



UMC Utrecht



Seminar PC2:

Hospital Mergers and the Centralisation of Production Services

Centralisation of Production and Compounding: the Dutch Perspective

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Disclosure

- Conflict of interest: nothing to disclose.

Self Assessment Question #1

Is the proportion of preparation and administration errors larger than 20% of all medication errors?

YES / NO

Self Assessment Question #2

Is moving to centralisation of manufacturing and compounding a proper way to reduce medication errors?

YES / NO

Self Assessment Question #3

Are the emotional pitfalls underestimated when centralising production services?

YES / NO

Topics to cover today

- Who am I?
- Necessity of Drug Manufacturing and Compounding
- Standardisation and Centralisation
- Dutch Perspective: in general
- Dutch Perspective: Apotheek A15
- Pitfalls
- Summary
- Acknowledgements
- Take home messages

Who am I?

- Hospital pharmacist
- **Until** January 1st, 2018:
 - Head of Pharmacy Apotheek A15 (Gorinchem, the Netherlands)
 - Senior staff member (focus on compounding & manufacturing), Dept. of Pharmacy, Erasmus Medical Centre (Rotterdam, the Netherlands)
- **Since** January 1st, 2018:
 - Head of the Department of Clinical Pharmacy of the University Medical Center Utrecht
- Past Board member of the Dutch Association of Hospital Pharmacists (Drug Manufacturing, Compounding, QC & QA; December 2011 – December 2015)

**“It's not enough
to have talent,
you also
have to be
Hungarian.”**

ROBERT CAPA

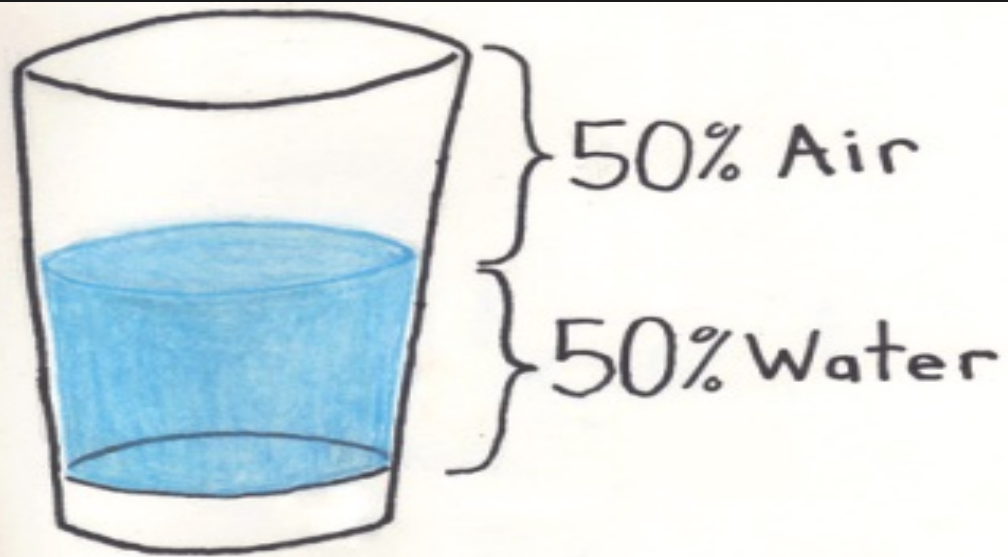


**WINE
IMPROVES
WITH AGE**

**I IMPROVE
WITH**

WINE





Technically,
The Glass is Completely Full.

Today

- I will be taking to you from my (former) Apotheek A15 perspective....



What is my intention with you for today?



NO



YES

Drug Manufacturing & Compounding

*On a hospital level is a hard
core necessity!!*

It's the real thing



DRINK

Coca-Cola®

Main Advantages

- Raising medication safety
- Raising quality levels, true specialisation & centralisation
- More time for nurses at the bed side of the patient (instead of performing pharmaceutical work)
- Minimising overall costs

Necessity for Drug Manufacturing and Centralized Compounding

- Therapeutically necessary, but not commercially available products
- Production problems with commercial products (temporarily / permanently)
- Investigator initiated drug research
- Medication safety (reducing medication errors)
- Service products (making things easier for nurses and patients)
- Individual needs of patients

Medication Errors (%)

Data from CMR = Dutch Registry of Medication Errors

Prevention of errors

- **Product**

 - Ready to Use (RTU)

 - Ready to Administer (RTA)

