Product description

# Aim

1. ~~Provide some existing examples as basis~~. Completed in product\_description\_examples.docx.

2. Decide on the product name/mechanism this week.

2. Reproduce the provided example - “Case Study Group C Drug Project Description.docx”.

3. To be uploaded to moodle by Thurs 1st Sept (but sooner would be better).

# Decided

1. Our drug is mAb oncology treatment.

2. It will be approved for subcutaneous administration: [example](https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-new-formulation-herceptin-subcutaneous-use).

3. From the four tyle of stems, it is a “-mig” multi-immunoglobulin (e.g. [BsMAb](https://en.wikipedia.org/wiki/Bispecific_monoclonal_antibody" \o "Bispecific monoclonal antibody)) which has [advantages](https://en.wikipedia.org/wiki/Bispecific_monoclonal_antibody#Advantages_over_ordinary_monoclonal_antibodies) over of naturally occurring Abs.

# Our product: option 1

**Product name**:

**Treatment**:

**Mechanism/target**:

**Discussion**:

# Our product: option 2

**Product name**: Hertumab

**Treatment**: Treatment of HER2 receptor positive breast cancer.

**Mechanism/target**: Similar to the mode of action from Pertuzumab and Herceptin (as illustrated in Figure 1), Hertumab targets a newly defined antigen of HER2 which inhibits the [dimerization](https://en.wikipedia.org/wiki/Protein_dimer) with other HER receptors, thereby preventing [signalling](https://en.wikipedia.org/wiki/HER2/neu" \l "Signal_transduction) in ways that promote cell growth and proliferation. HER2 positive breast cancer is caused by ERBB2 gene amplification that results in overexpression of HER2 in approximately 15-30% of breast cancer tumors. Stimulates cell proliferation and cell growth. (Text from Wiki, to be modified if used).

**Discussion**: Typical example of a hypothetical classical mAb. Similar to Pertuzumab (RG6264, Perjeta) from [Genentech](https://en.wikipedia.org/wiki/Genentech) which was first approved in 2012, Europe in 2013, etc. Similar to Trastuzumab, Herceptin from Genentech very well known, approval US 1998, EU 2000, WHO essential medicine.

Map

Description automatically generated

**Figure 1**. Cryo-EM map of HER2-trastuzumab-pertuzumab. Hao Y, Yu X, Bai Y, McBride HJ, Huang X (2019) Cryo-EM Structure of HER2-trastuzumab-pertuzumab complex. PLoS ONE 14(5): e0216095. <https://doi.org/10.1371/journal.pone.0216095>.

# Product Description

## Case Study: Development Plan for phase 1 clinical trial – Pharma.

Product Profile – Our product is a monoclonal antibody to be used in a phase 1 clinical trial in oncology. The company is named VaudBioTech with headquarters located in Switzerland. This company is the discoverer of the product in question. The planned phase 1 clinical trial will be conducted in Germany.

**Group: C**

**Group members:**

**Company:**

**Product name**:

**Treatment**:

**Mechanism/target**:

**Discussion**:

The nomenclature for our drug is defined according to the WHO International Nonproprietary Names (INN) (Programme and Classification of Medical Product) [1]. The current state of the art in anti-cancer monoclonal antibodies (mAbs) is overviewed by [Chiavernna, et al](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5319201/). [2]. Guidance for this clinical trian can be found in the [EudraLex Volume 10 Clinical trials guidelines](https://ec.europa.eu/health/documents/eudralex/vol-10_en) [3]. The drug development plan will be completed based on our template: Case\_study\_group\_C\_template.docx.

# Part A: Preclinical Plan

A preclinical plan will be completed summarizing the work that needs to be done and included in the application for the above mentioned Investigational Medicinal Product. This consistes of a short description of the preclinical studies to cover the clinical trial, namely the animal studies, the duration of treatment, pharmacology and toxicology studies in the appropraire animal model.

Guidance documents used in this plan include:

* [An introduction to little-known aspects of nonclinical regulatory writing](https://journal.emwa.org/preclinical-studies/an-introduction-to-little-known-aspects-of-nonclinical-regulatory-writing/); Nürnberg and Pierre [4].
* European Comission: ***EudraLex Volume 10 clinical trials guidelines*** (<https://ec.europa.eu/health/documents/eudralex/vol-10_en>) [3].
* European Comission: ***EudraLex Volume 10 clinical trials guidelines***: ***Guidance documents containing the common provisions on the conduct of GCP inspections by competent authorities of the different member states; To guidance for the conduct of good clinical practice inspections 2008***. (see chapter 4 <https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en>) [3].
* EMA committee for medicinal products for human use (chmp): ***Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials*** (<https://health.ec.europa.eu/system/files/2016-11/18540104en_en_0.pdf>).
* ICH harmonised tripartite guideline*:* ***Guidance on nonclinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals M3(R2) version step 4 2009*** (<https://database.ich.org/sites/default/files/M3_R2__Guideline.pdf>) [5].
* ICH harmonised tripartite guideline: (<https://www.ich.org/page/safety-guidelines>), specifically section ***S9 Nonclinical evaluation for anticancer pharmaceuticals version step 4 2009*** (<https://database.ich.org/sites/default/files/S9_Guideline.pdf>) [6].
* ICH harmonised guideline: ***Integrated addendum to ICH e6(r1): guideline for good clinical practice*** ***E6(r2)step 4 version 2016*** (<https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf>) [7].
* EMA Committee for medicinal products for human use (chmp): ***Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials 2022***
* (<https://www.ema.europa.eu/en/requirements-chemical-pharmaceutical-quality-documentation-concerning-investigational-medicinal>) [8].

