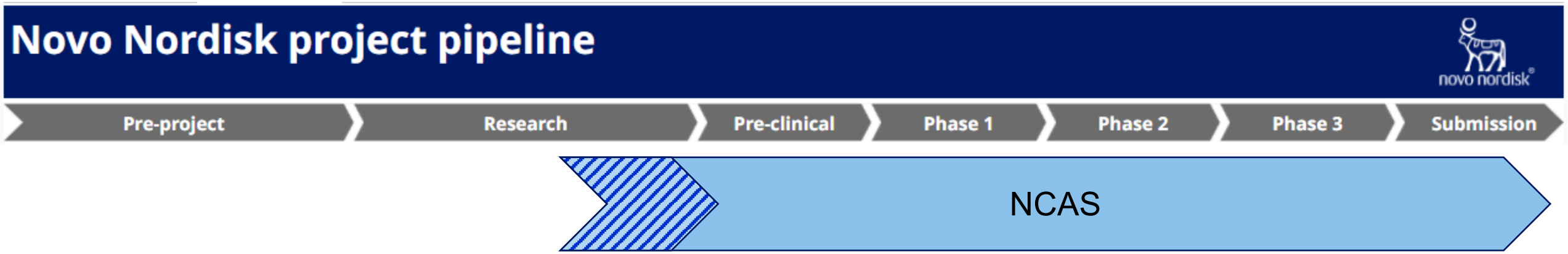
Full aspect of immunogenicity strategy (IS) according to guidelines

### Biomarkers (BM)

PAST: A few Core experts for biomarker assays in the team for Clinical Bioanalysis

- Biomarkers was traditionally often considered by stakeholders as a choice of technically validated assays to add to the study - most often outsourced
- Assays validated by inspiration from BMV **and/or** Fit for Purpose (e.g. clinical analysers/diagnostic labs)

# NCAS support in projects

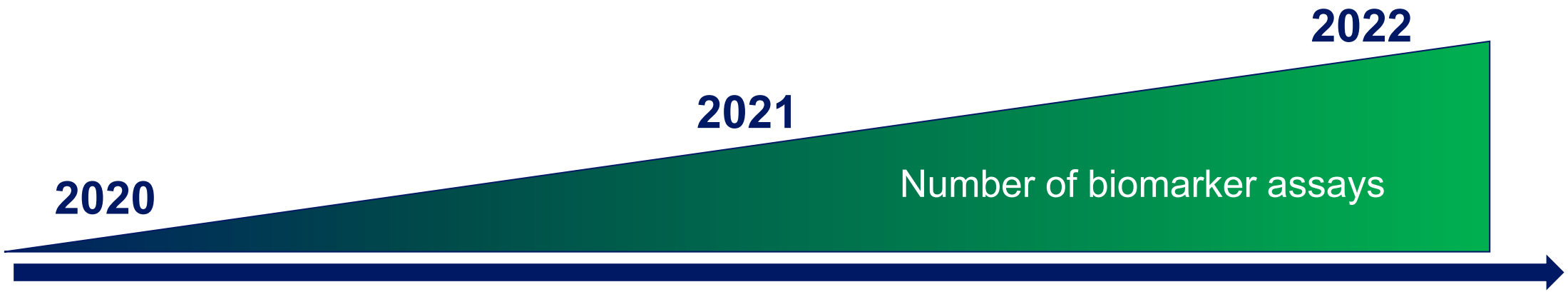



Depending on assay area (PK, Immunogenicity or Biomarker)
NCAS is involved in projects from research phase

