

# Therapeutic $\beta$ -lactam Antibiotics **Monitoring for Stratified Treatment** of Hospital-acquired Pneumonia, Improved Dose-dependent Efficacy, Decreased Treatment Duration, and Prevention of Emergence of Resistance

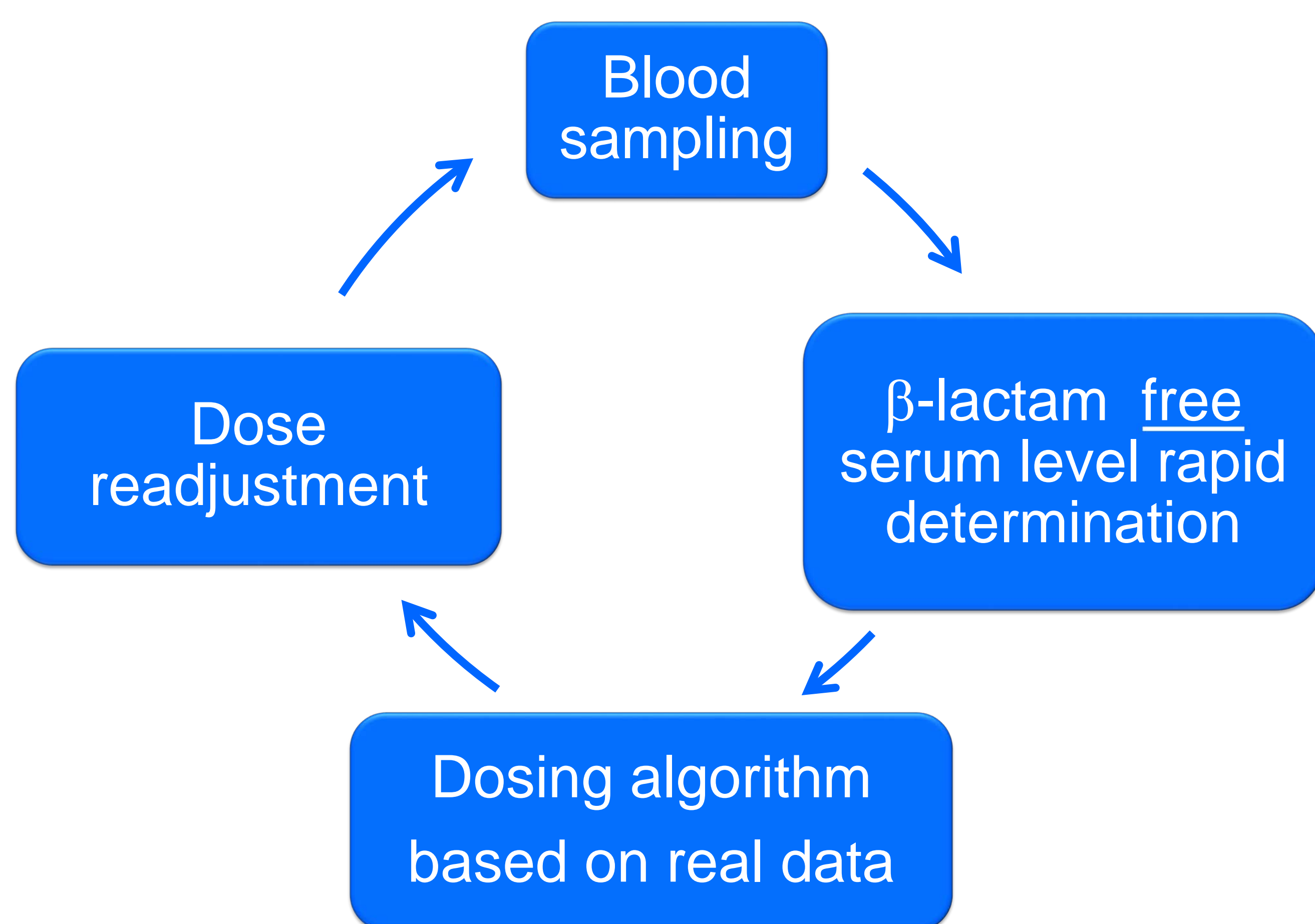
## Rationale

- The clinical efficacy of  $\beta$ -lactams is clearly linked to the percentage of the time during which their free concentrations remain above the MIC [ $f_t > \text{MIC}$ ] of the target organism.
- The minimal value (40%) is rarely achieved in difficult-to-treat patients, due to unpredictable variations of pharmacokinetics, leading to subtherapeutic concentrations.
- Increasing dosages in a blinded fashion is not without risk, as  $\beta$ -lactams may cause neurotoxicity, which often limits their use in severely-ill patients.
- Collectively, these concerns call for a on-line monitoring of  $\beta$ -lactams free blood levels, with rapid dosing readjustments based on real individual data.