- **Process**

 - Centralized compounding

 - Process help for ward preparation



RTU

- Ready To Use
- Standard dosage
- Prepared dose by the pharmacy
- Commercially available dosages



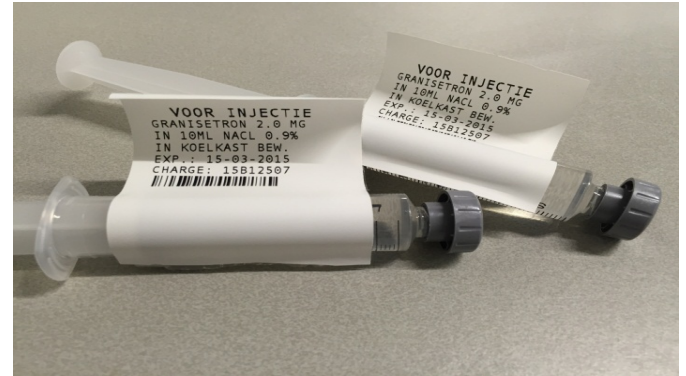
RTU availability: Pharmacy prepared

- Norepinephrine 50 mg = 50 ml
- Morphine 50 mg = 50 ml
- Midazolam (2)50 mg = 50 ml
- Furosemide 250 mg = 50 ml
- Heparine 25,000 IE = 50 ml
- Many electrolyte solutions
- Ropivacaine – Sufentanil
- etc



RTA

- Ready To Administer
- Commercial syringes, examples
 - Anticoagulants
 - Vaccines
 - LMWHs
 - Other
- Prepared in the pharmacy



Standardisation & Centralisation

Get the right balance of:

1. Centralised (and outsourced) manufacturing
2. Centralised compounding
3. Preparation on the ward

Standardisation & Centralisation

Get the right balance of:

1. Centralised (and outsourced) manufacturing

~~2. Centralised compounding~~

~~3. Preparation on the ward~~

The Dutch perspective

- Approx. 90 hospitals
- Twenty years ago: all hospitals had their own hospital pharmacy, including large scale manufacturing
- During the last two decades:
 - number of production sites has decreased
 - fusion of hospitals
 - concentration of specific expertise in specific centers
- Legislation: pharmacy preparation is only possible on an individual basis, for a specific patient with a specific prescription
- However: under strict circumstances it is possible to make preparations on stock and supply from pharmacy A to B

The Dutch perspective

- A relatively small portion of hospital pharmacies are still producing on a large scale and providing services and products for other pharmacies
- Also: there are several strictly commercial firms offering (production and compounding) services to pharmacies
- Basic concern: loss of control and expertise to manufacture necessary and clinically rational products within and for the hospital setting

Basic background idea of several academic hospitals:

- To assure necessary rational pharmaceutical preparations for (academic) hospitals and its patients
- Primary focussing on the needs of patients in the hospital as well as their out patient situation
- Providing products that are sustainable, expedient and have the highest quality standard
- Upholding expertise and control of pharmaceutical manufacturing for hospital pharmacist (in training)
- **Basic goal: availability of the essential and rational pharmaceutical care for the individual patient**

Apotheek A15

- Classic back-office (manufacturing, QC, QA, logistics, etc) of the Erasmus MC are placed outside of the hospital and outside of Rotterdam
- Apotheek A15: a totally separate pharmacy
- Legally: a private company in ownership of the two largest academic hospitals of The Netherlands (Erasmus MC Rotterdam and University Medical Center Groningen).

Apotheek A15

- *A state of the art* GMP licensed manufacturing facility
- 2000 m² of cleanrooms (GMP class B, C, D)
- Capable of manufacturing every type of product (non-sterile, sterile, aseptic) as well as performing individual and bulk compounding
- Contains a fully equipped analytical and microbiological laboratory and all other (logistic, etc) necessities.
- Functions under full industrial GMP situation and holds licenses for the manufacturing of products for Clinical Trial use as well as manufacturing products for other (hospital) pharmacies.