# Part B: Clinical Plan

* Clinical Trial Protocol will be drafted for inclusion in the application for the above-mentioned Investigational Medicinal Product. In this we define the main points of the clinical trial protocol and consider a master protocol.[Ledford 2013](http://www.nature.com/news/master-protocol-aims-to-revamp-cancer-trials-1.13176) reports on “‘Master protocol’ aims to revamp cancer trials” [9] and [Woodcock and LaVange 2017](http://www.nejm.org/doi/full/10.1056/NEJMra1510062#t=article) on requirements to “Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both” [10]. Consider[*PRIME*](https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines)and[*Breakthrough Designations*](https://www.fda.gov/regulatory-information/food-and-drug-administration-safety-and-innovation-act-fdasia/fact-sheet-breakthrough-therapies) (for comparison see FAQ 24. [here](https://www.fda.gov/regulatory-information/food-and-drug-administration-safety-and-innovation-act-fdasia/frequently-asked-questions-breakthrough-therapies)).
* Guidance and reference is found in the ICH harmonised guideline: ***Integrated addendum to ICH e6(r1): guideline for good clinical practice*** ***E6(r2)step 4 version 2016*** (<https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf>) [7].

# Part C: Chemistry, Manufacturing and Controls, CMC

Here we will write a clear CMC plan on the work that needs to be done and included in the application for the above mentioned Investigational Medicinal Product. (Emphasize the level of detail required.)

Guidance and reference can be found at

* European Comission: ***EudraLex Volume 10 clinical trials guidelines*** (<https://ec.europa.eu/health/documents/eudralex/vol-10_en>) [3].
* European Comission ***EudraLex Volume 10 clinical trials guidelines***: ***Guidance documents containing the common provisions on the conduct of GCP inspections by competent authorities of the different member states; To guidance for the conduct of good clinical practice inspections 2008***. (see chapter 4 <https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en> or PDF <https://health.ec.europa.eu/system/files/2016-11/18540104en_en_0.pdf>) [3].

# Part D: Pre-IND Meeting / Scientific Advice

Here we will include a summary of the project background, the questions with the opinion of the company, number of attendees, and the time for the meeting (ideally).

Advice can be found at the Paul-Ehrlich-Institute, Federal Institute for Vaccines and Biomedicines webpage (<https://www.pei.de/EN/information/license-applicants/advice/scientific-advice/scientific-advice-node.html>) and the EMA Human Regulatory webpage for Scientific advice and protocol assistance (<https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance>).

# Part E: Inspection Readiness

Here we will write a summary of the work that a company needs to have ready before the inspection to ensure compliance to GxP. Extract some details from the Week 3 presentation. Important is the know the points the inspector normally go through during an inspection.

Guidance can be found at

* European Comission ***EudraLex Volume 10 clinical trials guidelines***: ***Guidance documents containing the common provisions on the conduct of GCP inspections by competent authorities of the different member states; To guidance for the conduct of good clinical practice inspections 2008***. (see chapter 4 <https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en>) [3].
* European Comission: Guidance documents containing the common provisions on the conduct of GCP inspections by competent authorities of the different member states. G***uidance for the conduct of good clinical practice inspections (***<https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2008_11/vpl10_an5_10-2008_en.pdf>).

# References

[1] R. Balocco, S. D. S. G. Koch, R. Thorpe, K. Weisser, and S. Malan, “New INN nomenclature for monoclonal antibodies,” *The Lancet*, vol. 399, no. 10319, p. 24, 2022.

[2] S. M. Chiavenna, J. P. Jaworski, and A. Vendrell, “State of the art in anti-cancer mAbs.,” *J Biomed Sci*, vol. 24, no. 1, p. 15, Feb. 2017, doi: 10.1186/s12929-016-0311-y.

[3] “EudraLex Volume 10 Clinical trials guidelines.” 2014. [Online]. Available: https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10\_en

[4] A. Nürnberg and H. Pierre, “An introduction to little-known aspects of nonclinical regulatory writing,” *Medical Writing*, vol. 26, pp. 9–19, 2017.

[5] I. C. H. Guideline, “ICH: Guidance on nonclinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals M3 (R2). Version step 4 2009.,” 2009. [Online]. Available: https://database.ich.org/sites/default/files/M3\_R2\_\_Guideline.pdf

[6] I. C. H. Guideline, “ICH: S9 Nonclinical evaluation for anticancer pharmaceuticals. Guidance on nonclinical safety studies for the conduct of human clinical trials and marketing authorization for pharmaceuticals M3 (R2). Version step 4 2009.,” 2009. [Online]. Available: https://database.ich.org/sites/default/files/S9\_Guideline.pdf

[7] I. C. H. Guideline, “ICH: E6(R2) Good Clinical Practice (GCP). ICH Efficacy Guidelines.,” 2016. [Online]. Available: https://database.ich.org/sites/default/files/E6\_R2\_Addendum.pdf

[8] “EMA: Guideline on the requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials.” [Online]. Available: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-requirements-chemical-pharmaceutical-quality-documentation-concerning-investigational\_en-1.pdf

[9] H. Ledford, “‘Master protocol’ aims to revamp cancer trials.,” *Nature*, vol. 498, no. 7453, pp. 146–147, Jun. 2013, doi: 10.1038/498146a.

[10] J. Woodcock and L. M. LaVange, “Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both.,” *N Engl J Med*, vol. 377, no. 1, pp. 62–70, Jul. 2017, doi: 10.1056/NEJMra1510062.