Ready to use injectable medicines: is there a need for them and how do we get them?

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Disclosure

- Conflict of interest: nothing to disclose

Background

Central Hospital Pharmacy, The Hague (AHZ)
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Head production department

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Definitions

- RTA: a presentation of the medicinal product at the required concentration and volume, **in the final** container (syringe, infusion bag or elastomeric device), and ready to be adminstered to the patient.

- RTU: a presentation of the medicinal product at the required concentration in a container. The required volume is **transferred** to a final administration device (syringe, infusion bag or elastomeric device) for administration to the patient

Why do we need RTU/RTA? Patient safety!

Medication errors regarding reconstitution

- Possible failures in the reconstitution process
  - Reconstitution of the wrong dose
  - Calculation errors leading to administration of the wrong dose and/or at the wrong concentration or rate
  - Incorrect reconstitution (insufficient mixing, incomplete dissolution, use of the wrong diluent)
  - Incompatibility between diluent, infusion, other medicinal products or administration devices
- Risk of microbiological contamination

From: Scheepers HPA, et al. Eur J Hosp Pharm 2015

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Quality of products: ranking (low to high)

- Preparation on the the wards
- Preparation in the pharmacy
- Preparation supplied from stock (pharmacy, outsourcing)
- Commercially available products

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Consider a strategy

- Pharmacy takes over preparations (make or buy)
- All??
- Not possible; therefore training and instructions
  - Education program
  - Information data base (Parenteral manual)

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Preparation: categorisation where, who and how

- Central:
  - high risk medication/process
    - Patient
    - Technician
  - Efficiency: RTU, RTA

- Satellite
  - As much as possible
    - Quality
    - Efficiency
- Patient bed
  - Immediate use

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Two obvious examples to start with

- RTA: homecare treatment of a CF patient with ceftazidim 2000 mg and tobramycin 300 mg in an elastomeric pump for 14 days

- RTU: use of a syringe pump with noradrenaline for a patient on the ICU

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Ceftazidim 2000 mg and tobramycin 300 mg

- Ceftazidim powder for injection
- Tobramycin ampoules 40 mg = 1 ml, 3ml
- Water for injection
- NaCl solution
- Elastomeric pump

- Preparation facilities and skills

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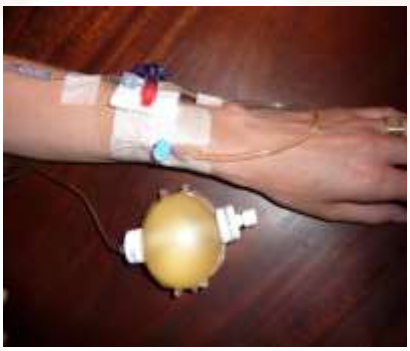
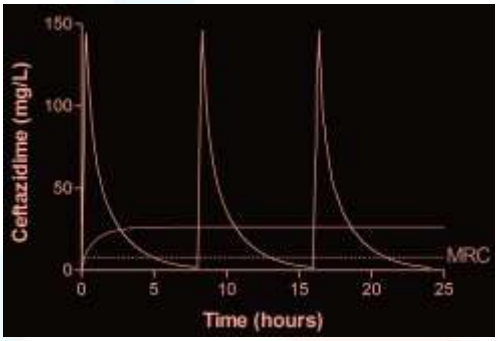


Stability of the performance of the device

Stability of the drug at room temperature.

Continuous versus intermittent

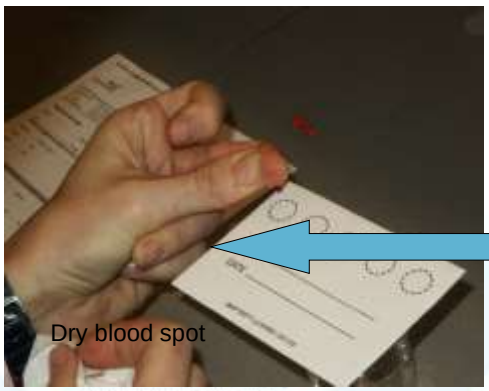


Aminoglycosides.