Apotheek A15

- Manufacturing necessary but not commercially available drugs for primary care & drugs for investigator initiated trials
- Developing new products to ensure regular patient care as well as medication safety
- Production site for Erasmus MC (full scale), Academic Centre Groningen (full scale) as well as approx. 50 other parties (non-full scale)

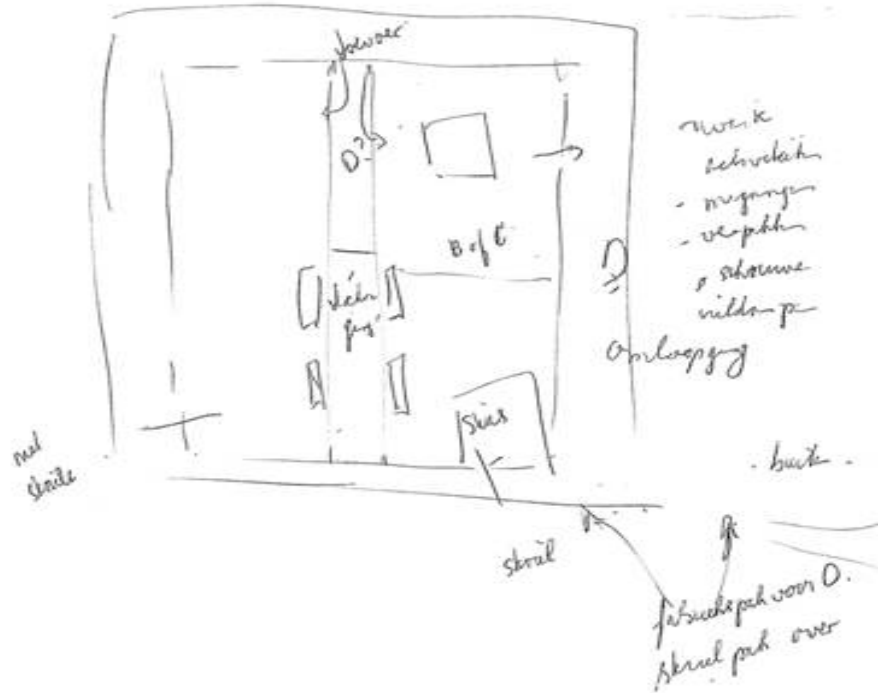
Activities 2010-2014

- June 2010: basic plan was formulated to perform all back-office pharmacy tasks of the Erasmus MC outside of the hospital and outside of Rotterdam
- February 7th, 2011: first meeting with architect (EGM) and primary technical advisor (RHDHK)
- June 16th, 2011: final design ready
- June 2011- Feb. 2012: preparations for starting construction
- March 15th, 2012: start of construction
- May 8th, 2012: official 1st pole was placed
- June 18, 2013: hand-over of the finished building
- January 1st, 2014: pharmacy totally operational

Timelines

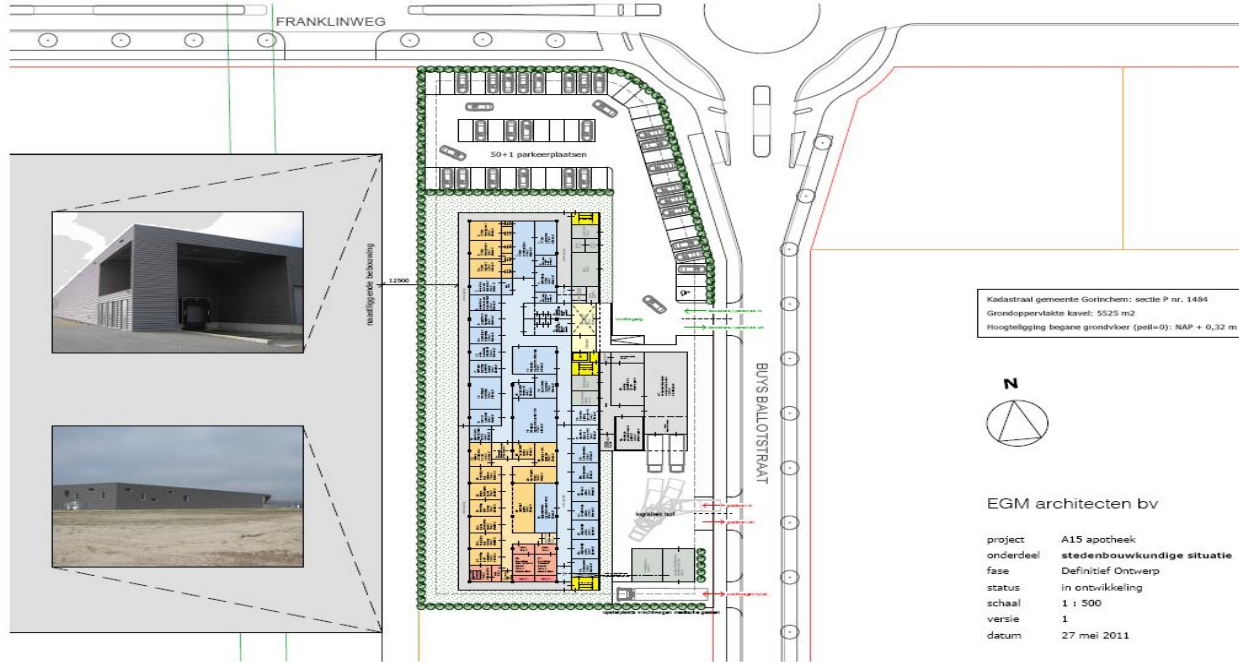
- 1st thought – fully operational 3.5 years
- Total construction time, including initial validation of installations 15 months
- Total construction time, excluding validation 11 months
- Total time for initial validation of processes 7 months

