Code for Proper Use of Human Tissue

- an update –

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Code of Proper Use of Human Tissue

- 2001 – update May 25, 2011
- FEDERA (Dutch Federation of Biomedical Societies / Federatie van Medisch Wetenschappelijke Vereningen)
- COREON (Committee on Regulation of Research / Commissie Regelgeving Onderzoek

Code of Proper Use of Human Tissue

- Observational versus Experimental scientific research with humans
- Fills vacuum in current laws & regulations
  – Self regulation of/for relevant stakeholders
- Human Tissue Act (WZL)

Code of Proper Use of Human Tissue

- Applies to observational research on human tissues
- All Human Tissues, except:
  - Fetal tissue
  - Organs meant for donation
  - Tissues of deceased persons

Related Dutch laws

Wet medisch-wetenschappelijk onderzoek met mensen (WMO)

- Lichaamsmateriaal dat voor wo is afgenomen: toestemming vereist
- Onduidelijk wat mag met restmateriaal

Wet op de geneeskundige behandelovereenkomst (WGBO) (BW Art. 7:467)

- Zeggenschap over nader gebruik van anoniem restmateriaal voor wetenschappelijk onderzoek: geen-bezwaar systeem.
- Er wordt vanuit gegaan dat patiënt geïnformeerd wordt over mogelijkheid tot bezwaar maken, maar wettelijk ligt dit niet vast.

Embryowet

- Handelingen met geslachtscellen en embryo's: toestemming vereist. Voor WO dient de CCMO goedkeuring te geven.

Wet foetaal weefsel (WFW)

- Regelt voorwaarden voor de terbeschikkingstelling van foetaal weefsel na spontane abortus of abortus provocatus. Toestemming vereist.

Wet op de Orgaandonatie (WOD)

- Regelt voorwaarden voor het verwijderen van organen voor transplantatie. Voor transplantatie ongeschikte organen mogen voor w
- Wetenschappelijk onderzoek gericht op implantatie worden gebruikt, behalve als de donor uitdrukkelijk anders heeft bepaald.

Wet inzake Bloedvoorziening (WiB)

- Verzekert de kwaliteit, veiligheid en beschikbaarheid van bloed en bloedproducten

Wet op de Lijkbezorging (WLB)

- Begraafplicht
- Regelt voorwaarden om een lijk na overlijden te bestemmen voor ontleding in het belang van de wetenschap

[**Code Goed Gebruik (zelfregulering)**]

Code of Proper Use of Human Tissue

- Biobanks
  - ‘secondary use’
  - ‘de novo’
- Not a law, not a standard protocol
- Gives a direction: “apply or explain”
- FAQ

