COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

CBG-MEB Workshop
BCF Career Event

28 May 2025

GOEDE MEDICIJNEN
GOED GEBRUIKT

Presenters

Ineke Havinga - Sr. Regulatory Project Leader (RPL)
Biomedical sciences

Emmely de Vries – Senior Clinical Assessor
Biomedical sciences/Neuroscience/PhD

What is your background?

- Pharmacy
- Biomedical sciences
- Drug innovation
- Medicine
- Health sciences
- Other?

Who is familiar with the CBG-MEB?

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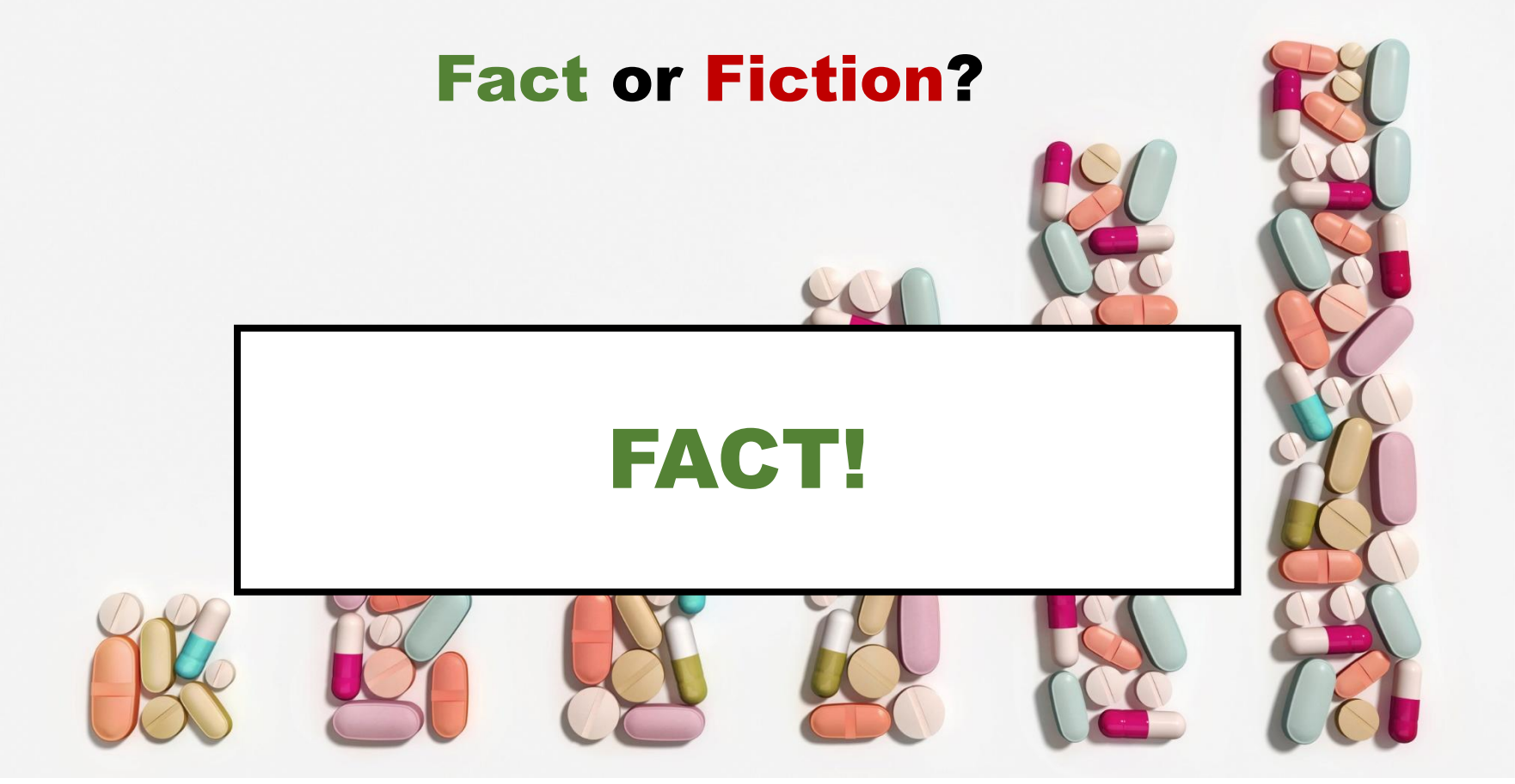
The CBG-MEB develops medicinal products

Fiction!

There are more than 17.000 approved medicinal products in the Netherlands



Paracetamol was the first approved medicinal product in the Netherlands.

Fact or Fiction?

Fiction!

The CBG-MEB also assesses medicinal products for the European market.

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Fact or fiction?

FACT!

