Karlsruhe Institute of Technology

Modeling of DTPA decorporation therapy

Still puzzling after all these years

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Bundesamt für Strahlenschutz

KIT
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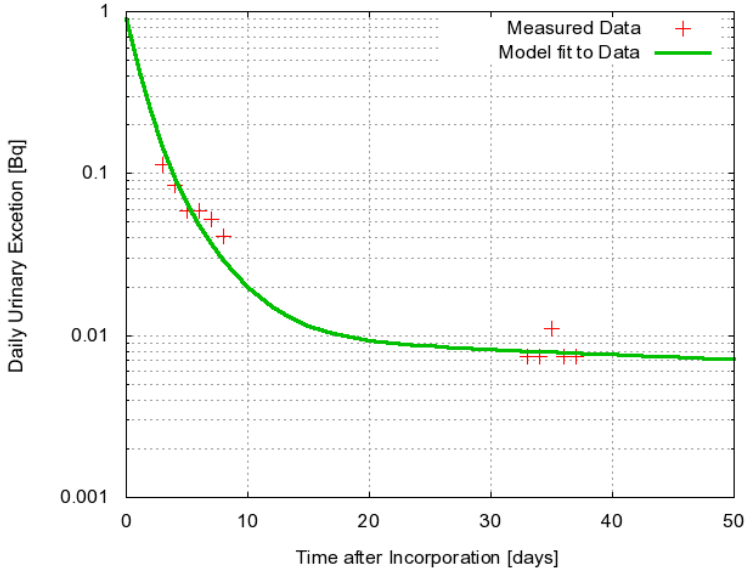
EURADOS

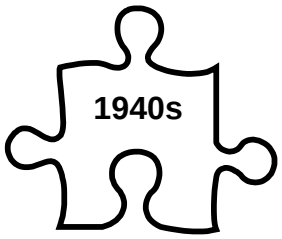
DTPA – still puzzling after all these years

- Dose assessment after Incorporation of Radionuclides is based on
  - **Measurements**
    - Urinary or fecal analysis
    - Whole/partial body counting (where possible)
  - **Modeling**
    - Biokinetic behaviour of radionuclide
    - Distribution of dose deposition



DTPA – still puzzling after all these years

- Studies on Biokinetics of Plutonium and other Actinides
  - First human injection studies
    - Langham et al.



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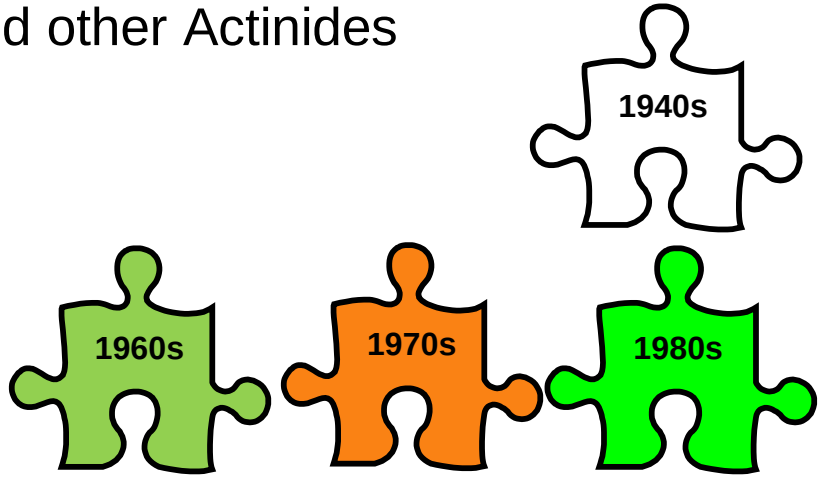