Code of Proper Use of Human Tissue

Basic principles related to the donor

Management of biobank

Responsibility of researcher

1. Basic principles related to the donor

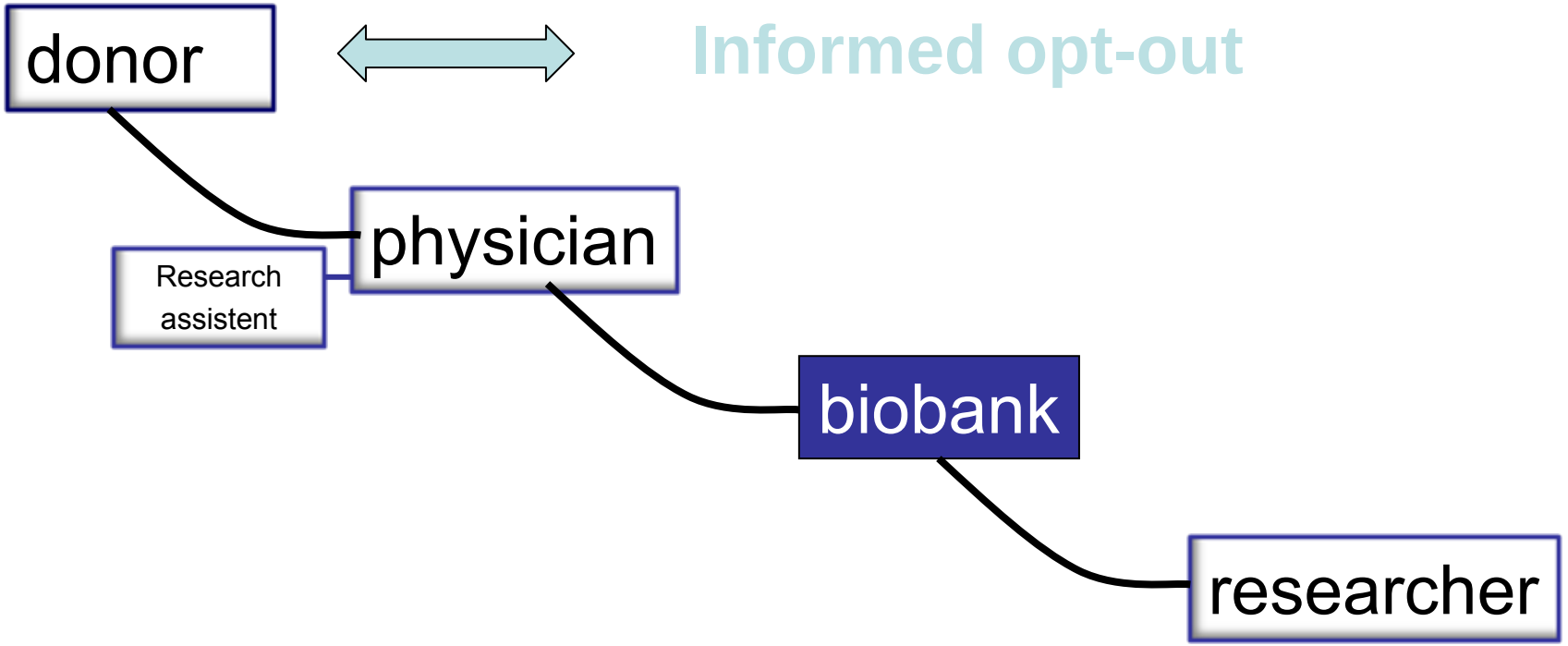
- No risk or minimal risk for donor
- Optimal privacy protection
- Well-balanced donor control
- Well-considered policy on incidential finding

´Secondary use´ biobank

- Two aims:
  - Keep tissue for primary aim
  - Keep tissue for secondary aim
- 2nd aim must not cross 1st aim
- Manager biobank:
  - Decide what is possible given the two aims
  - Intermediate between donor/physician and researcher

