Person in Plant for early development projects: from a small biotech customer perspective

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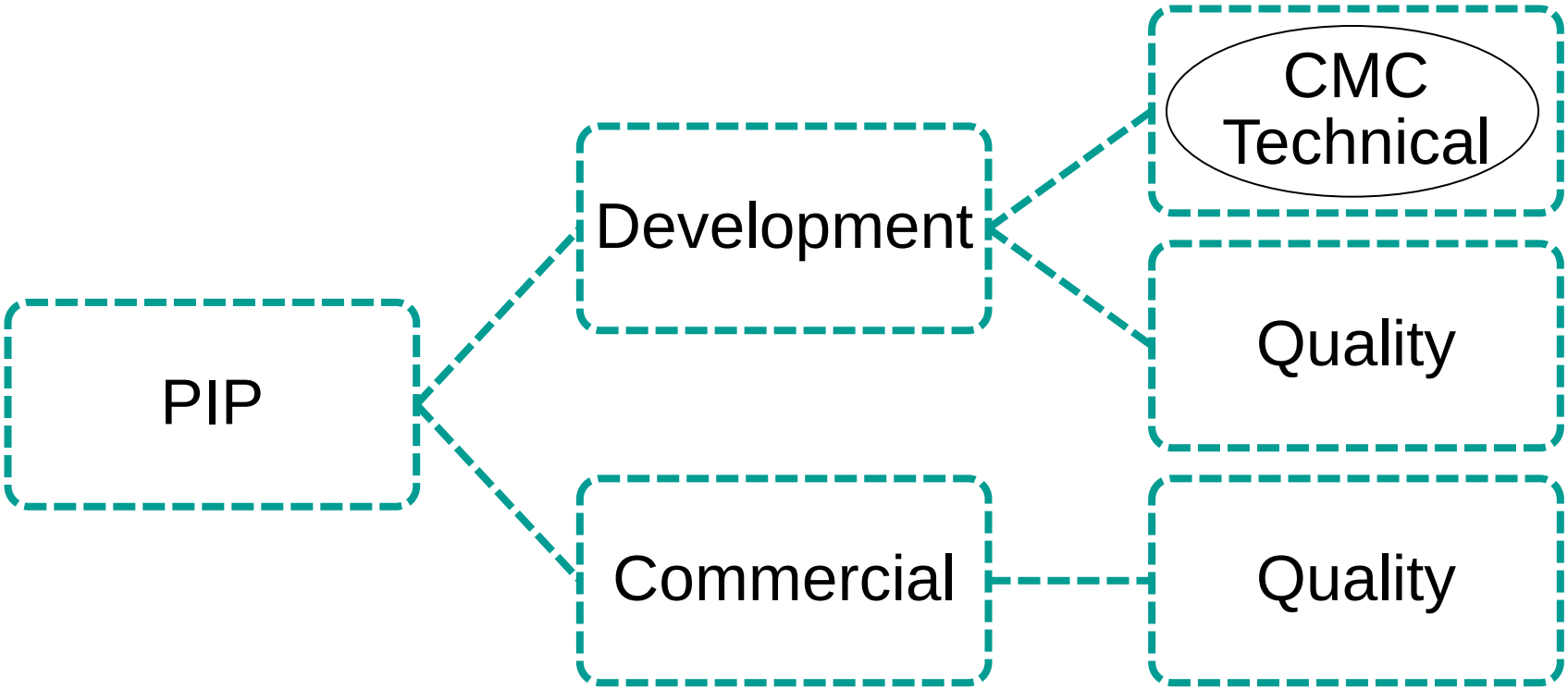
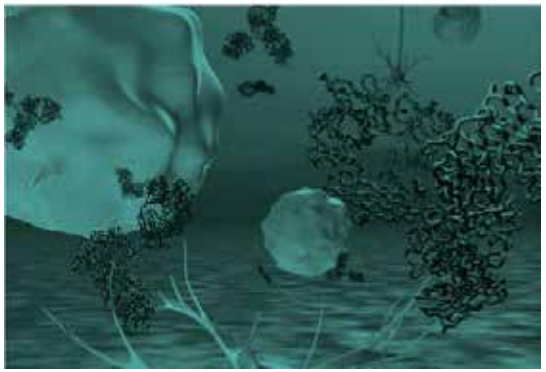
Genmab