Apotheek A15: initial drawing



Feb 2011

Apotheek A15: final drawing



Feb 2012

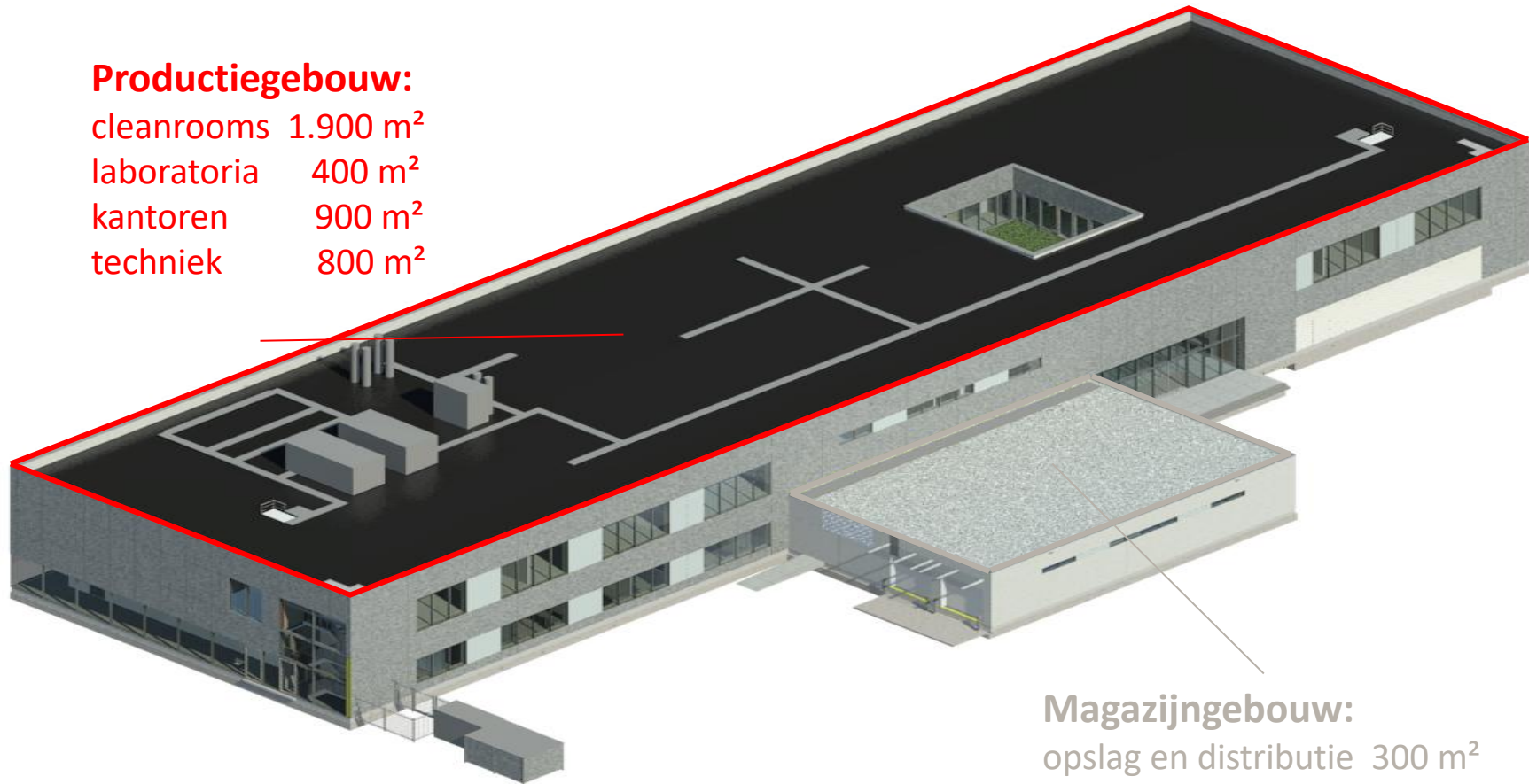
Productiegebouw:

cleanrooms 1.900 m²

laboratoria 400 m²

kantoren 900 m²

techniek 800 m²

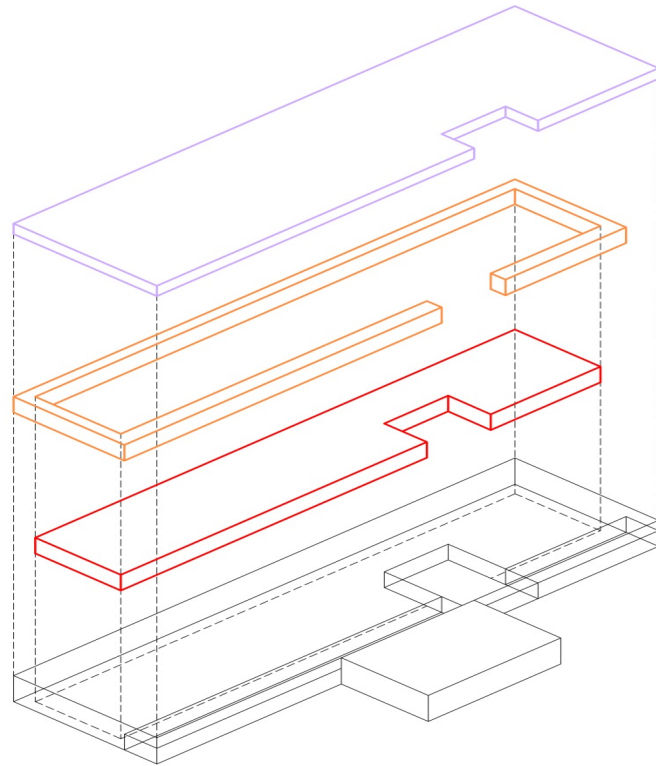


Magazijngebouw:

opslag en distributie 300 m²

Apotheek A15

- Available lot: 5525 m²
- Building consists of two levels (2225 m² ground floor & 1940 m² first floor)
- Ground floor: entrance, reception, cleanrooms, small portion of technical area
- Ground floor: logistical area (warehouse, quarantine, expedition, etc)
- First floor: larger portion of technical area, water production, laboratory, offices, conference rooms, canteen, kitchen, etc)
- Fully equipped with circulation corridor & walkable technical ceiling for maintenance.