Chain of responsibilities

´secondary use´ biobank

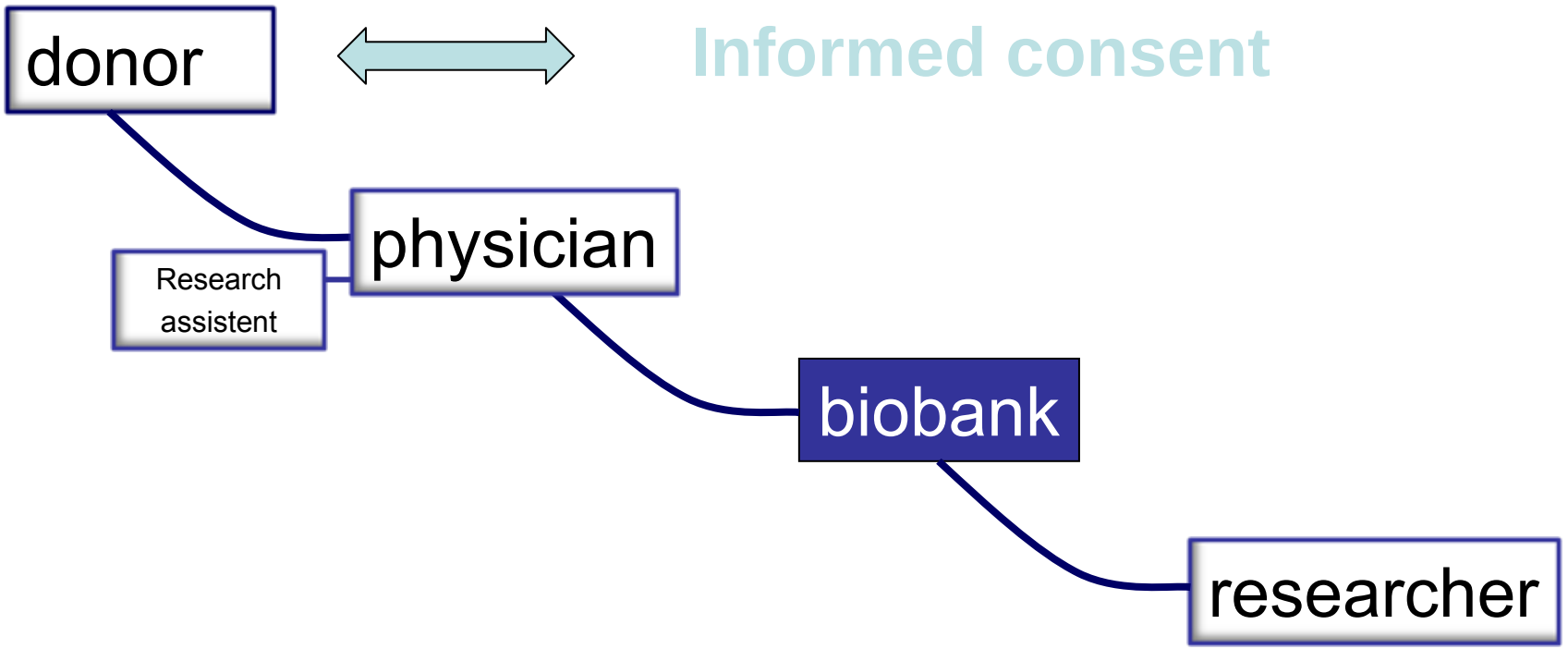


‘De novo’ biobank

- Define scientific and social aims
- NO or minimal risk to donor
- Tissue collection embedded in larger data collection
- Methods to reach aims are flexible
- Define donors, informed consent procedure, expected future donor contacts, opt-out and complain procedures
- **Donors are stakeholders**

Chain of responsibilities

´de novo´ biobank



Informed Opt-out system

´Secondary use´ biobank

Information on:

- Tissue → coded- anonymous data
- Aim of the research is to improve prevention and treatment
- May lead to spin off with ‘commercial applications
- Findings will not be communicated on an individual basis, but applied to all

Informed Opt-out system

'Secondary use' biobank

Additionally, informed opt-out system implies:

- Several contact persons in the institute that may explain the procedure
- Easy to opt-out registry!
- Opt-out implies the entire chain
- Easy to complain officially

Informed Opt-out system

'Secondary use' biobank

not sufficient if:

- Anonymity cannot be guaranteed at the research level
- Incidental findings can be expected
- Observational research within an RCT
- Study aim does not relate to human health
- Commercial setting

´Anonymity cannot be guaranteed´

Research that uses

tissues from a ‘secondary use’ biobank

and

identifiable data

needs

explicit informed consent of the donor!

General *informed consent* *'de novo' biobank*

acceptable if information is clear on:

- General aims of the research
- What other study-related contacts may be expected in future
- Where to find actual information on the project
- How to opt-out and/or officially complain
- No profit for donor: no individual feedback

  AND
- None of the former exceptions for opt-out system of secondary use apply

However, specific consent is needed if:

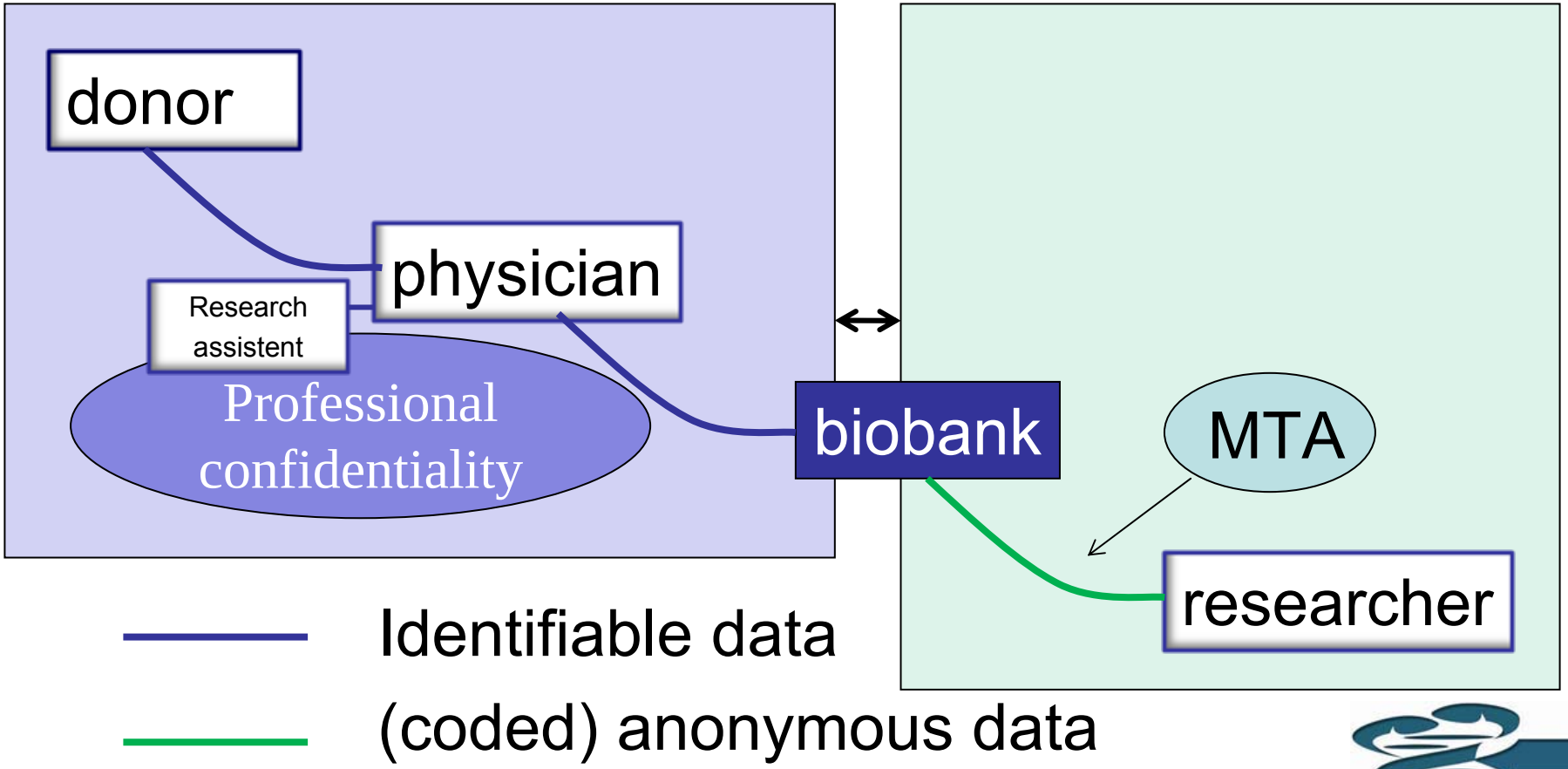
- Risk are not minimal
- Incidental findings are expected not to be rare
- Opt-out procedure is not effective
- Information on incidental findings cannot be given
- Additional personal data are needed
- Personal information from other sources than from the donor him/herself

1. Basic principles related to the donor

- No risk or minimal risk for donor
- **Optimal privacy protection**
- Well-balanced donor control
- Well-considered policy on incidental findings

Privacy Protection

'secondary use' and 'de novo' biobanks



Data management

Anonymous data		Personal data		
Fully anonymous	Coded anonymous (=pseudo-mised data)	Indirectly identifiable data		Directly identifialbe data
		Coded, but coding is insufficiently secure Or Securely coded and aggregation level too low	Not coded, but aggregation level too low	

However:

‘Can human tissue be anonymous?’

'Can human tissue be anonymous?'