Definition & Scope



About Genmab

- International biotechnology company
- Focus on human antibodies to treat cancer
- Proven ability to bring product to market
  - One marketed product (Arzerra®) with growing sales
  - First-in-class daratumumab next potential product
- Strong innovation focus
  - Proprietary technology – DuoBody® & HexaBody™ platforms
  - Innovative pre-clinical pipeline
  - World class antibody know-how
- Collaborations with blue chip partners incl. GSK and Janssen



International locations

3 offices with ~ 177 employees worldwide

Denmark ~ 55

Clinical Development, CMC and QA, IPR, Legal, IR

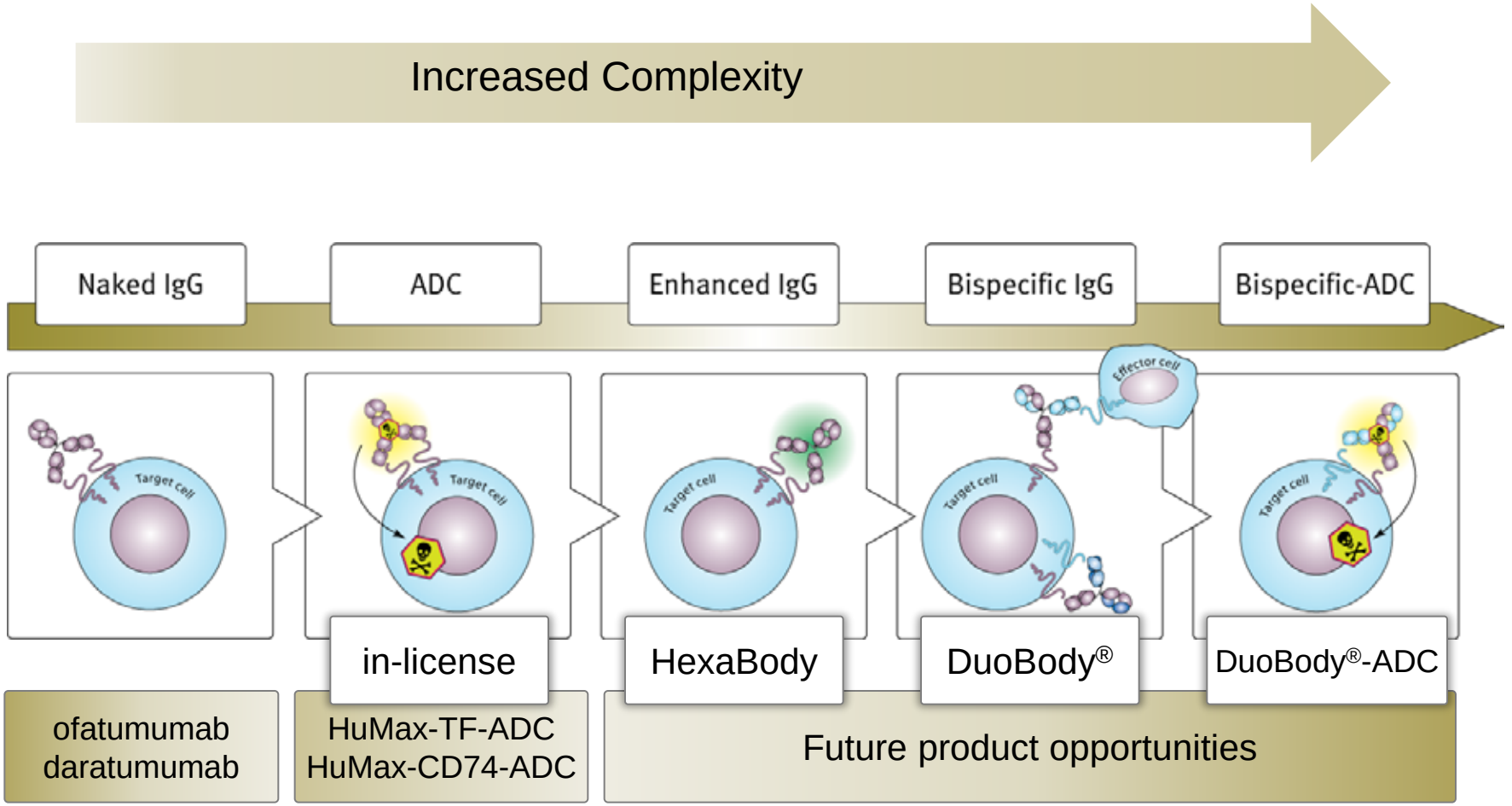
The Netherlands ~ 113

Discovery, Preclinical Development

US - Princeton ~ 9

Finance and Business dev.