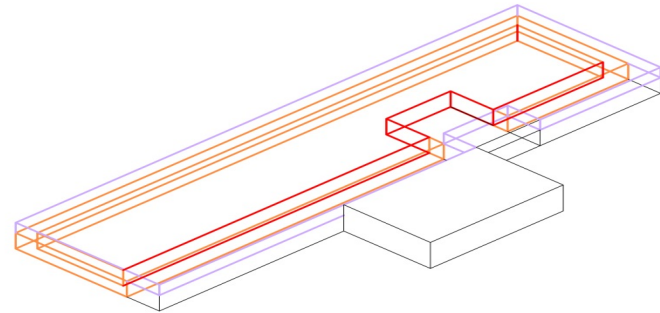
bezoekbaar technisch serviceplafond

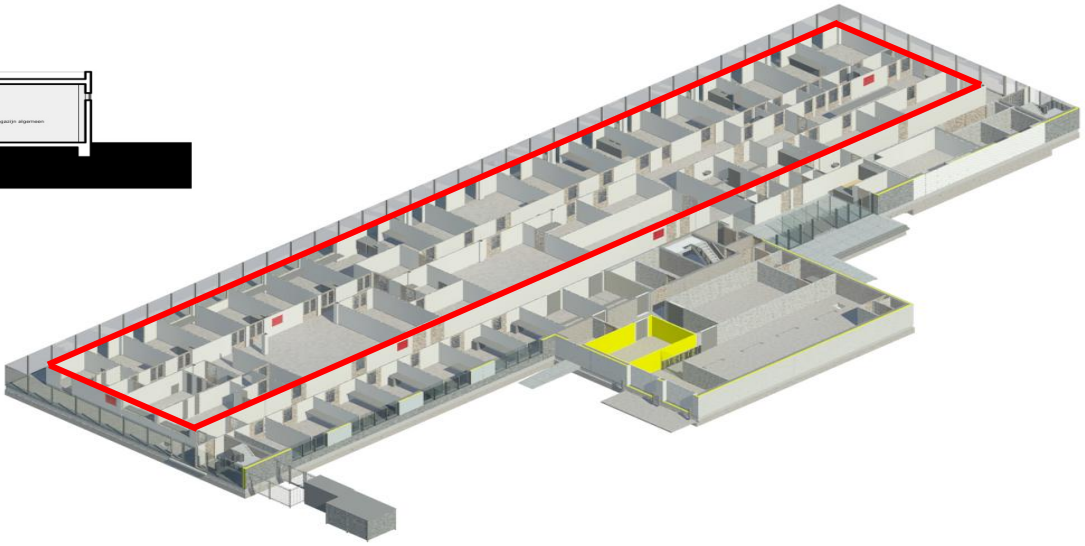
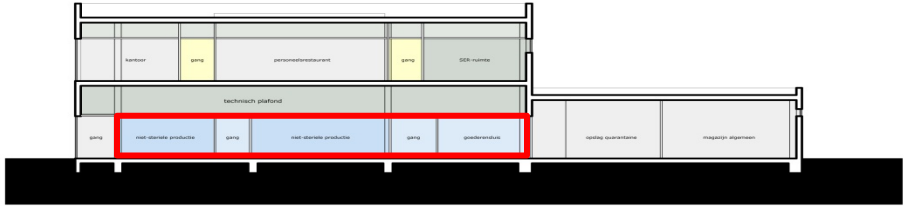
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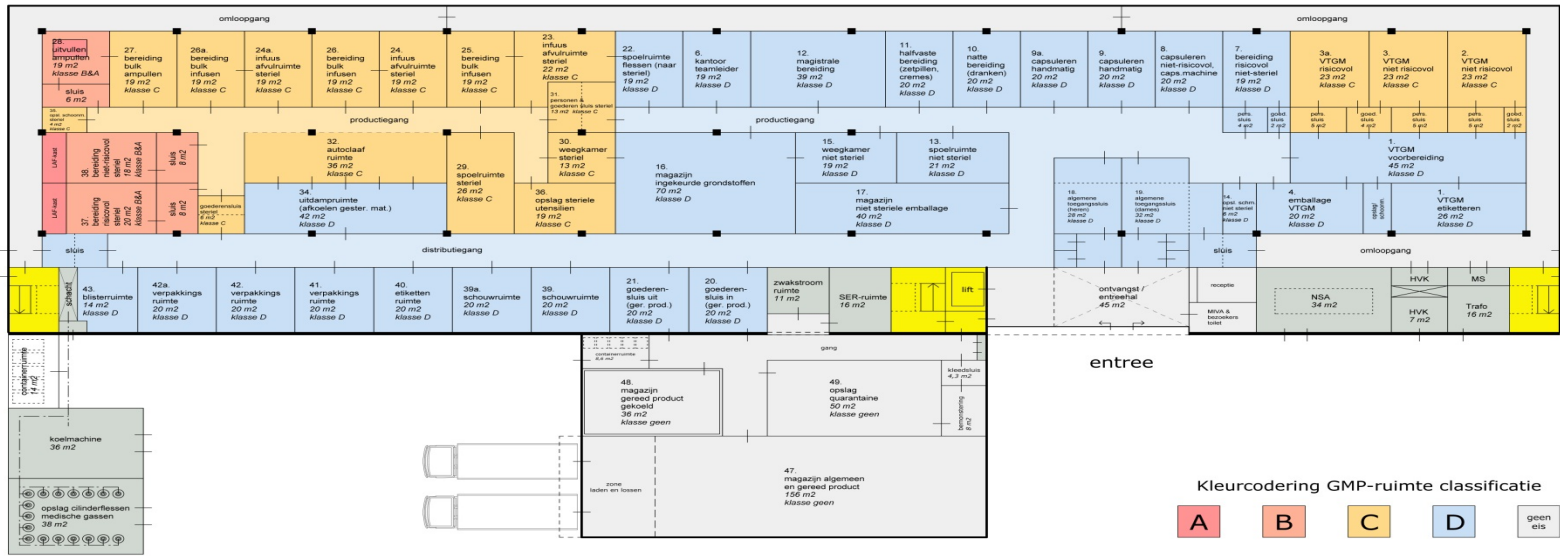
cleanrooms