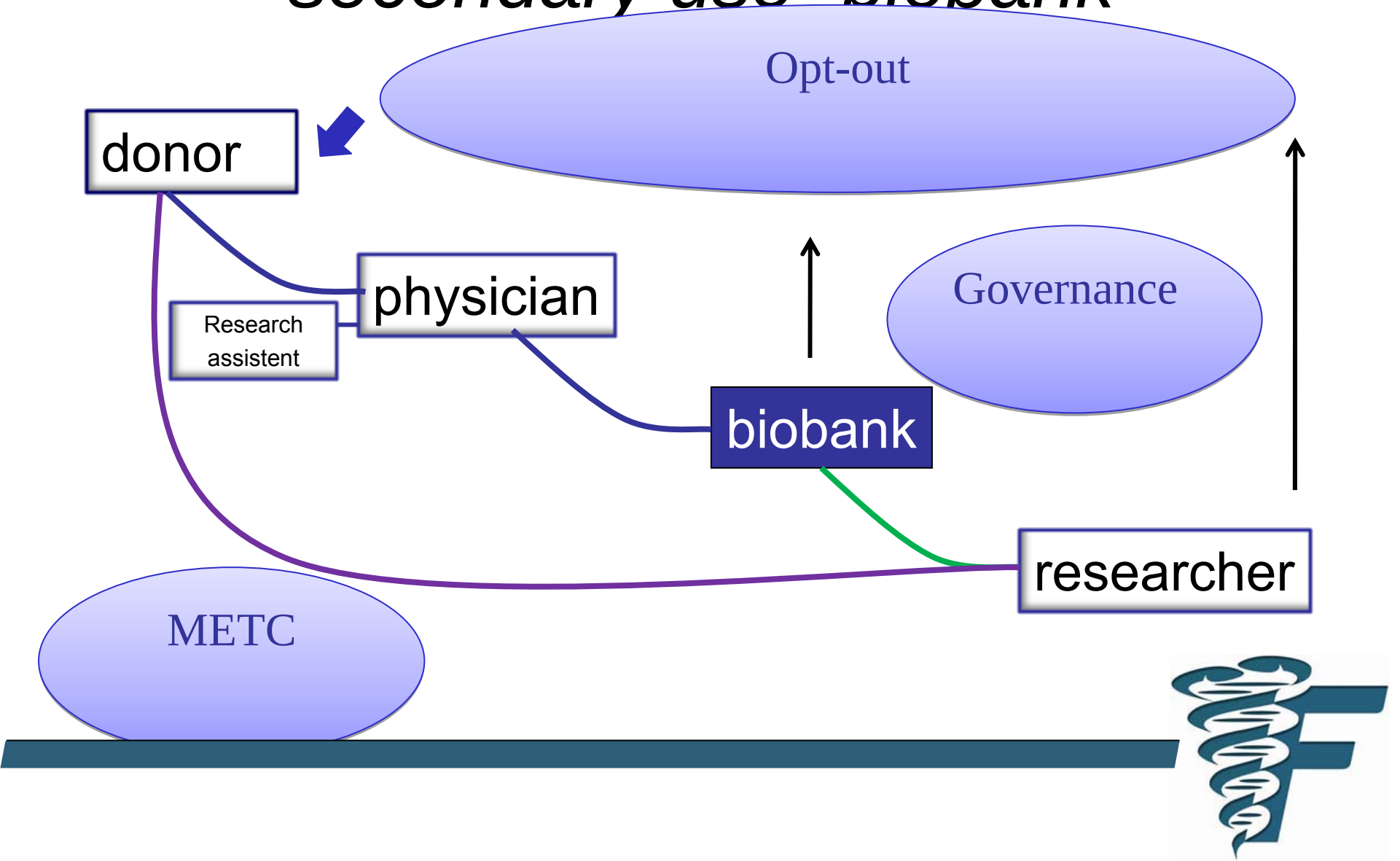
- Yes, no different status for genetic data
- As for fingerprints you need a database with identifiable genotypic data to identify a person through the genetic profile

1. Basic principles related to the donor

- No risk or minimal risk for donor
- Optimal privacy protection
- **Well-balanced donor control**
- Well- considered policy on incidental findings

Donor control

´secondary use´ biobank



'What after opting-out?'