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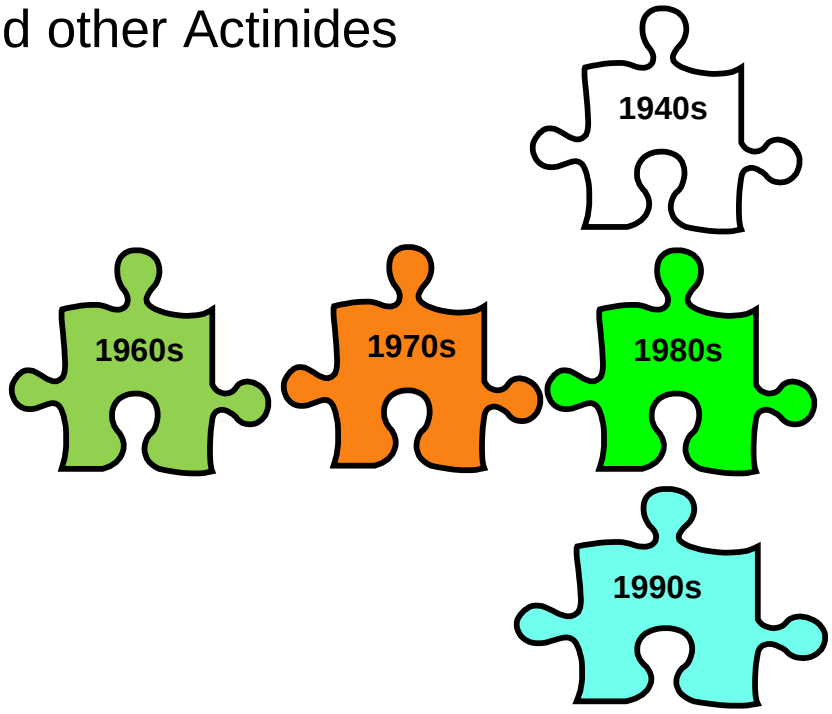
  - Latest Studies with human volunteers
    - Talbot et al., Newton et al.



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  - Latest Studies with human volunteers
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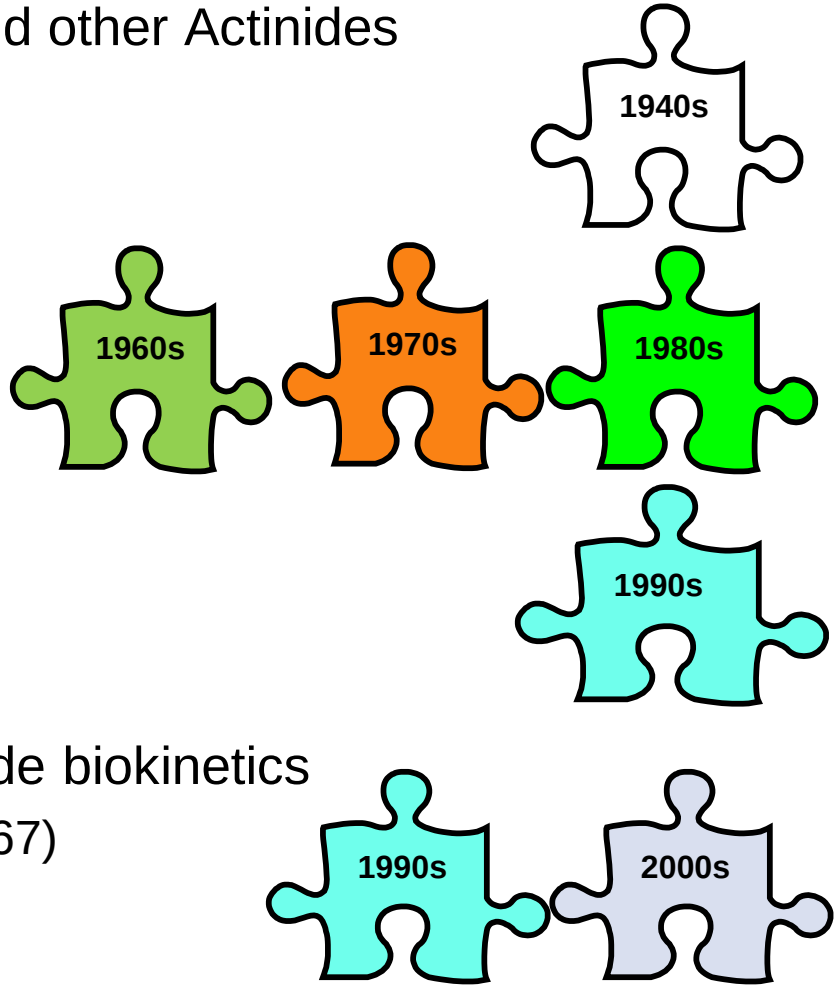
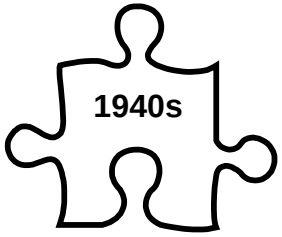
- Mathematical models of Pu and Actinide biokinetics
  - ICRP models (ICRP Publications 48, 67)
  - Latest model: Leggett et al. (2005)