Most resources are used for regulated studies

# New modalities, New therapy areas and Translational Science

- Biomarker focus in NCAS

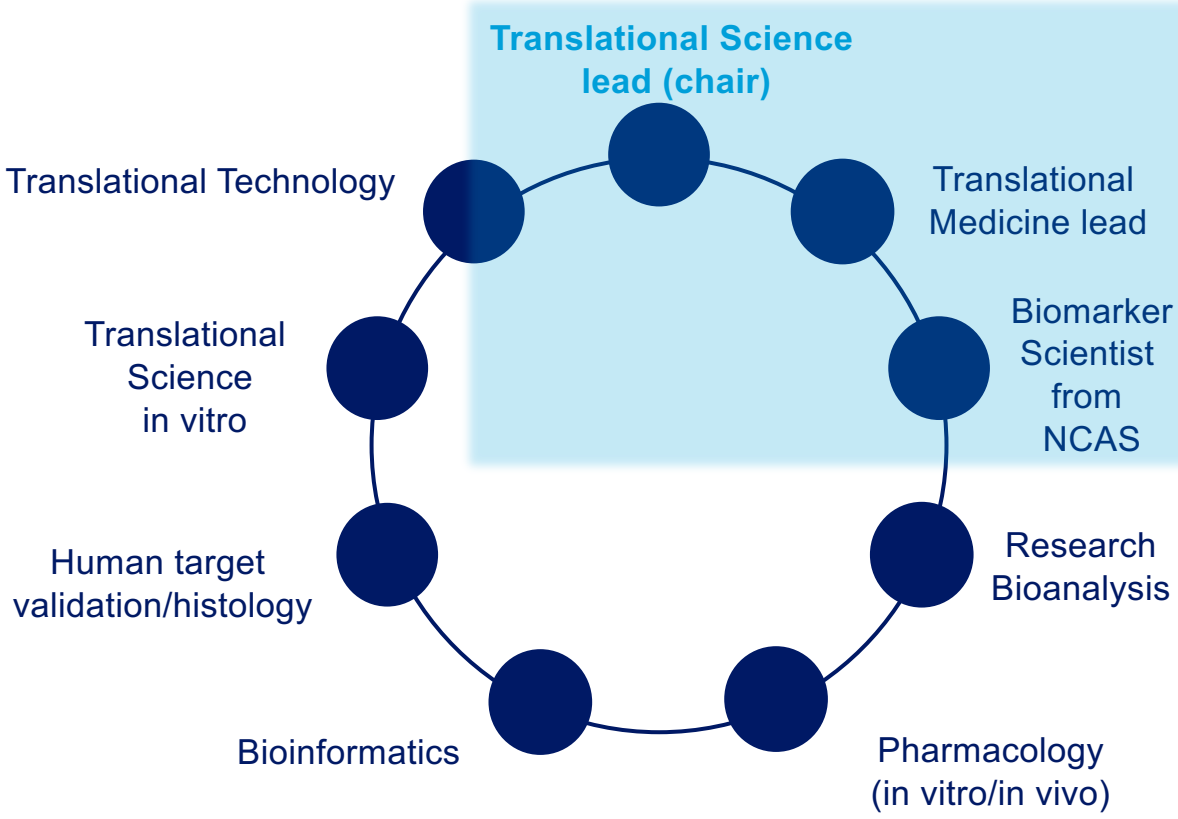



- With a growing number of Biomarkers expected additional resources and focus is being added in NCAS teams
- Added resources have experience from Biomarkers, PK assays, Immunogenicity and Diagnostics
- Strategies are being formed with stakeholders to fully consider translational aspects
- Learnings from the past and inspirations from outside Novo Nordisk are used to form the future