Content

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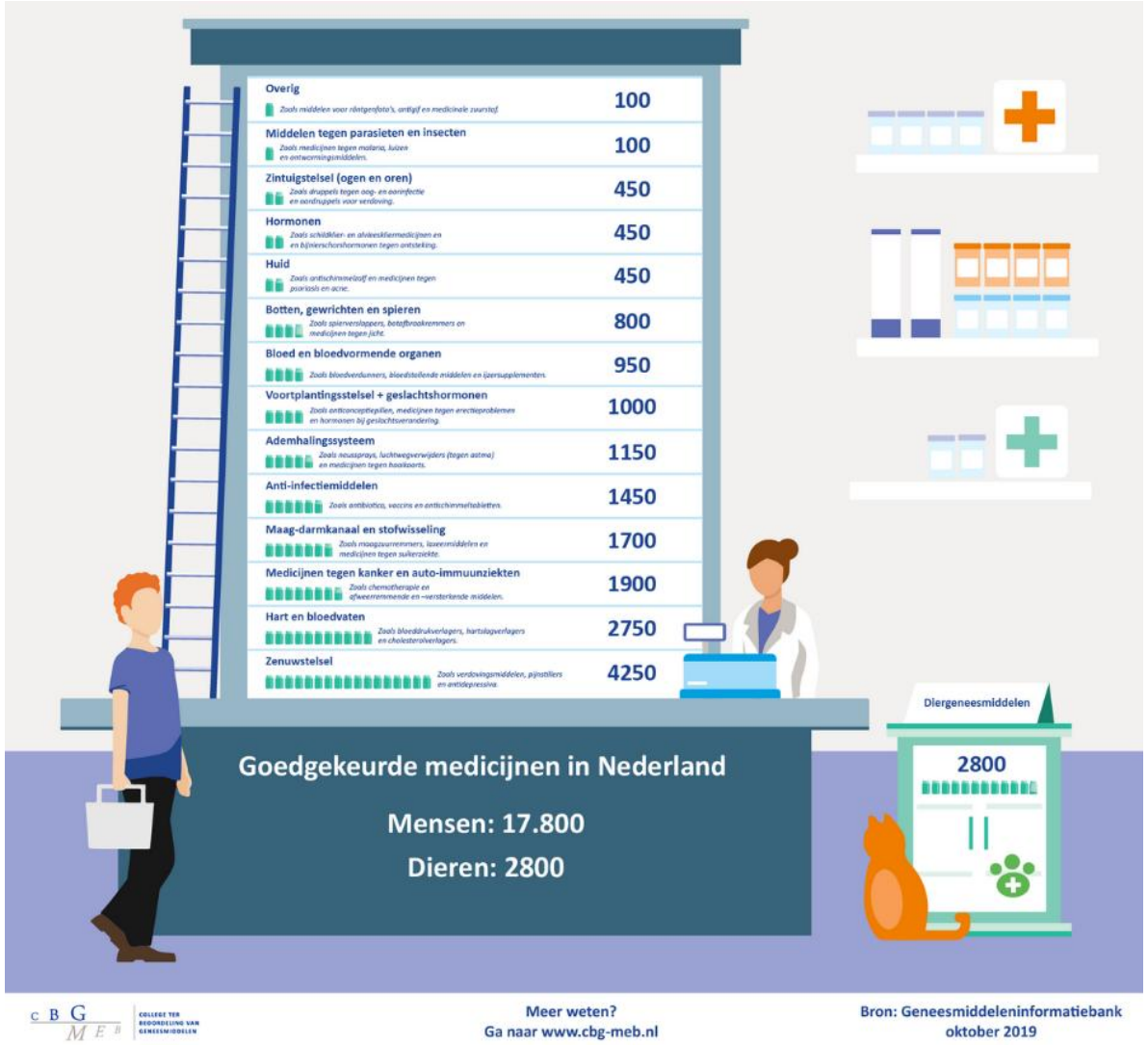
6. After approval



Why do we regulate?

In NL, the regulatory agency is the CBG-MEB, founded in 1963.

What was the indirect reason for the foundation?