gebouw

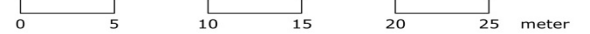
Box-in-box principle



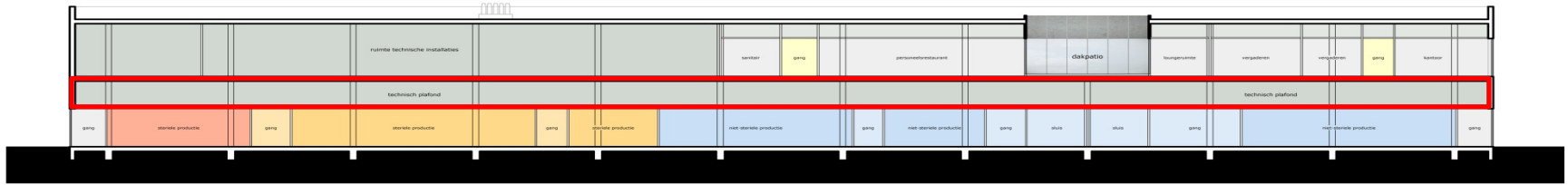




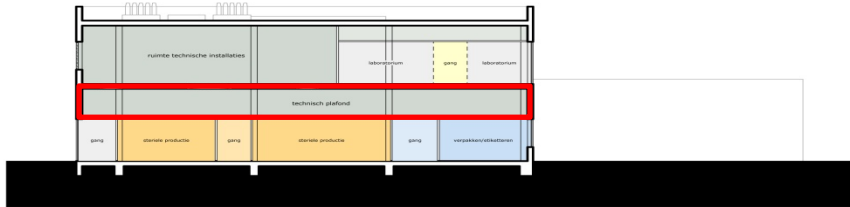
Plattegrond begane grond



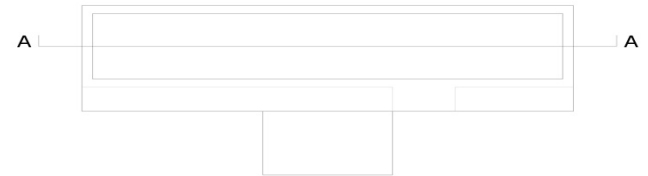




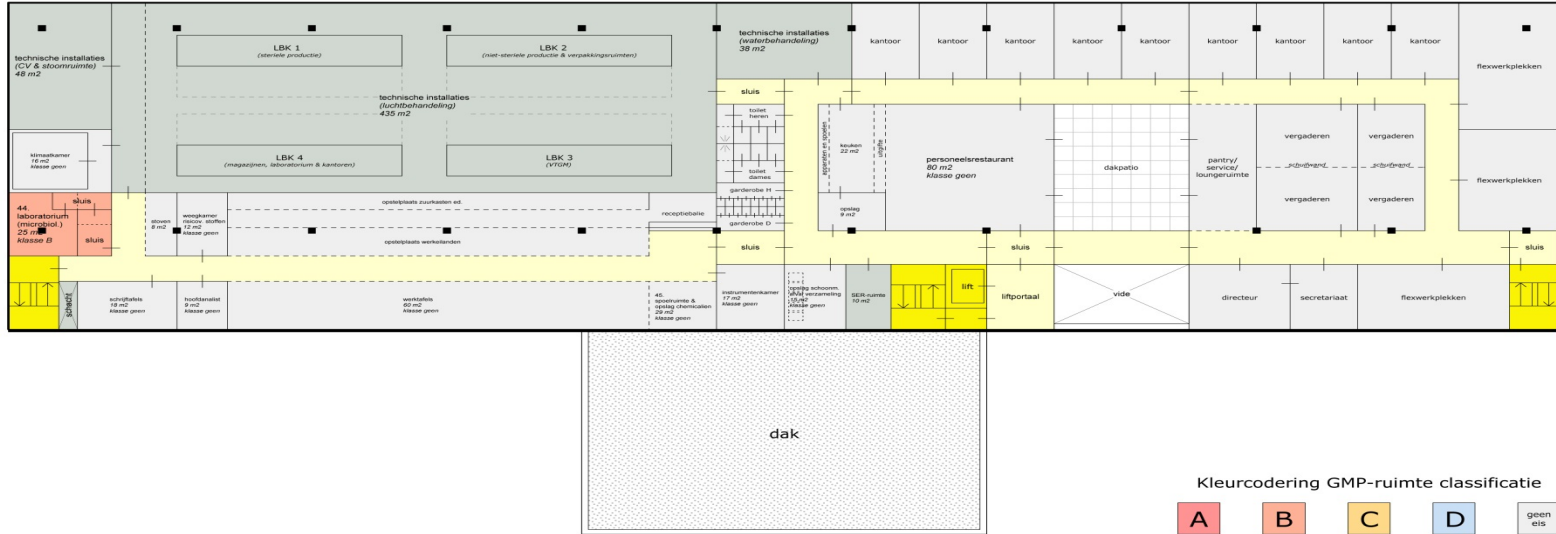
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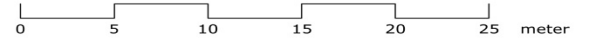
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Plattegrond 1e verdieping