Optimal dosing, limited blood samples, dry blood spot
Preparation of elastomers in pharmacy
Distribution by outpatient pharmacy

Hospital Pharmacy

Outpatient Pharmacy



RTU example: noradrenalin available in 1 mg = 1 ml while 50 mg = 50 ml is used

Service and
patient safety

Advantages are evident

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Adrenalin	Insulin
Cefamandol	Potassium chloride
Cefotaxim	Midazolam
Ceftazidim	Midazolam / Morphine
Dobutamin	Morphine
Dopamin	NaCl 0,9%
Phenylephrine	Nitroglycerin
Furosemide	Nitroprusside
Glucose 5%	Noradrenalin
Heparine	Propofol

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Special example from Isala Hospital

- Automatic filling and closing machine:

Prefillable and sterilizable syringe

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Ref: Karin Larmené- Beld, hospital pharmacist Isala, Zwolle, The Netherlands

Source of products in the examples: hospital pharmacy

- Process RTA (in general):
  - Buy a licensed product
  - ‘ handling’
  - Storage and delivery
  - Documentation

- Process RTU (in general)
  - Buy raw materials
  - Design a product (including dossier, validation etc.)
  - Production, storage and delivery
  - Documentation

Legislation???

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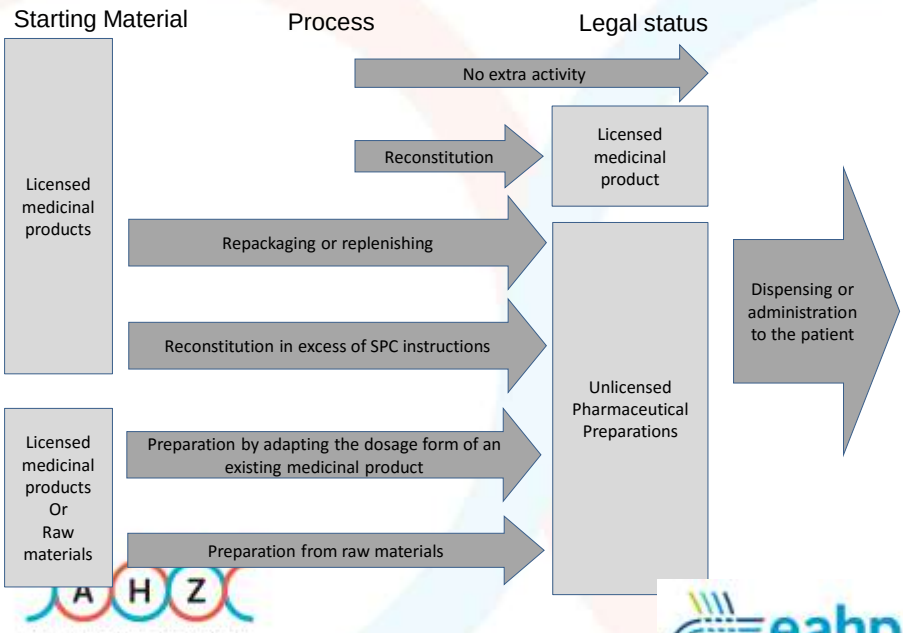

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Preparation of unlicensed medicines

- Legislation in Europe: Directive EU 2001/83
- Art. 3: Pharmacy preparations: clear!
- Delivery between pharmacies? Allowed in several countries
- But: Abcur case in Sweden!
- Consequences?
  - Delivery between pharmacies is necessary (some countries) but will it continue
  - Quality demands for pharmacy preparations (Resolution 2011)
  - How to consider equivalence with licensed preparations

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Again: Quality of products: ranking (low to high)

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- **Commercially available products**

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RTU's availability; just a few examples

Commercially availabe:
Gentamicin solutions and midazolam

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Always usefull??

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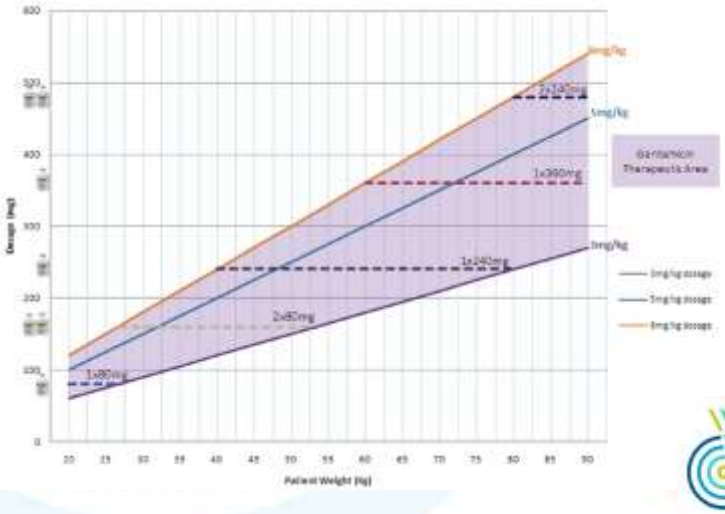
Standardized versus individual dosing?
Dose banding!