The medicines development program

CBG-MEB

National competent authority

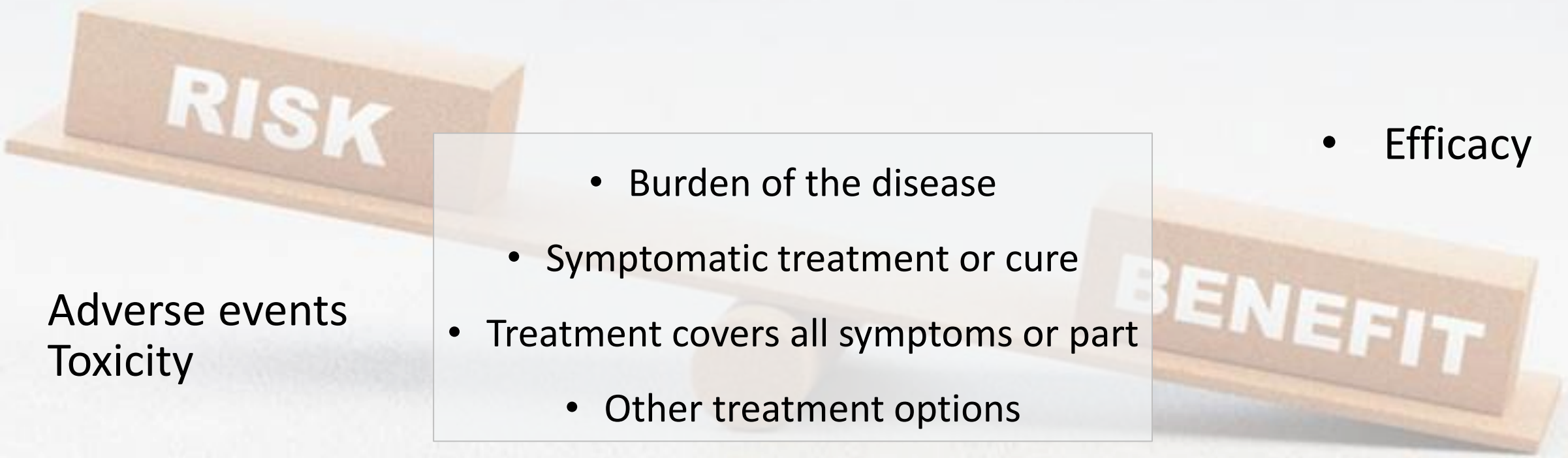
Decides on marketing authorisations of medicinal products and monitors after approval.

Main task is to ensure that medicines are:

- Effective
- Safe in normal use
- Of good quality

- Works in a European context
- Coordinated by European Medicines Agency

Clinical: Benefit risk assessment



- Adverse events
- Toxicity

- Burden of the disease
- Symptomatic treatment or cure
- Treatment covers all symptoms or part
- Other treatment options

- Efficacy

Post-marketing: PharmacoVigilance!

The dossier

Then …

And now….

Regulatory Project Leader (RPL)

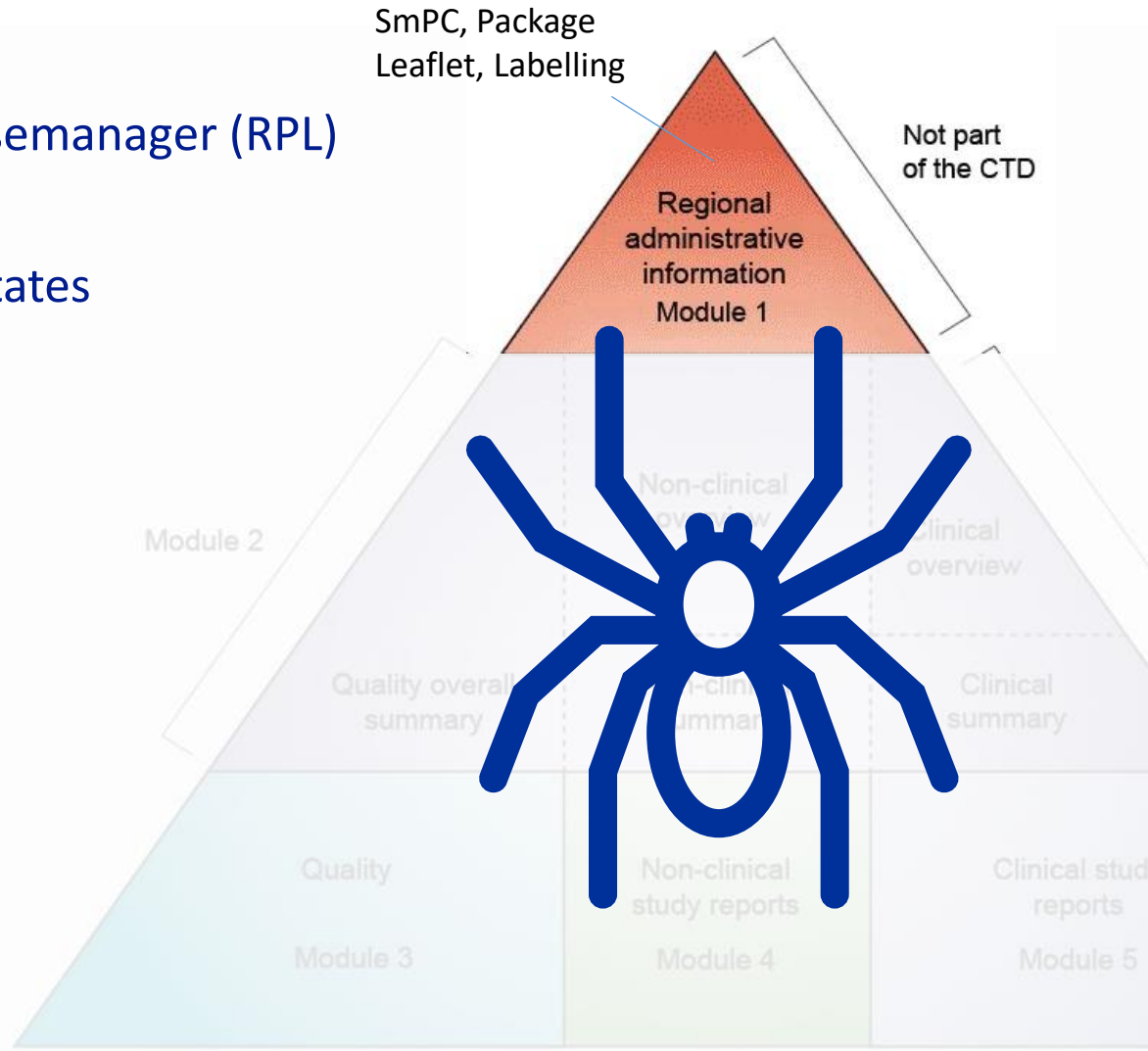
Responsible for the case from start to end → 1 case = 1 casemanager (RPL)