# TE and MoA Biomarker strategy – a cross-function collaboration

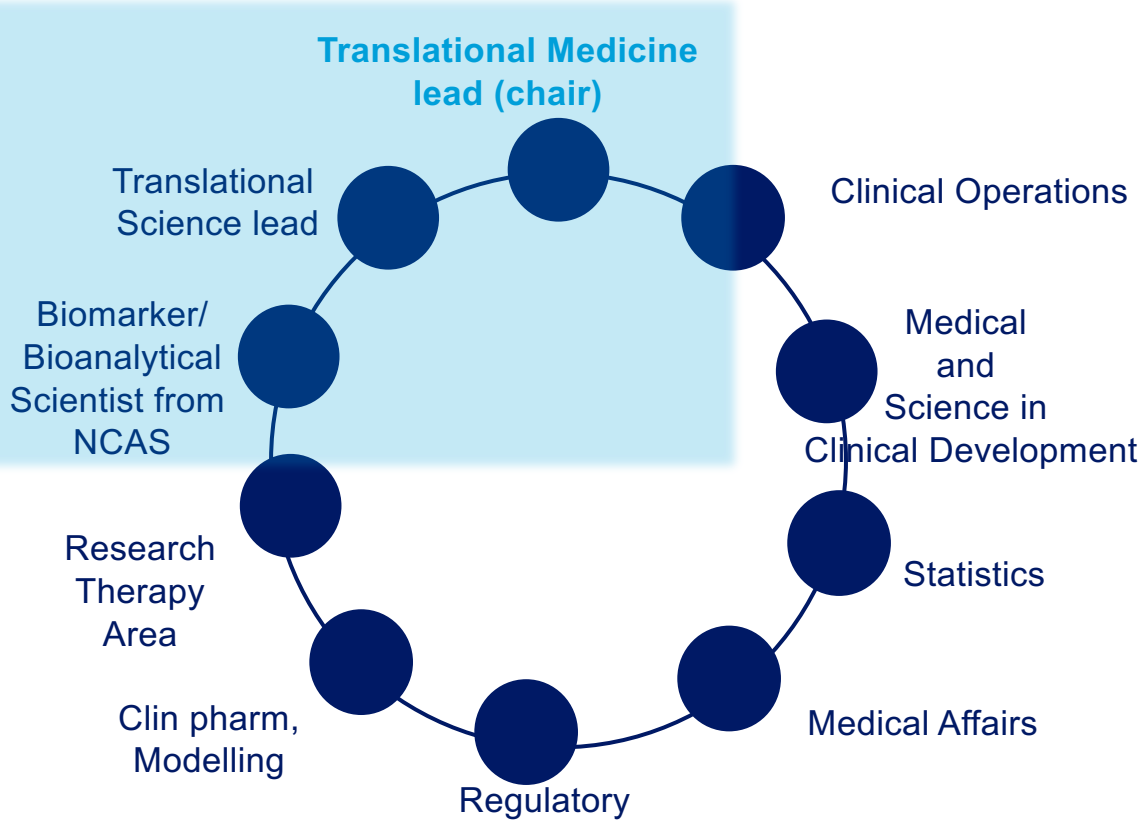
## Early Research

**Delivering biomarker strategy:**
**Translational Science responsibility**

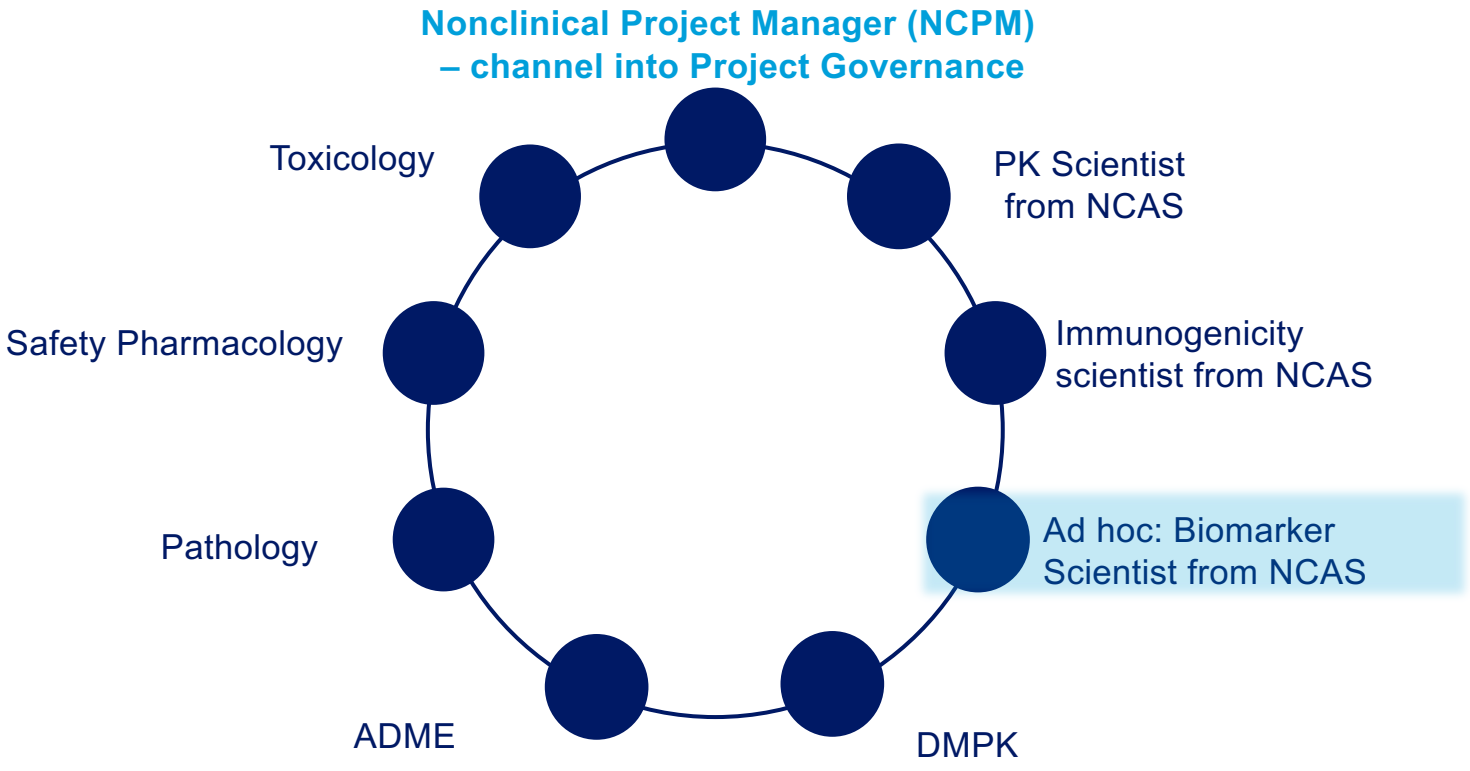



## Clinical Development

**Implementing biomarker strategy:**
**Translational Medicine responsibility**



# NCAS in Nonclinical teams: projects in regulated safety animal studies




NCAS are represented by a scientist (s) focusing:

- PK assays
- Immunogenicity
- AD hoc: Biomarkers

One scientist can represent all of above, or different scientists for different areas. Most often Immunogenicity is separate from PK and Biomarkers

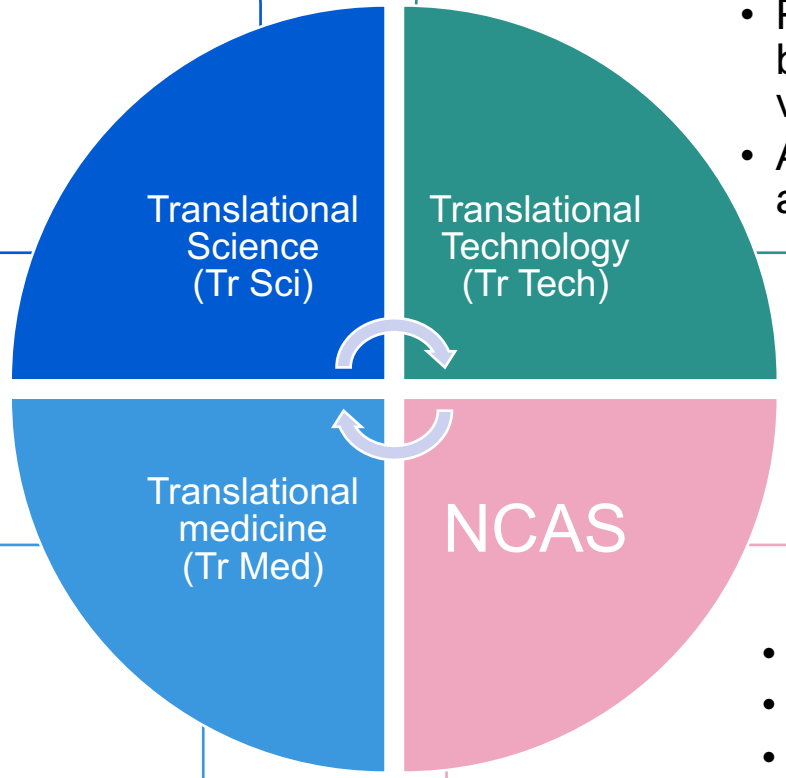
**Purpose 1:**
Ensure study validity (safety/efficacy)

**Purpose 2:**
Gain more translational knowledge

# Biomarker strategy – new cross-functional Translational project teams with defined responsibilities

## Definitions started to be rolled out in 2020

- Biomarker strategy and feasibility
- Preclinical evaluation of biomarker and ”biomarker validation”