- Implies the entire chain
- Recoding in biobank: tissue no longer available for research, only for primary use
- Inform researchers that have tissue samples:
  - Sample should be destroyed except for part necessary for validation of publications (temporally)
- Data already obtained from tissue do not need to be destroyed: opt-out applies to future research on tissue

Transparency for donor

- Secondary use: *informed opt-out procedure*
- ‘de novo’: *Informed consent with clear general study aims*
- METC and Governance committee
- Clarify: *data management, what happens after opting out procedure for complain*

www.studyinformation.nl

1. Basic principles related to the donor

- No risk or minimal risk for the donor
- Optimal privacy protection
- Well-balanced donor control
- **Well-considered policy on incidental findings**

Should I always give feedback on incidental findings?’

What is an incidental finding?

- Very rare, not screened for at entry of biobank
- Findings that can be of direct importance for the future health of the donor

'Should I always give feedback on incidental findings?'

Secondary use biobank: 'No", only if:

- There is a high risk of a severe condition
- Prevention, treatment or follow-up is available
- The donor did not opt-out of feedback
- Standard test or treatments are not certain to lead to diagnosis
- **To be decided by an expert-committee!**

'Should I always give feedback on incidental findings?'

- 'de novo'biobank:
- Same conditions, AND only accept tissues from donors who agree in feedback of incidental findings

'And what about feedback to family members?

No, only if:

- There is a high risk of a severe condition
- Prevention, treatment or follow-up is available
- The donor did not opt-out of feedback
- It is uncertain whether standard test or treatment will not lead to finding or treating the condition

To be decided by committee!

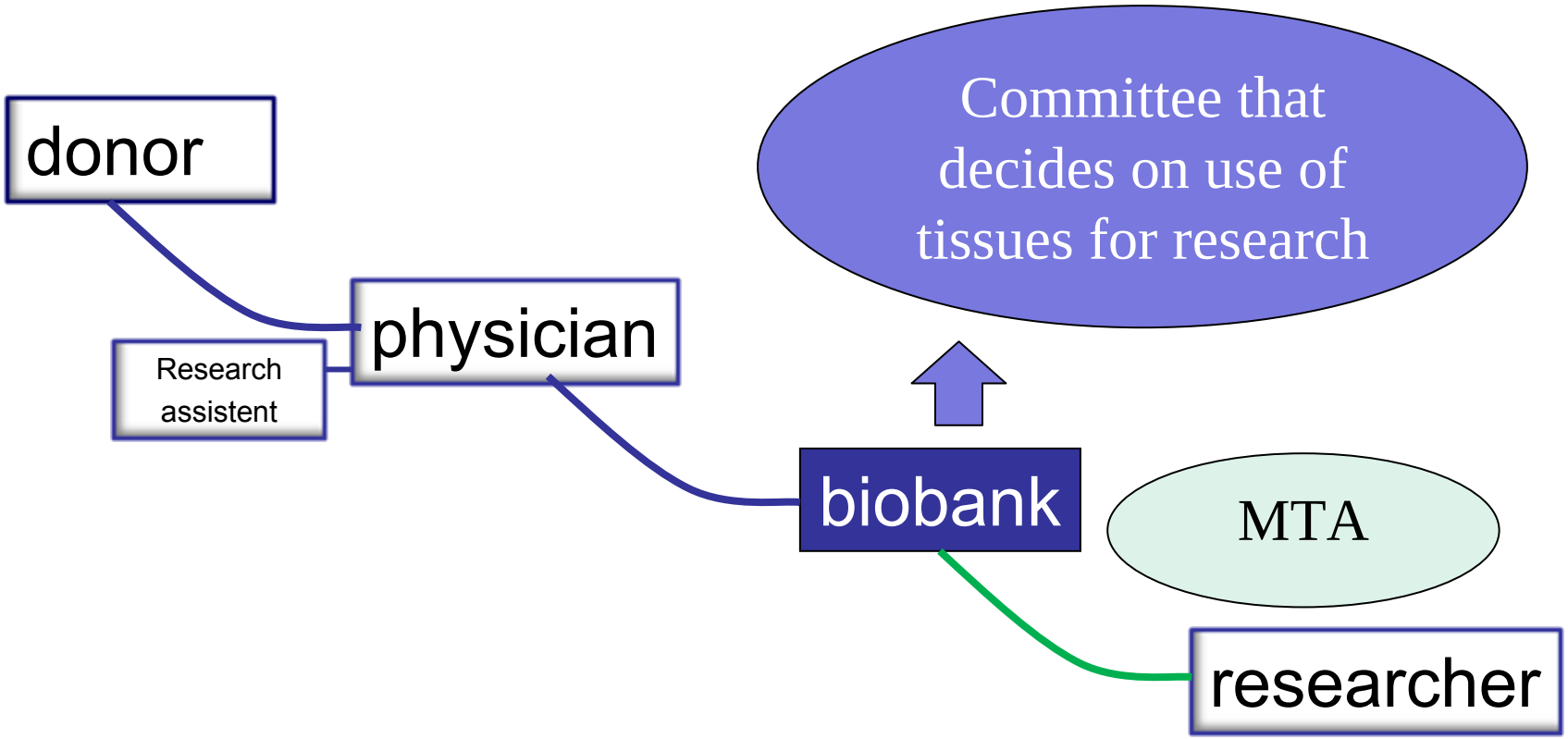
- Whit even more restraint
- Family members not known in healthcare system, they did not seek genetic counseling based on family history
- Not dear that the condition applies to the specific family member