RPL = Contact with companies, EMA, assessors, Member States

RPL controls processes

- Validation of application
- Deadline submission reports
- Internal consultation with assessors
- Board meetings, meetings with companies, task forces

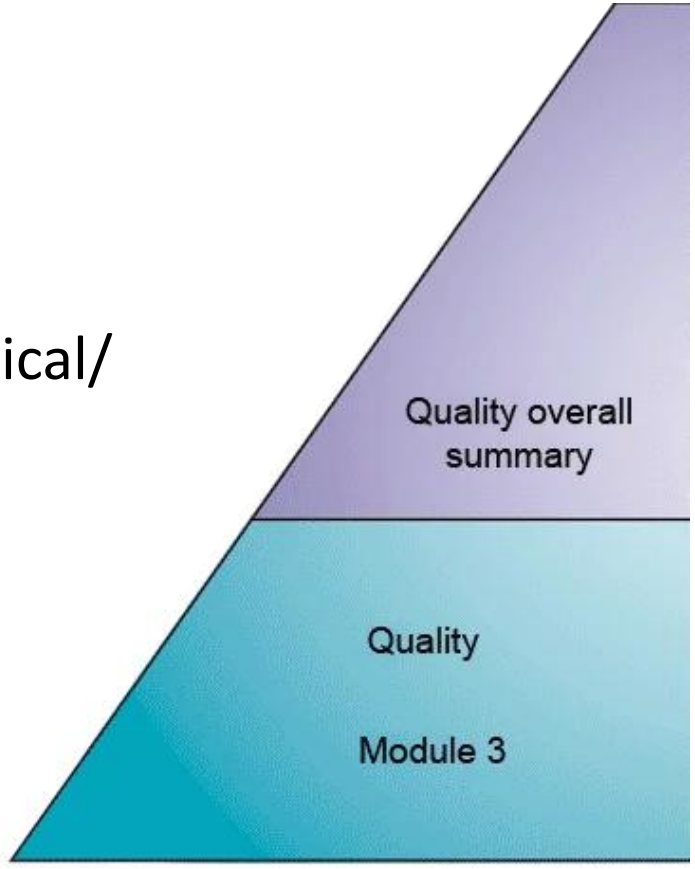
Very diverse, like a spider in a web!



The assessors: what do they do?