Genmab Product Innovation



Innovative Pipeline

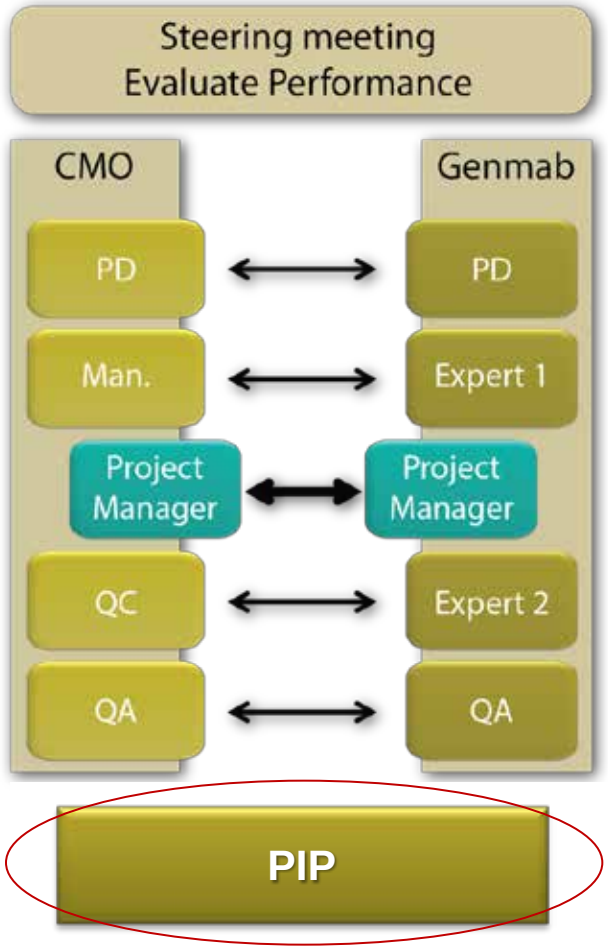
Product	Disease Indications	Development Phase: Pre-clinical	I	I/II	II	III	IV
Ofatumumab 18 studies Partner: GSK	Chronic lymphocytic leukemia (CLL)			■	■	■	■
	Follicular lymphoma (FL)		■		■	■	
	Diffuse large B-cell lymphoma (DLBCL)				■	■	
	Pemphigus vulgaris (PV)					■	
	Relapsing remitting multiple sclerosis (RRMS)				■		
	Waldenström's Macroglobulinemia (WM)				■		
Daratumumab 4 studies Target: CD38 Partner: Janssen	Multiple myeloma (MM)		■	■	■		
Teprotumumab Target: IGF-1R Partner: River Vision	Active thyroid eye disease				■		
HuMax-TF-ADC Target: TF Partner: Seattle Genetics	Solid cancers		■				
> 10 Active Pre-clinical Programs	HuMab, Enhanced HuMab, HuMab-ADC, DuoBody or DuoBody-ADC	■					

Business model – Operations

The Genmab business model is focused on innovation: All operational tasks are outsourced to contract partners in the product creation phase.

Genmab's CMC Collaboration Philosophy

- Direct communication lines – no funneling
- Leave disputes for the responsible contract manager – keep it out of the technical teams
- Evaluate performance and align expectations every 6-12 months in steering meetings
- Face-to-face meetings to build relationships