## Objectives

- To bring to the clinics a method for fast and *quasi* “on line” monitoring of the **free serum concentration** of  $\beta$ -lactams, with results made available to the prescriber **within less than 1 h** together with **suggestions for dose adaptation** based on both **actual data** and modeling of the **individual patient’s pharmacokinetic parameters**.
- On this basis, tailor **individualized treatments**, meeting **optimal efficacy** as well as a **reduced risk of emergence of resistance** and **avoidance of toxicity**.
- To develop and demonstrate at the clinical level the usefulness of this approach in the context of a typically **difficult-to-treat infection** (nosocomial pneumonia).

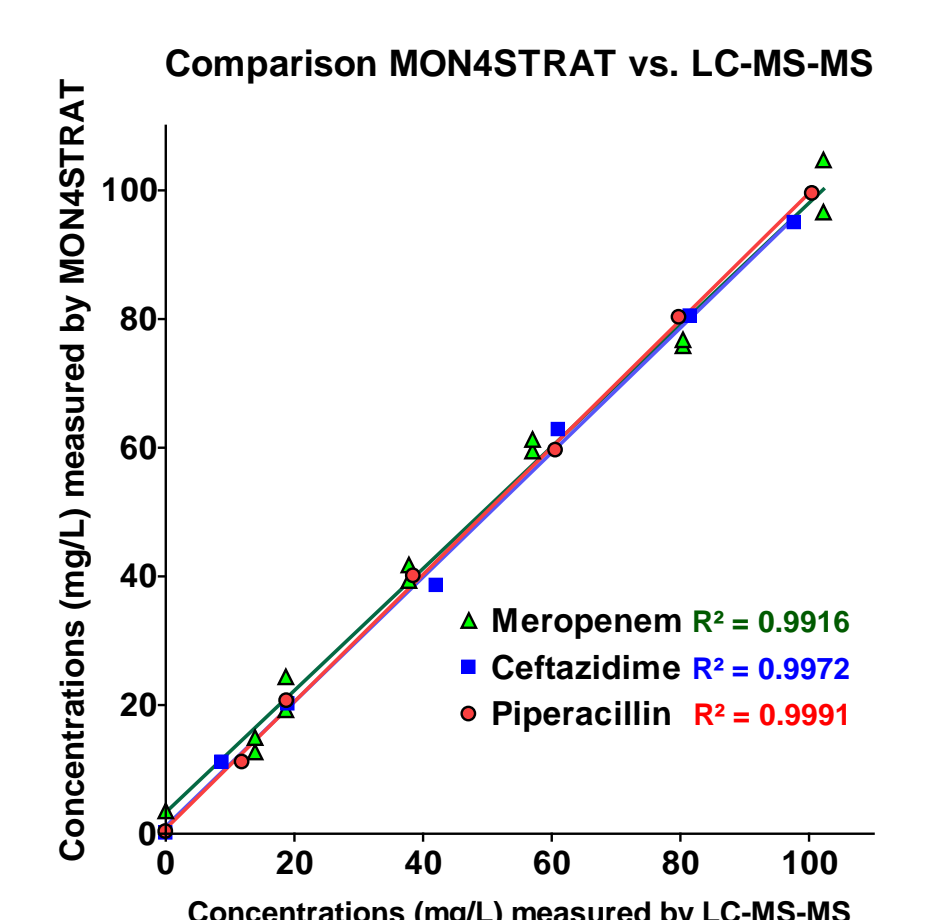
## The approach



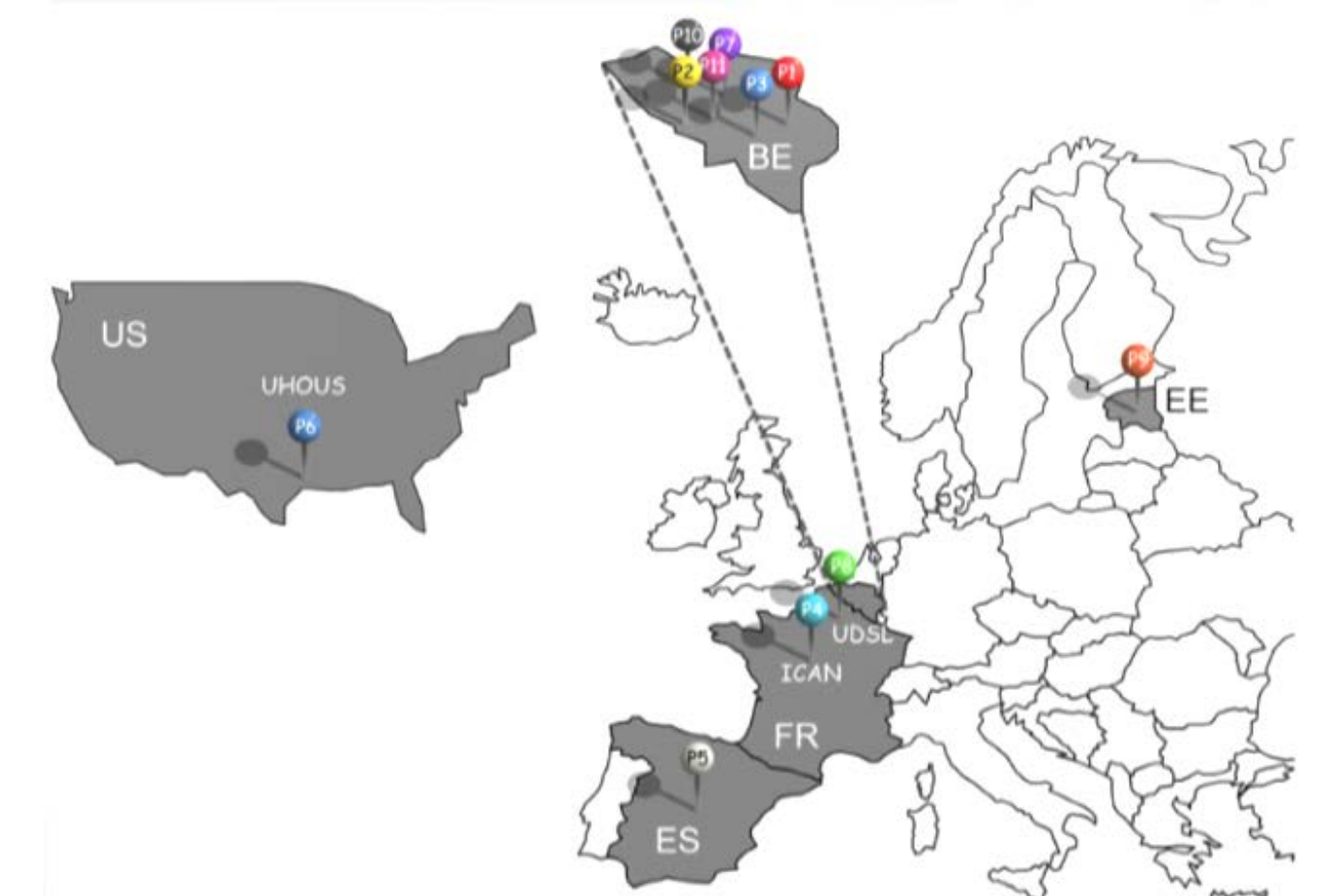
## The machine and its calibration



- Can be placed in a clinical ward and operated by the nursing team
- Provides results within < 1 h (including sample preparation and machine pre-test calibration)
- Coupled with a lap-top for calculation of patient’s individual PK parameters and suggestions for doses readjustment based on deviation between actual and desired free serum levels ( $C_{\max}$ ,  $C_{\min}$ , AUC, time > defined threshold, ...)



## The team



- Specific, sensor-based assay of **free**  $\beta$ -lactam concentrations (at bed-side);
- Calculation of deviations from predicted values and construction of a patient-**specific** pharmacokinetic profile;
- Correction of dosing in order to maintain the **free** serum concentration within predefined optimal limits.

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