- **Assess** the relevant part of the dossier and write an assessment report

  - **Quality assessors** → chemical/ pharmaceutical attributes

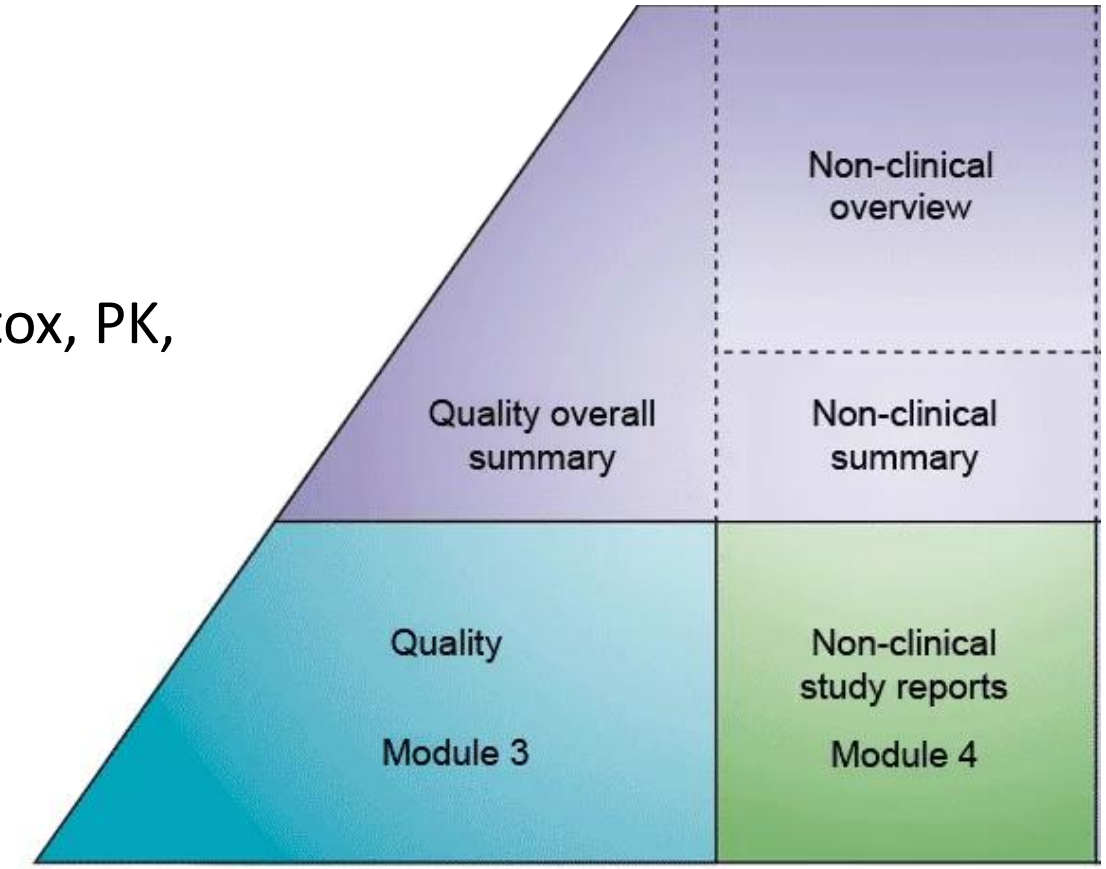


The assessors: what do they do?

- **Assess** the relevant part of the dossier and write an assessment report

  - **Preclinical assessors** → tox, PK,

    PD in vitro/in vivo

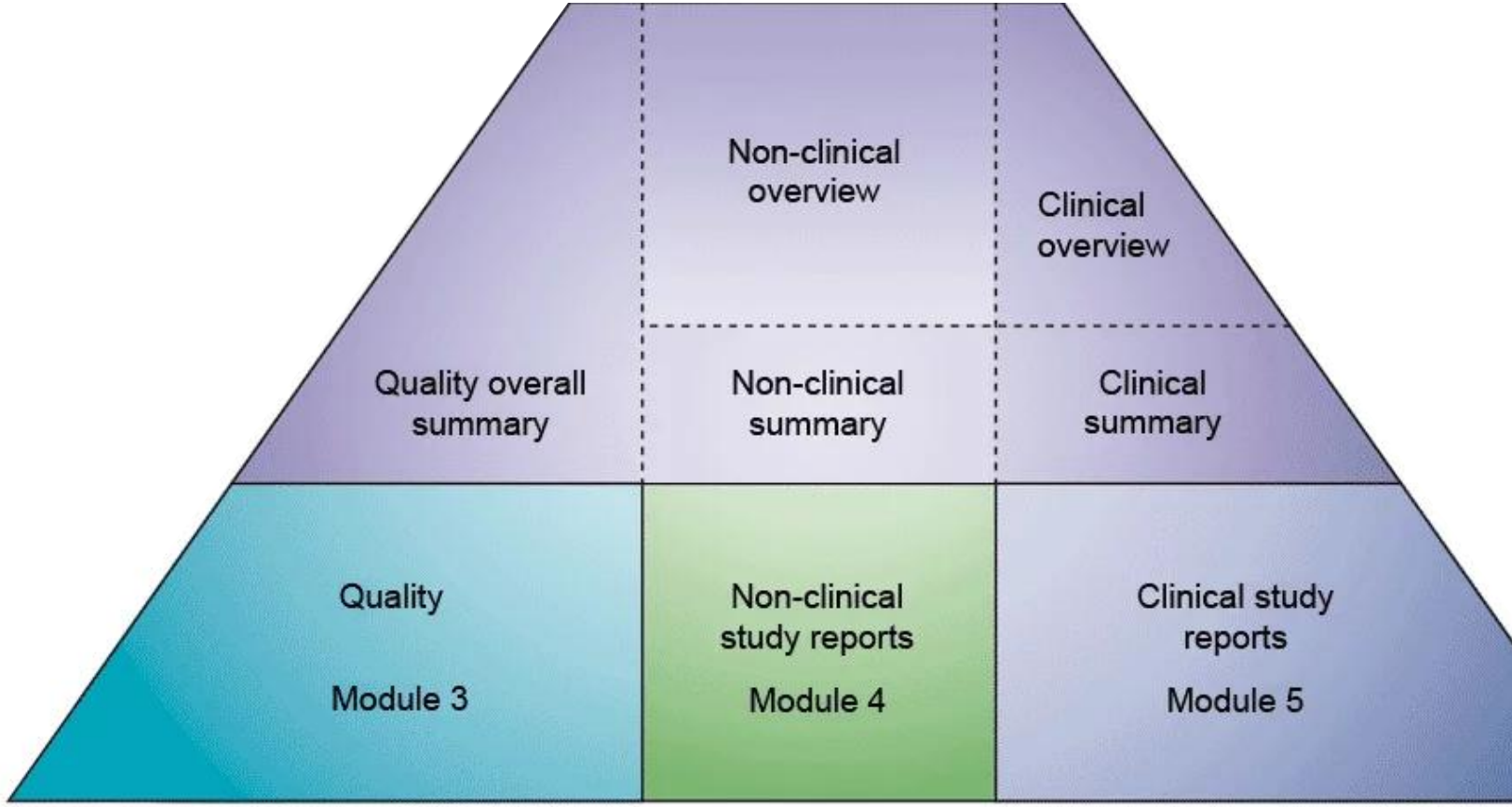


The assessors: what do they do?