2. Management of ‘secondary use’ biobank - *functions*

- Agreement with physicians (clarify both aims)
- Keep tissues in such a way that both aims can be met
- Keep and deliver tissues such that donor control can be fulfilled (MTA)
- Transparent procedures to decide on tissue delivery
- Deliver tissues to researcher according to these decisions

Management

´secondary use´ biobank



Organisation of ‘de novo’ biobank

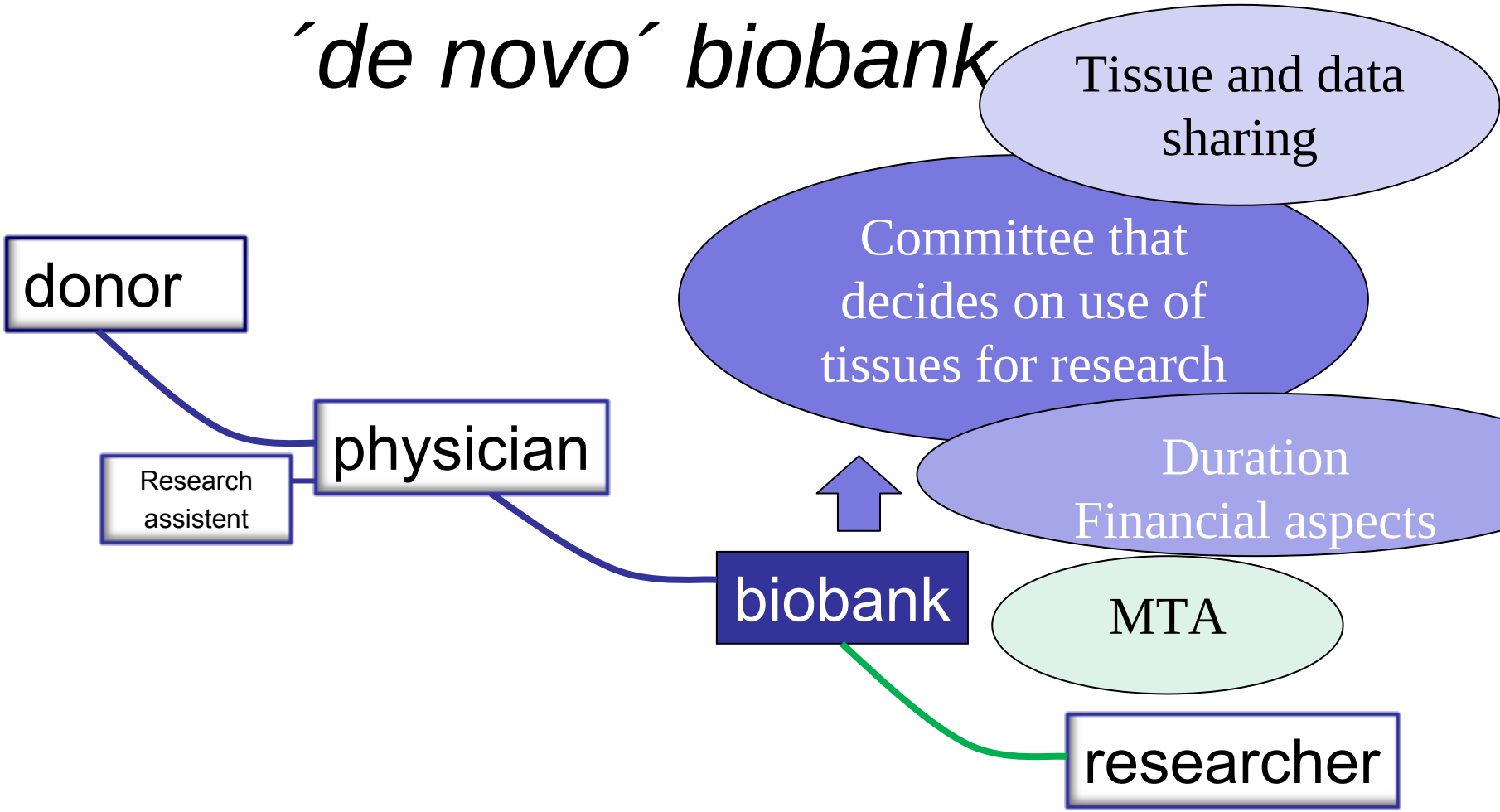
- Make distinction in functions for:
  - Tissue and data collection
  - Tissue and data management
  - Tissue and data use for research
- Time plan
- Financial plan: what if budget fails
- Plan for tissue and data sharing
- Embedded in governance structure