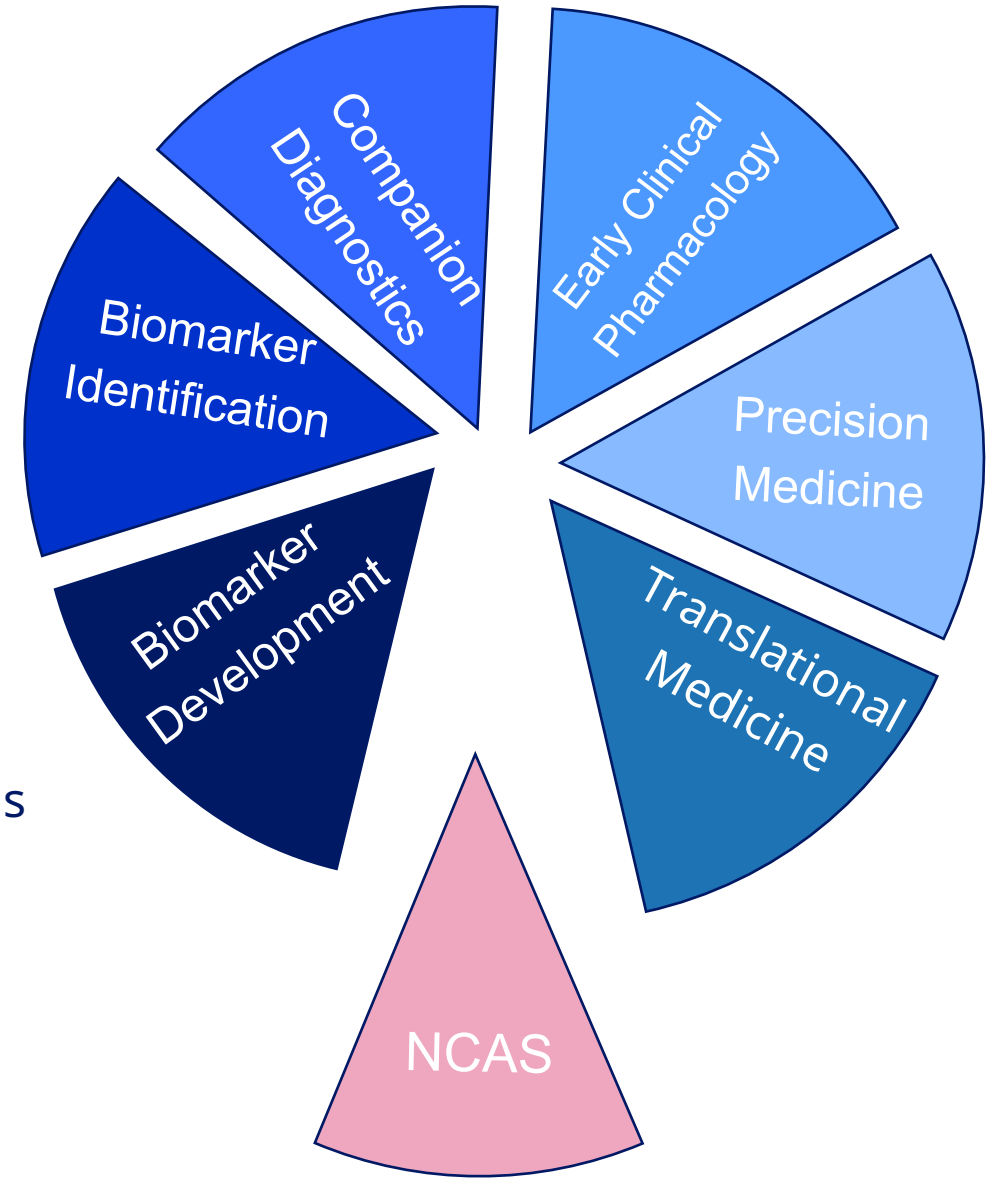

- Preclinical evaluation of biomarker and ”biomarker validation”
- Assay prototype, development and qualification

- Evaluate target value & lower reference value
- Decide on stop/go

- Technical Validation for its CoU
- In-house or outsourced
- Scientific responsible for clinical study sample analysis

# Reorganisations – new responsibilities

- Rocade in Translational Departments
- Individual stakeholders with new responsibilities
- NCAS responsiblities stays the same:
  - Technical Validation for its CoU
  - In-house or outsourced
  - Scientific responsible for clinical study sample analysis



# Early realisation between the stakeholders: Need for harmonisation of definitions

## WHAT IS VALIDATION AT NOVO NORDISK?

### Species validation

*Can the species be relevant for the target?*

”Research level”

### Biomarker validation

*Is the biomarker suitable for the given project?*

Preclinical evaluation of biomarker

No formal technical assay validation used – characterization/ feasibility needed

### Technical assay validation

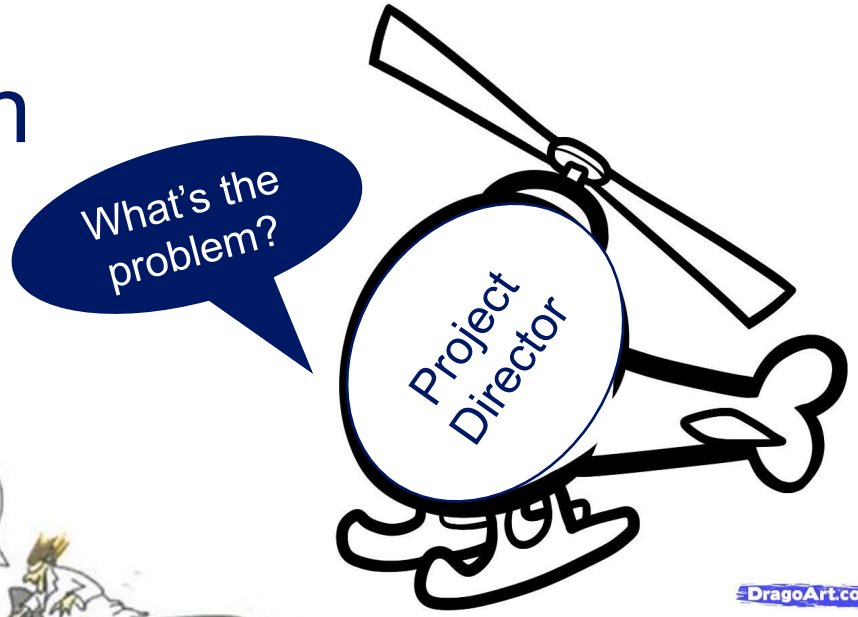
*Does the assay preform consistently within pre-defined acceptance criteria?*

Formal ”rubber stamp” documented with a validation plan and report that is included during for drug submission