- **Assess** the relevant part of the dossier and write an assessment report

  - **Clinical assessors**→

    efficacy/safety



The assessors: what do they do?

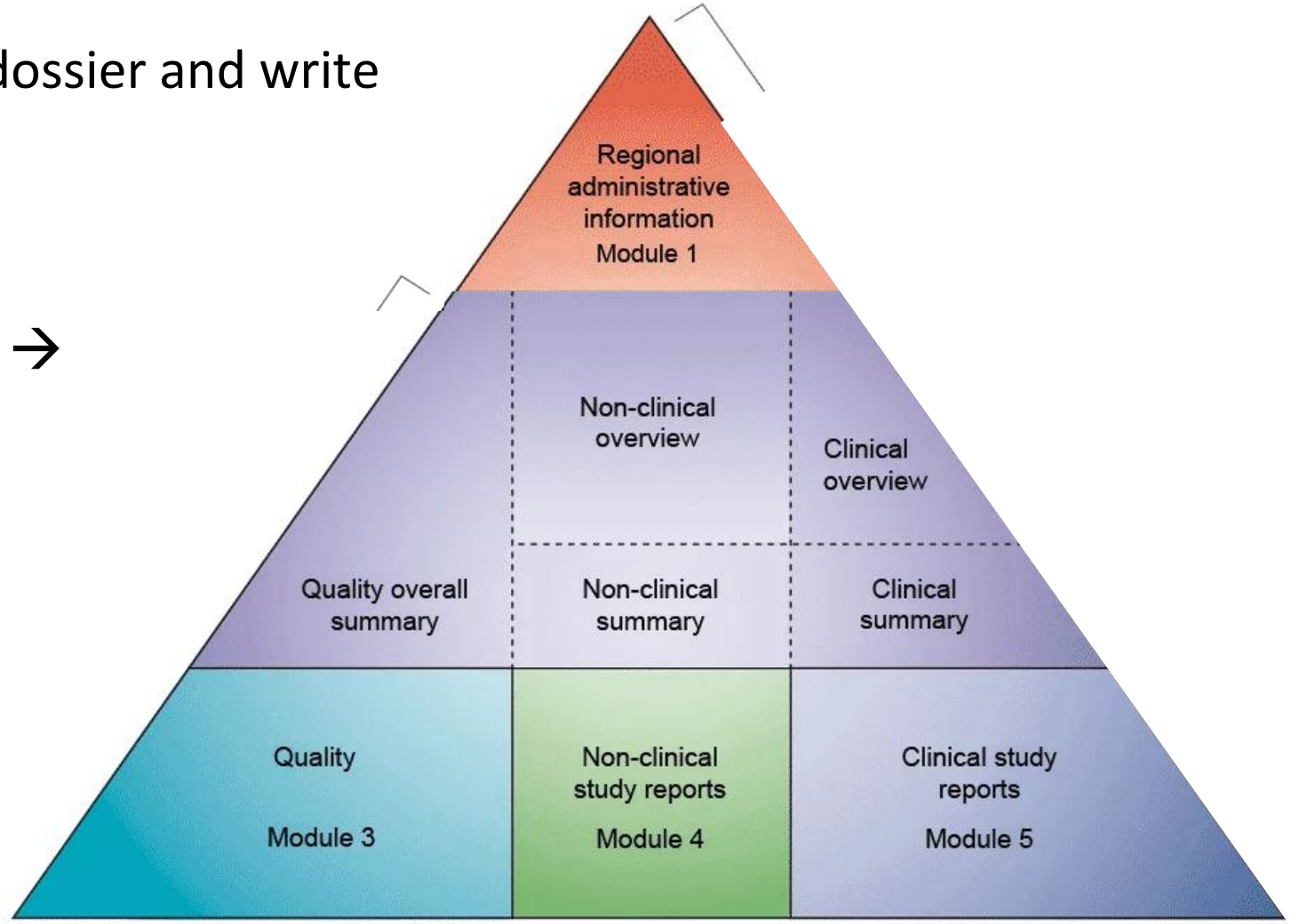
- **Assess** the relevant part of the dossier and write an assessment report

  - **PharmacoVigilance assessors** →

    post-marketing

  - **Methodology**

    study design & statistics



The assessors: what do they do?

- **Assess** the relevant part of the dossier and write an assessment report
- Gives **advice** to the **board** and **NL CHMP** members.

As an assessor you need to have

- expertise in the **relevant area**
- A **suitable** (scientific) **background**
  For example:
  - MD,
  - biomedical sciences,
  - pharmaceutical science,
  - biochemistry,
  - etc!