Key Figures

- At the basis: combination of the necessary products of Erasmus MC & University Medical Centre Groningen (combined & filtered)
- Approx. 360 unique preparations on stock & standardised individual preparations
- Approx. 20 new products in several stages of development
- Approx. 2,000 batches of product a year
- Approx. 1,000,000 units of drugs a year
- Nearly 70 employees (65 FTE)

Greatest pitfalls

- Negative vibe
- Combining stuff
- Financial issues
- Inspectorate
- Too far off

Greatest pitfalls: negative vibe

- From many colleagues (other hospital pharmacies)
- Fear of losing a proper basis for their own production facility
- Personal opinion: missing the larger picture, self-centred state of mind
- Lots of meetings and visits were planned with colleagues
- As well as offering excellent services and high quality from the start
- Give it some time.... (typical (Dutch?) pharmacist characteristic...)
- ...And the negative vibe will turn around to positive!

Greatest pitfalls: negative vibe

- From the own organisation and its employees
- People fear to lose their jobs (at the start, when production was planned to stop at the academic centers them selfs)
- Lives are shook up
- People have to make adjustments in their lives
- Some join, some don't
- Long and hard process; lots of talks and meetings
- Gaining trust by listening and understanding peoples challenges
- First two years: extra bonus to cover extra costs and necessary life adjustments

Greatest pitfalls: combining stuff

- Formulary choices have to be made on every side
- Rotterdam: from 220 to 130 stock preparations
- Groningen: from 550 to 200 stock preparations
- Combining cultures and opinions
- Combining ways things are usually dealt with (and people are used to)

Greatest pitfalls: financial issues

- Strict business plan
- First few years you lose money; how to compensate?
- Gaining trust from hospitals to start buying (specific) products
- Fear of not getting enough serious partners and large customers
- From the start: don't exclude any possible partner, what ever direction they come from
- Selection (and exclusion) of partners and clients is something for future times

Greatest pitfalls: inspectorate

- New concept in The Netherlands
- Dutch Inspectorate was watching the situation closely from the start (positive mind set, but also cautious)
- From the start you need to get the quality issues up to speed as soon as possible
- No slip ups or failures
- Invest in all areas of quality from day 1
- Transparency and open mind towards inspectorate

Greatest pitfalls: too far off

- Too far away from the hospitals
- Too far away from regular hospital pharmacy
- Telling the strategic background over and over again
- Change the state of mind of people
- Legally a separate pharmacy; emotionally (and strategically) a part of the academic centers that are the owners (it is ours, just a bit further away)
- Hard to convince hospital pharmacists to apply for job vacancies
- Although, how must do you actually need...?!

Summary

- Drug Manufacturing and Compounding on a hospital level is a hard core necessity
- Standardisation and centralisation is the way forward (when adequately balanced with preparation on the ward for specific situations)
- The goal is to minimize medication errors and to get the highest quality standard of necessary and rational products
- There are many pitfalls to cover when engaging the process of merging production services
- Do not underestimate the emotional pitfalls in the process of centralisation

Acknowledgements

Apotheek A15 and its full staff!



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YES

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Is moving to centralisation of manufacturing and compounding a proper way to reduce medication errors?

YES

Self Assessment Question #3

Are the emotional pitfalls underestimated when centralising production services?

YES

Take home messages

- Drug Manufacturing and Compounding on a hospital level is a hard core necessity
- Standardisation and centralisation is the way forward (when balanced)
- The goal is to minimize medication errors and to get the highest quality standard of necessary and rational products
- Do not underestimate the emotional pitfalls in the process of centralisation

BE NICE TO
PHARMACISTS
BECAUSE
WE **KILL** U
CAN **WITH ONE**
mistake
☺

***Thank you for your
attention!***