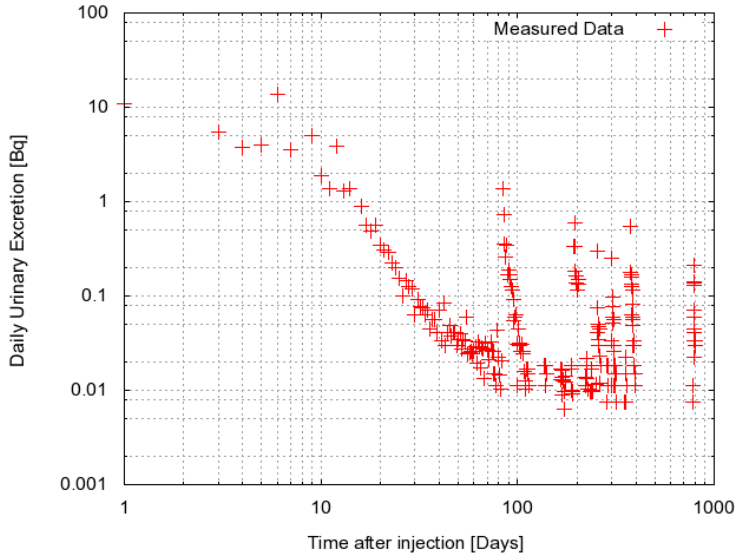


DTPA – still puzzling after all these years

- Decorporation therapy: Idea
  - mask the metal ion from it‘s „standard“ processess
  - Rapid excretion of masked metal-ion
  - If plutonium/actinide is removed from body it cannot deliver a dose inside

    → averted dose





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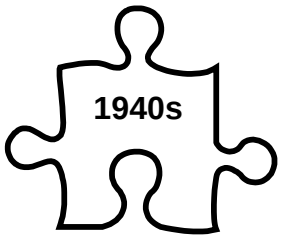
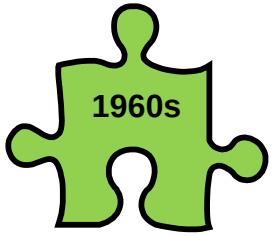
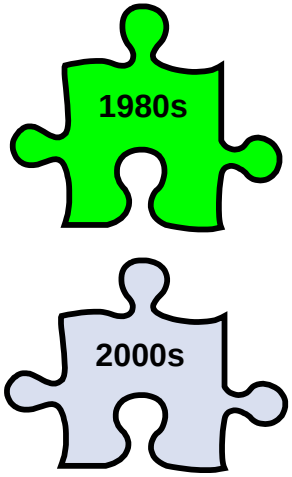


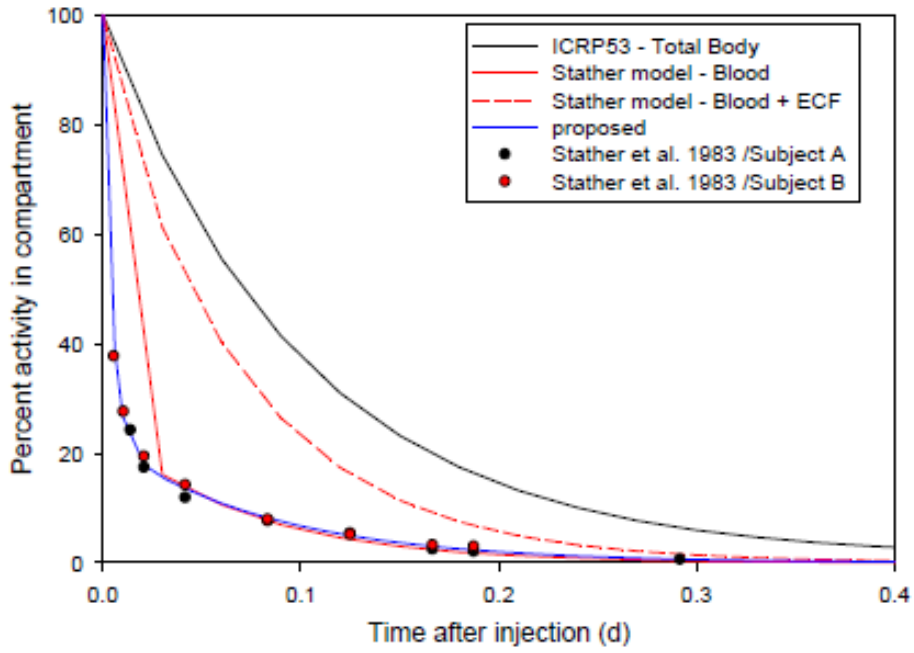
- Development of several chelating agents
  - DTPA available since 1960s



DTPA – still puzzling after all these years

- Biokinetics of DTPA
  - Human Study: Stather et al. 1983
  - Reinterpretation: CONRAD Project 2008