Required at GLP and primary/secondary endpoints in clinical studies (GCP) – ie when decision is an outcome of marker in a GLP/GCP study

Based on Context of Use and previous technical characterization of the assay

# Realisation: Different perspectives on biomarkers and assay validation



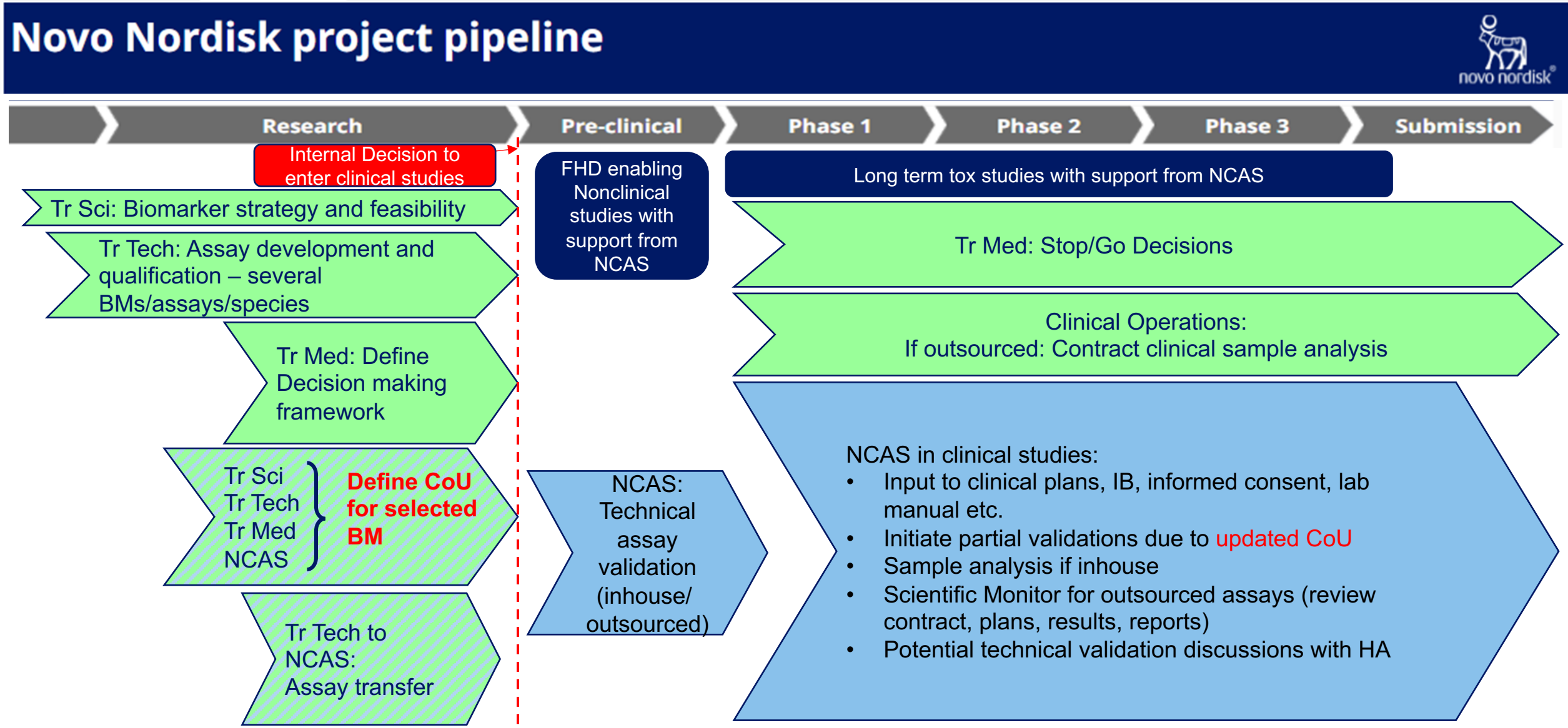

Develop and validate the right assay for the COU – main steps:

- Agree on responsibility split
- Define the COU
- Communicate

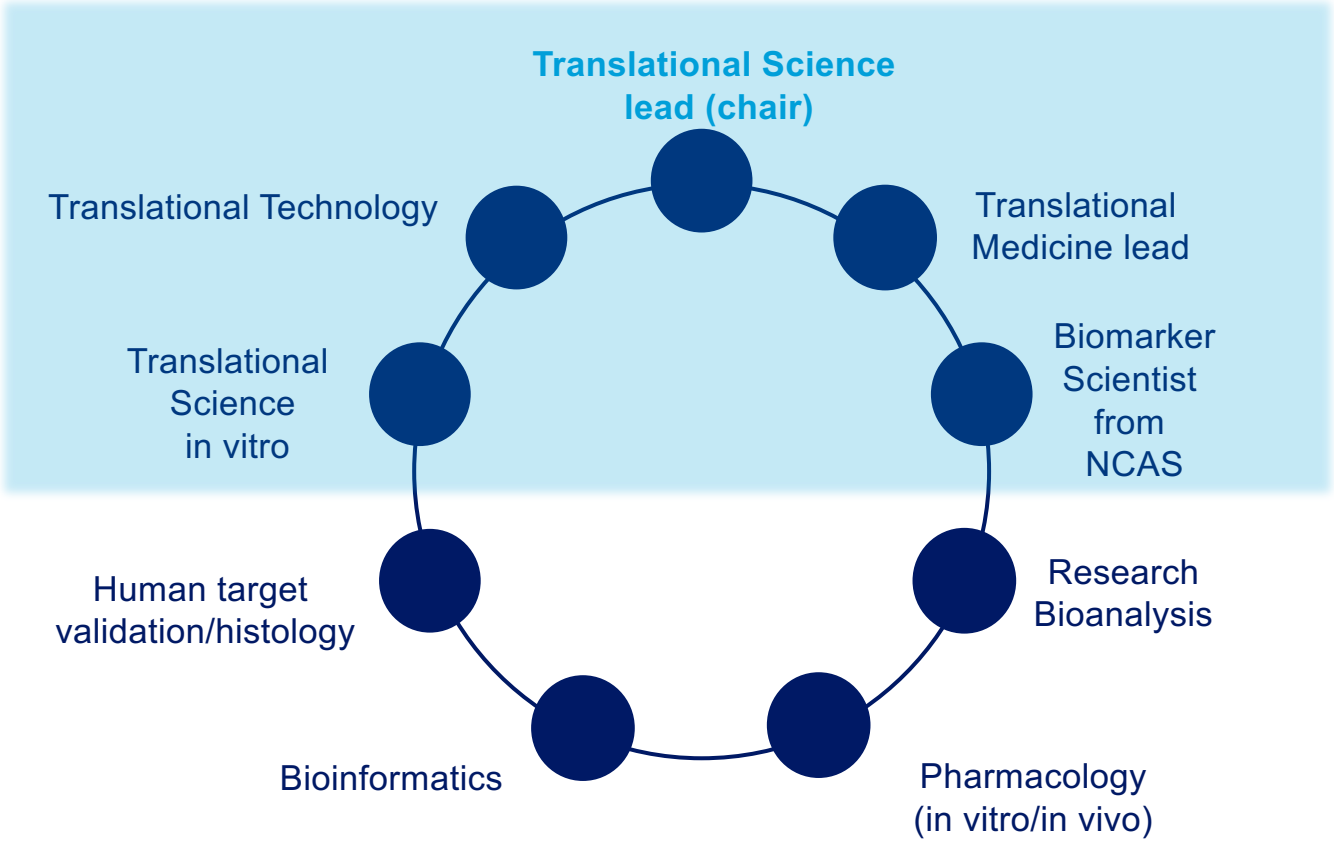
# Updating the organisational process for Biomarkers at Novo Nordisk

- Optimising collaboration and responsibility split while we work in the projects
- Workshops within NCAS and between close stakeholders to define future processes