Management of 'the novo' biobank - *functions*

- General informed consent
- Keep tissues in such a way that both aims can be met
- Keep and deliver tissues such that donor control can be fulfilled (MTA)
- Transparent procedures to decide on tissue delivery
- Deliver tissues to researcher according to these decisions

Management

´de novo´ biobank



3. Responsibility of researcher
protocol

- Study aim
- What tissue and which data are needed
- Methods
- Incidental findings expected to be rare?
- **Clarification of ‘the chain ’for this specific research (other partners involved, etc.?)**
- Duration of use
- Opt-out procedure
- Protection of privacy of donor
- Handling of remaining tissue

3. Responsibility of researcher
advise

- Involvement of donors
- Enable control of protocol
- For large cohorts: ‘privacy committee’
- Ensure the chain is limited (don’t loose track of the tissue)
- Data sharing

‘What should I be aware of if I collaborate with a commercial partner?

‘What should I be aware of if I collaborate with a commercial partner?’

MTA describes:

- What can be done with the tissue
- Results should become available
- **Ownership is not transferred** to the commercial partner
- Remaining tissue should be returned

  (= suggestion not in code)

Basic principles related to the donor

- No or minimal risk for donor
- Optimal privacy protection
- Well-balanced donor control
- Well-considered policy on incidental findings

No micro management

Balance between interests of the donors and the public

‘*Do I always need informed consent for research with human tissues?*’

Do I always need informed consent for research with human tissues?’

In case of secondary use: **‘No’** if:

- Study aim within broad consent
  - Coded data
- Effective opt-out system:
  - Registry of refusals
  - Optimal transparency
  - Subjects are able to ask questions
  - Easy to opt-out, also later

‘*Do I always need informed consent for research with human tissues?’*

If case of a ‘de novo’ biobank: **‘Yes’**,

At least general consent

'Is general consent not always preferable to specific consent?'

'Yes' – also for a study with a specific study question general consent is preferable, because in case secondary use is aimed to investigate a topic not covered by the first specific consent, new informed consent should be asked

(not in code)