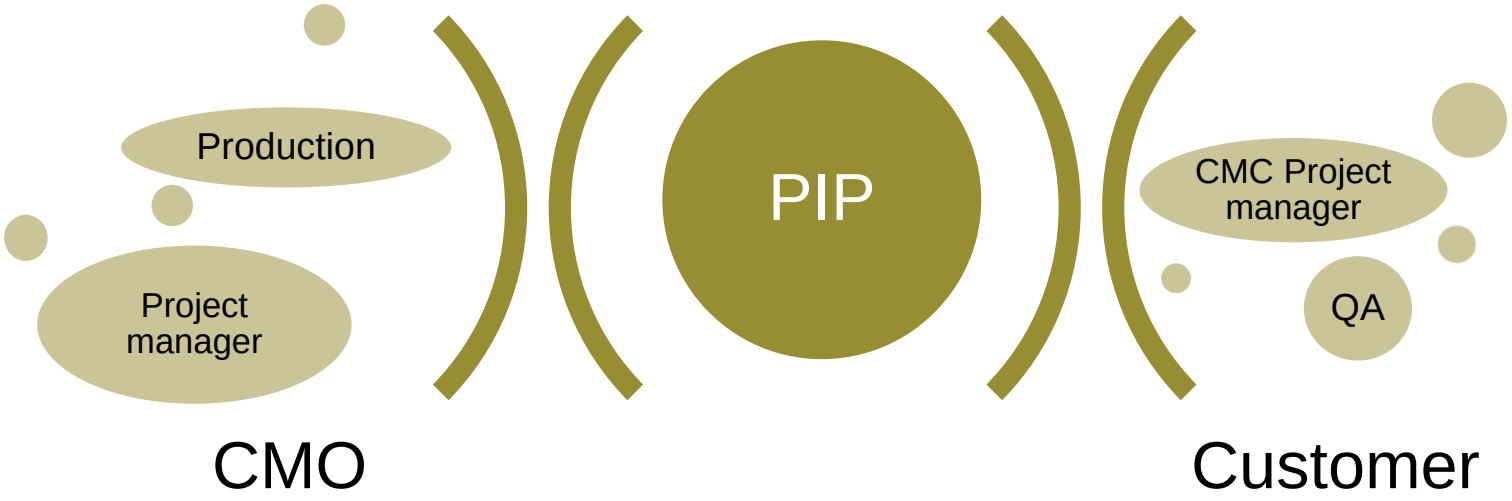
What is PIP

- PIP refers to having a project sponsor's employee or designee present at a contract manufacturing site (CMO) in order to observe operations.

Dilemma I: Resource vs. Accountability of control

- Efficient use of resource especially for small, virtual company
- “The Contract Giver is ultimately responsible to ensure processes are in place to assure the control of outsourced activities.”

Dilemma II: Mixed expectations from two sides



Case 1: PIP for one large international CMO

J

- Share product knowledge - ”How to handle the product”
- Trouble shooting: input from expert in product development

L

- OK to observe, but not hands-on
- While product-related questions are welcome, an ”audit-like” PIP is not expected.

Knowledge sharing and trouble shooting

Case 2: PIP for a small, virtual company (customer)

J

- To get an insight into the process at CMO
- Part of the outsourcing control strategy

L

- Resource
- Very limited access to certain areas

Joint Product & Process understanding

"Aaaaaaaaaaah"

Continuous learning and improving process

- QbD
  - FDA guidance on the lifecycle approach of process validation, a collaborative and continuous learning and improving process comprised of
  - Stage 1 - Design
  - Stage 2 - Process Qualification
  - Stage 3 - Continued Process Verification

  - *When has it to be done?*
  - *How about small virtual companies?*

Sponsor has regulatory accountability, but how to be in control?

- These processes should incorporate risk management principles. Supplier controls are to be based upon an evaluation of the risk of the supplier and its impact to product quality, safety, and efficacy.

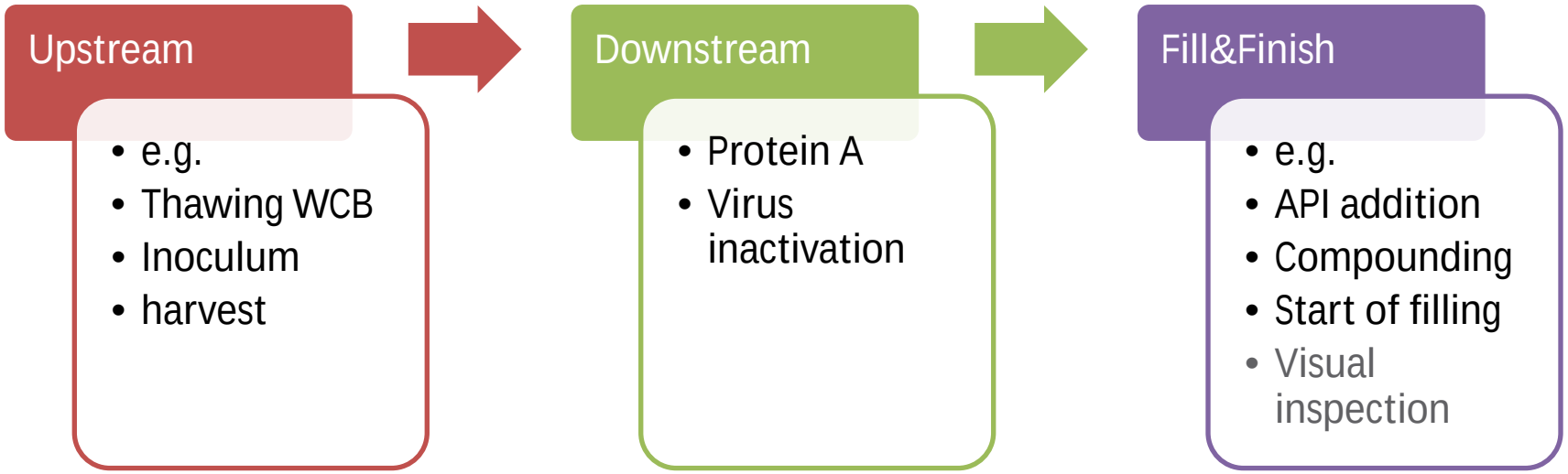
  --- Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Chapter 7: Outsourced Activities, June 2012