# Current scenario: Responsibility split for clinical biomarkers



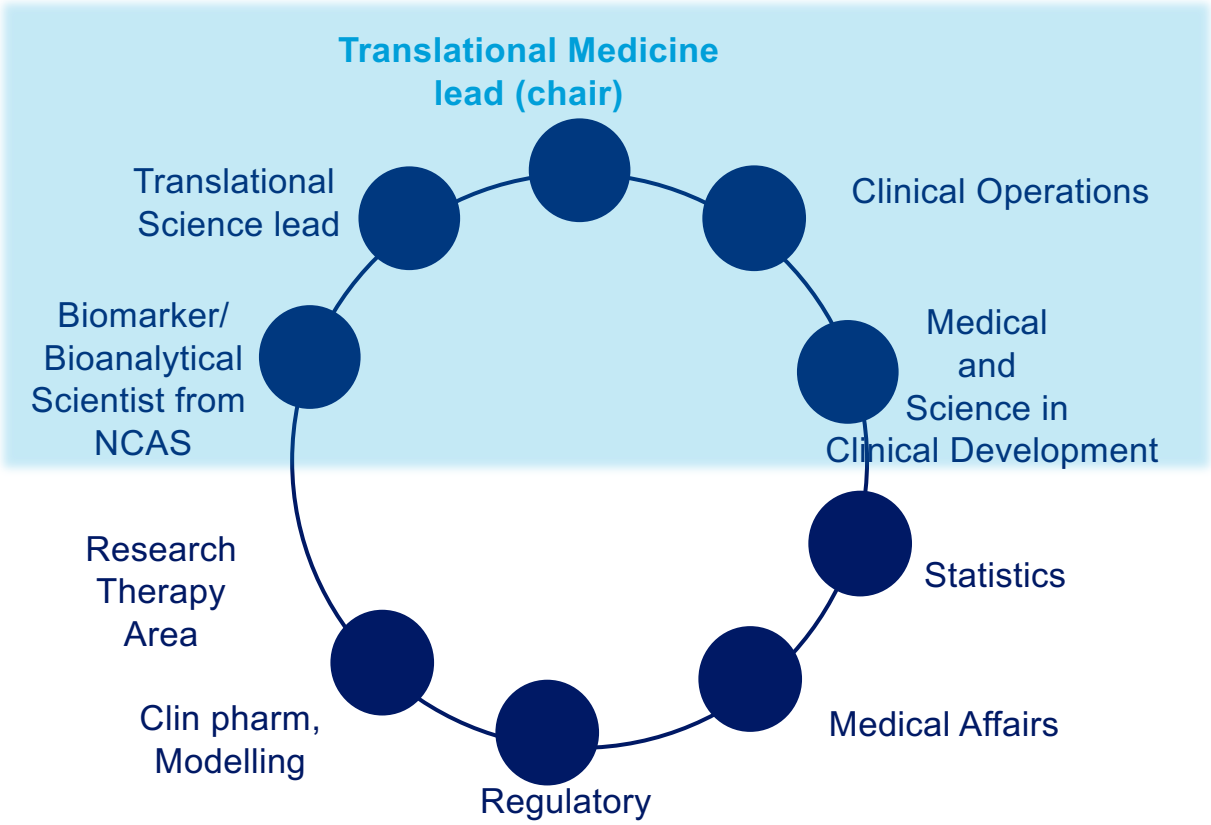
# Early communication is important to define CoU




- Subteams meet on regular basis to share updates on selection of relevant biomarkers
- CoU defined for each biomarker
- NCAS decides on inhouse vs outsourcing activities
- Information on CoU can later be integrated in assay strategy (submission documents), validation plans, potential outsourcing

# Continued communication is important to maintain CoU

- Translational Team meet on regular basis to share updates on relevant biomarkers
- NCAS BM scientists is included in Translational Team and Clinical Operations team
- NCAS BM scientists:
  - Is updated on clinical strategies
  - Decides on inhouse vs outsourcing activities and technical assay validation
  - Is included in regulatory considerations
- Maintained/updated CoU is ensured



# Current process for biomarker assays

## Feasibility/Qualification (Translational Science/ Translational Technology)

- Antibody pair selection and calibrator material
- Commercial kit

- Use a Scientific Case-by-Case mindset:
  - Frontload relevant parameters potentially included in validation
  - Communication on what is needed for CoU

- Test important parameters:
  - Choice of matrix and calibrator material
  - Stability
  - Matrix effect – Minimum required dilution and parallelism
  - Confirm literature data (range) in HS vs Disease biobanks
  - Precision of assay and stability of analyte
  - Total/free assay (Drug interference if relevant)

- Results for internal communication

## Technical Validation (NCAS)

- A priori defined acceptance criteria based on qualification and CoU

- Parameters to consider based on Scientific Case by Case:
  - Precision
  - Accuracy (or relative accuracy)
  - Parallelism
  - Stability
  - Range: Sample testing HS vs Disease
  - Sensitivity LLOQ/ULOQ
  - Total/free assay (Drug interference if relevant)
  - Specificity (cross-reactivity)
  - Selectivity
  - Calibrator/ Reagents

- Results and conclusions in a Validation Report

# Key points – Biomarker Assays in the new framework

- A holistic approach and communication is required
- The whole process is considered from the start of the project:
  - ✓ Assay reagents, design and analytical qualification – consider the long term use early
  - ✓ Qualification in pilot human research cohorts/exploratory testing – confirm literature data
  - ✓ Discussions on Inhouse and Outsourcing activities
  - ✓ CoU validation based on:

    Biology, understanding of assay and how the results will be used clinical trials

Does it work? Not always – ongoing optimisation of the process!

# Acknowledgements


- NCAS
  - All colleagues in NCAS
  - The biomarker team within NCAS
    - Lone Hummelshøj Landsy
    - Marie Rossen
    - Solvej Lund Lippert
    - Mette Loftager
    - Annette Rosendal
    - Christian Herling
    - Julie Overgaard
    - Mette Stougaard Kyhn

- Management that have understood the need for change and that work should not be done in silo
- Project leaders
- Past colleagues that have formed our biomarker considerations

Stakeholders in
- Translational Science
- Translational Technology
- Translational Medicine

CROs for exellent collaborations

EBF community for inspiration

THANK YOU!