You are the assessor now!

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Benefit risk assessment: example

100 people have the common cold.
They receive a drug for common cold, as a result, they suffer from a runny nose for 3 days, instead of 14!
Does this drug work, or not?

However, if 100 people take this drug, 50 people get very severe side effects and have to be treated in the hospital for these side effects for 10 days.
Is this drug safe, or not?

Conclusion: the drug works (proven efficacy) but it is not so safe.

Benefit risk assessment: example

But, what if?
People had a runny nose for 13 days instead of 14.
Does the drug work or not?

And what, instead of 50 people ending up in the hospital for side effects,
2 people get a bit of nausea.
Is the drug safe, or not?

Conclusion: the drug does not really work very well, but it is safe.

Benefit risk assessment: example 2

There are 100 patients with a fatal disease. Without treatment, they will likely not survive past 2 months.

With a new drug, 30 patients will be cured. 20 patients will live 6 months instead of 2. The remaining 50 patients will not respond to this new drug, and will not survive past 2 months.

Does this drug work or not?

Of the 100 patients treated, 95 patients have side effects of which 70 severe and require hospitalisation for 1 week.

Is this drug safe, or not?

Conclusion: the drug works, but it is not very safe.

Does it matter?

Examples of B/R balances

Effect	Short Description	Unit	Vaccine	Placebo	Uncertainties/ Strength of evidence
Favourable Effects					
Vaccine efficacy	Occurrence of infection	Cases/ Number of subjects at risk for the endpoint	**8/ 17411**	**162/ 17511**	Robust data with similar efficacy confirmed in all age sub-groups
Unfavourable Effects					
Pain at injection site		%	83	14	Transient events, majority mild to moderate intensity
Headache		%	42	34	
Facial paralysis		number of cases	4	1	Small number of cases, short duration of follow-up

Positive opinion, MA granted

Adapted from the effects table in the Comirnaty EPAR

Examples of B/R balances

Effect	Short Description	Unit	Aduhelm	Placebo	Uncertainties/ Strength of evidence
Favourable Effects					
CDR-sb	Composite cognitive and functional scale	-	1.46	1.64	(difference -0.17, p=0.1) Both pivotal Studies were terminated for futility
Unfavourable Effects					
ARIA-E	Different imaging and clinical severities	%	35	2.7	Imaging phenomena with heterogeneous clinical presentation and unclear long-term clinical consequences. Incidence with intensive MRI monitoring of uncertain feasibility in practice
ARIA-H	Different imaging and clinical severities	%	19.1	6.5	

→ Negative opinion, MA denied.

Adapted from the effects table in the Aduhelm EPAR

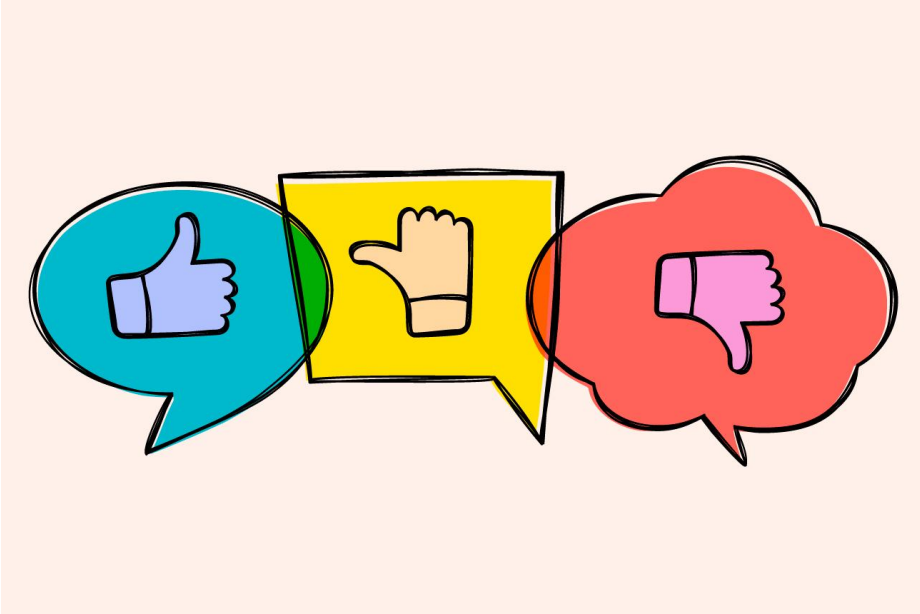
Advice to the MEB and CHMP

Request for additional information

major objection / potential serious risk to public health

other concern

Positive or negative opinion



But is does not end there!

Example: Picato

Picato (ingenol mebutate): a gel authorized for treating the skin condition actinic keratosis.

In Europe, review was started of a study comparing Picato with imiquimod (another medicine for actinic keratosis). After 3 years, 6.3% of patients treated with Picato (15 out of 240 patients) compared with 2% of patients treated with imiquimod (5 out of 244 patients).