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Standardised dose?

- Yes for a standard patient, but always consider patient characteristics such as (for gentamicin)
  - Bodyweight
  - Gender
  - Renal clearance

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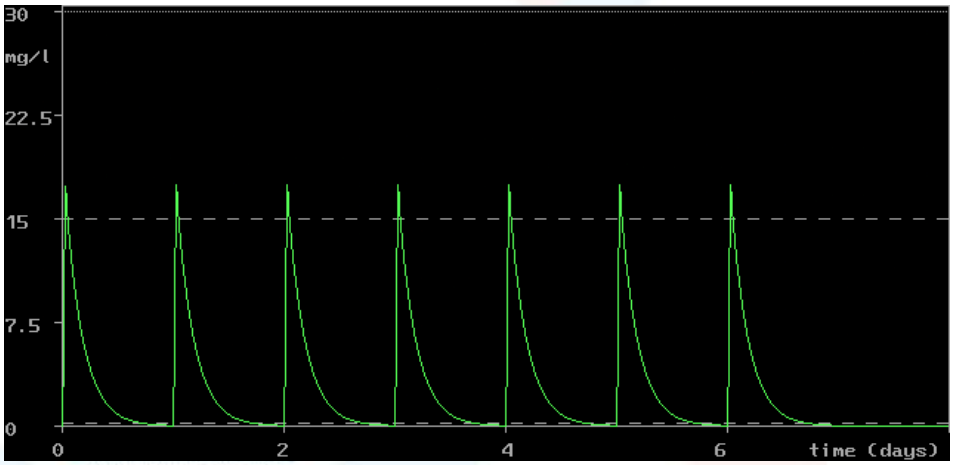
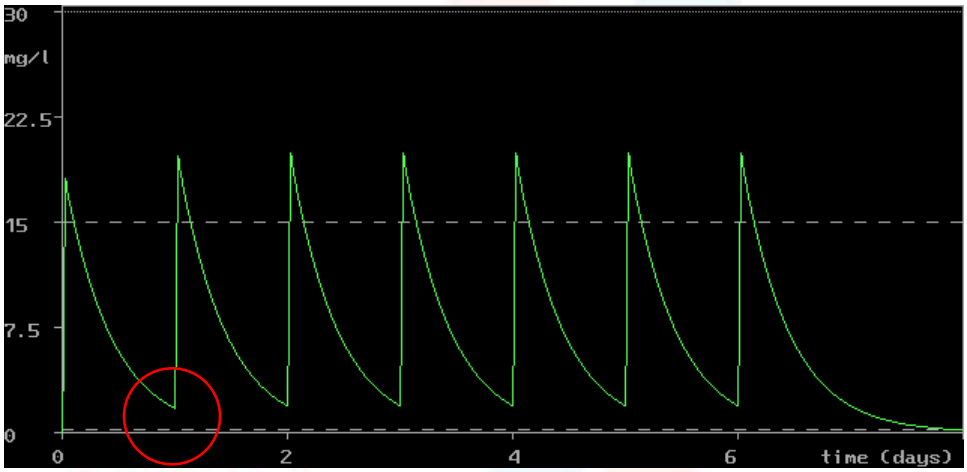
Male, 72 kg, creat 70, 1 dd 360 mg gentamicin



Male, 72 kg, creat 200, 1 dd 360 mg gentamicin



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Ready to use

- Yes, but be aware of (changes) in patient characteristics

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Summary

- In order to improve patient safety in IV's there are several options to consider.
- Process support (education, information)
- Prepare in pharmacy if possible
- But consider legislation and quality demands
- Standardise with RTU's RTA's if applicable
- Make or buy RTU's and RTA's
- Choices depend on local situation and in general a combination of the options will be used
- Be aware of (new) risks

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Any questions from yc