Genmab Internal guideline requirement for PIP

“The contractor **can** be visited (Person in Plant), during production at **critical stages** of the manufacturing process or for evaluation of data. A brief visit report is then created.”

When to PIP

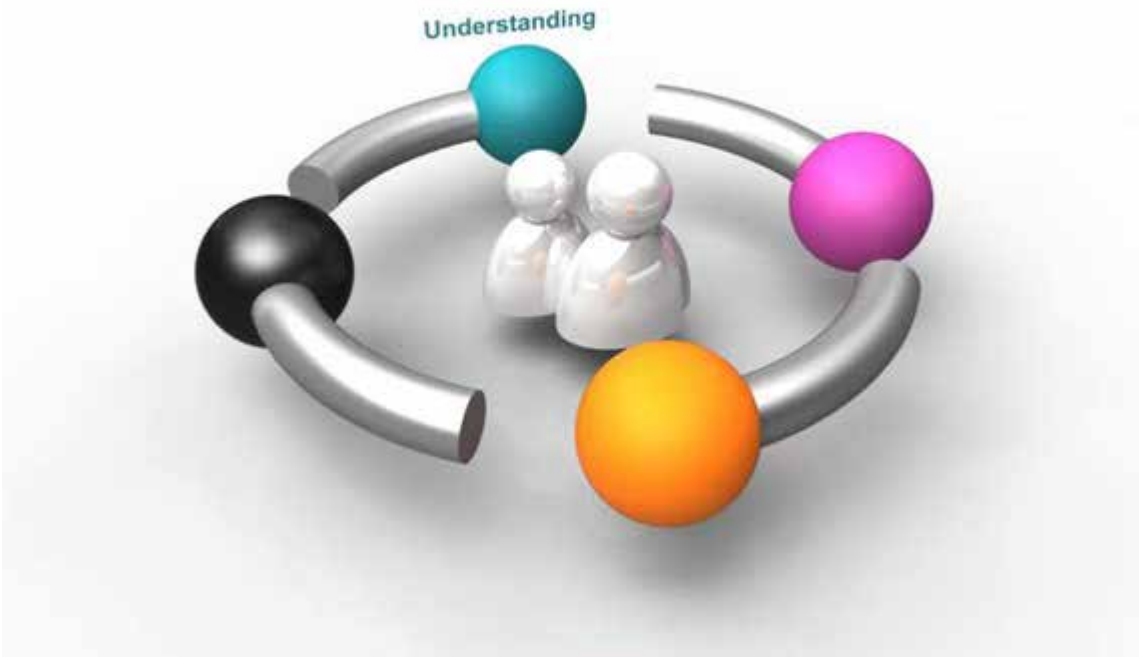
- Risk assessment per project, CMO and process.
- Very often for critical initial batches (first 1- 3 batches)
- Critical Step/stages, safety related
- Afterwards, only process changes, tech transfer or incident/trouble happens.



Who to PIP

- Mostly one person, max. 3
- At least one has some knowledge in product development, preferably involved in the specific product development.
- Possibly a QA, depending on the CMO / the situation.
- QA could obeserve if the procedures were being followed, BUT be aware that it’s NOT an audit.

Tips for sponsor PIP

- PIP is part of risk-based supplier oversight, only benificial with right ”dose” at right time
- Comunicating in a proper manner, and showing respect and trust. Don’t make an operator nervous.
- Choosing the right communication channel, perhaps through the CMO PM or supervisors, but not to the operators directly.
- Be aware of not blurring the lines of legal liability, by interfering with operations at the contract site.

Long-lasting Partner relationship