Conclusion: the medicine may increase the risk of skin cancer and that its risks outweigh its benefits.

Picato is no longer authorized in the EU as the marketing authorization was withdrawn.

Example Ozempic

Authorised for: treatment of diabetes type 2.

Due to off-label use of Ozempic (to loose weight): shortages

Role of CBG-MEB:

- Monitor shortages of medicinal products
- Inform and communicate (general public and healthcare providers)

CBG waarschuwt voor aanhoudend tekort diabetesmedicijn Ozempic

Nieuwsbericht | 17-03-2023 | 09:30

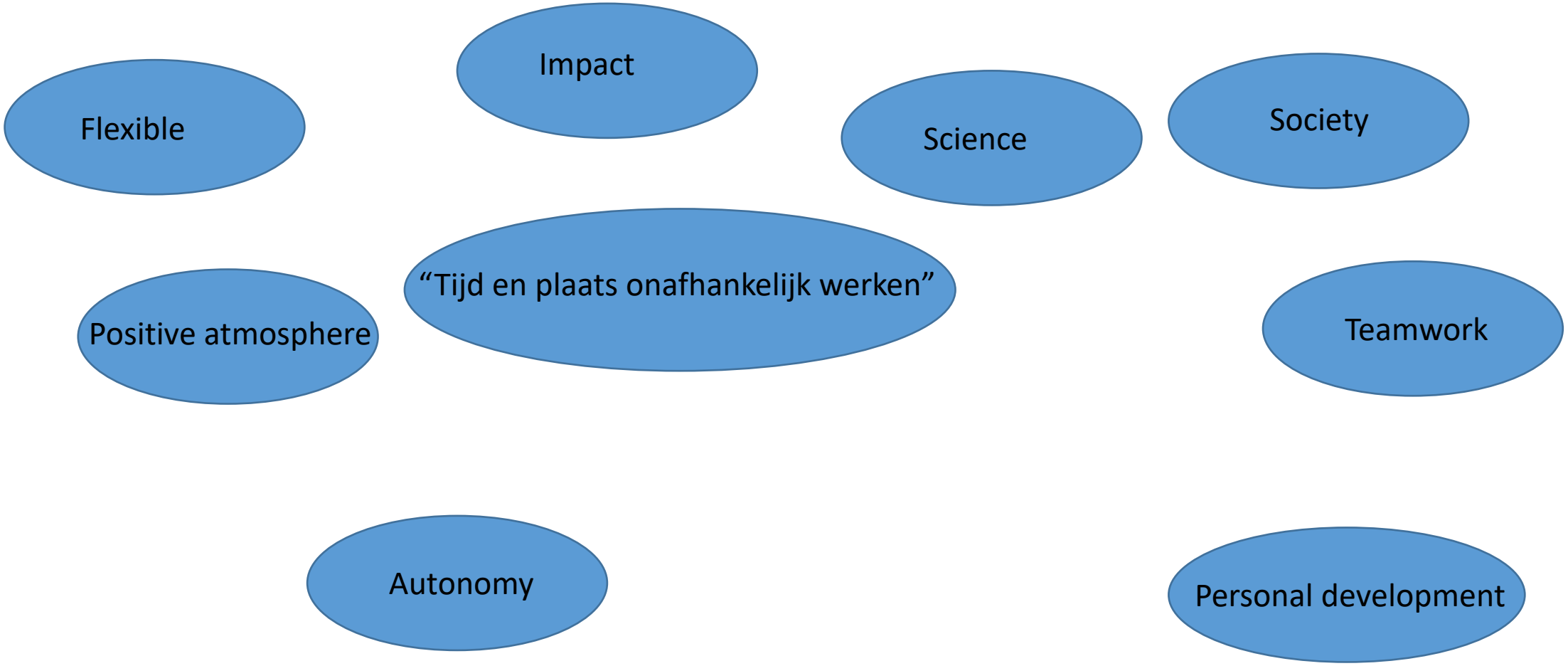
Het wereldwijde tekort aan diabetesmedicijn Ozempic blijft nog het hele jaar aanhouden. Dat verwacht de fabrikant. Het tekort is ontstaan door een snel gestegen vraag naar het medicijn. Ozempic is de laatste maanden veel in de media omdat het (off-label) gebruikt wordt als afslankmiddel. Medicijnautoriteit CBG waarschuwt om dit medicijn niet zonder toezicht van een arts te gebruiken.

Vorig jaar toename ernstige tekorten medicijnen

PW11 - 08-03-2023

Farmaceutische bedrijven hebben vorig jaar meer verwachte leveringsproblemen gemeld dan in 2021. Ook was er een toename van het aantal ernstige tekorten. Fabrikanten, groothandels en apothekers kregen 132 keer toestemming een alternatief geneesmiddel uit het buitenland te halen. Dat blijkt uit het jaarverslag van het Meldpunt Geneesmiddelentekorten en -defecten.

Why work for CBG-MEB?



Are you interested?

https://www.cbg-meb.nl/onderwerpen/over-cbg-werken-bij-het-cbg

Questions?