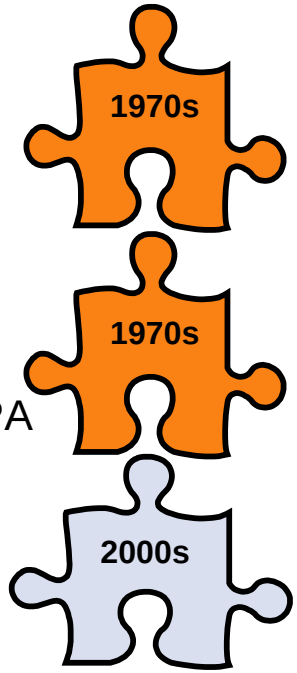


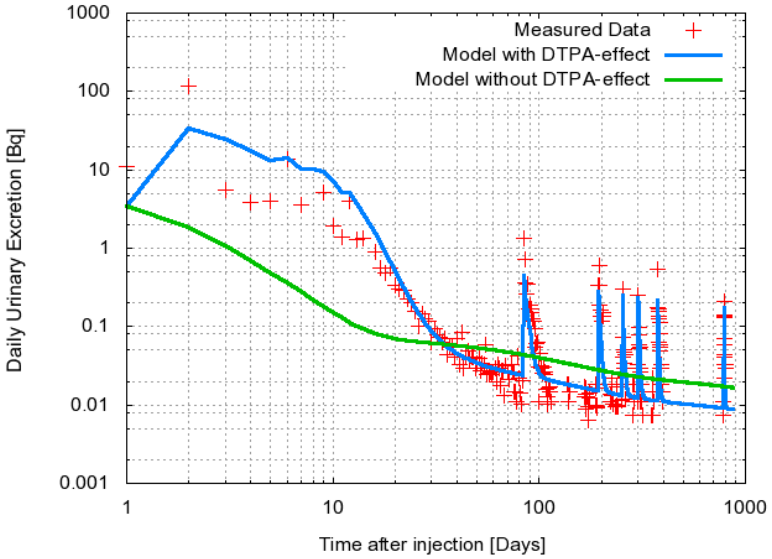


Taken from: Lopez M.A. et al., Final Report of CONRAD Work Package 5, CIEMAT-Report, Madrid

DTPA – still puzzling after all these years

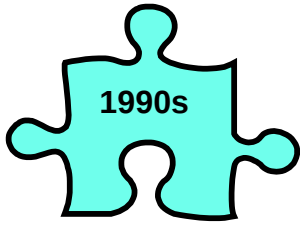
- Models of DTPA-decorporation therapy
  - „Wait and see“ Approach
    - Ignore data from first (100) days after therapy
  - Empirical Approach
    - Description of urinary excretion by mathematical function
    - Add terms describing (independent) additional excretion of Pu-DTPA

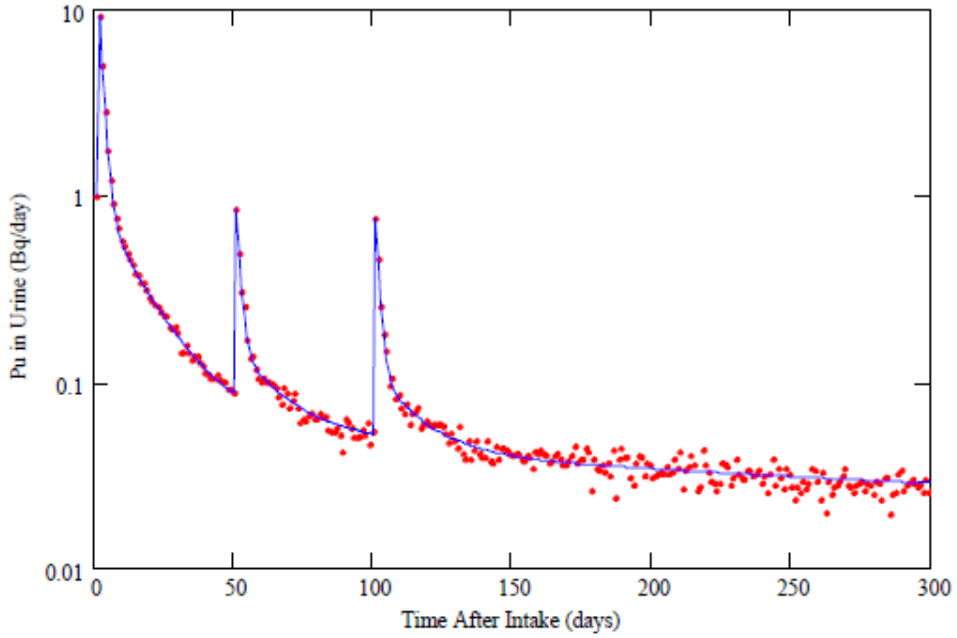




DTPA – still puzzling after all these years

- Models of DTPA-decorporation therapy
  - „Stop and go“ approach
    - Stop undisturbed model at time of therapy
    - Shift part of compartmental contens to urinary excretion
    - Continue calculation

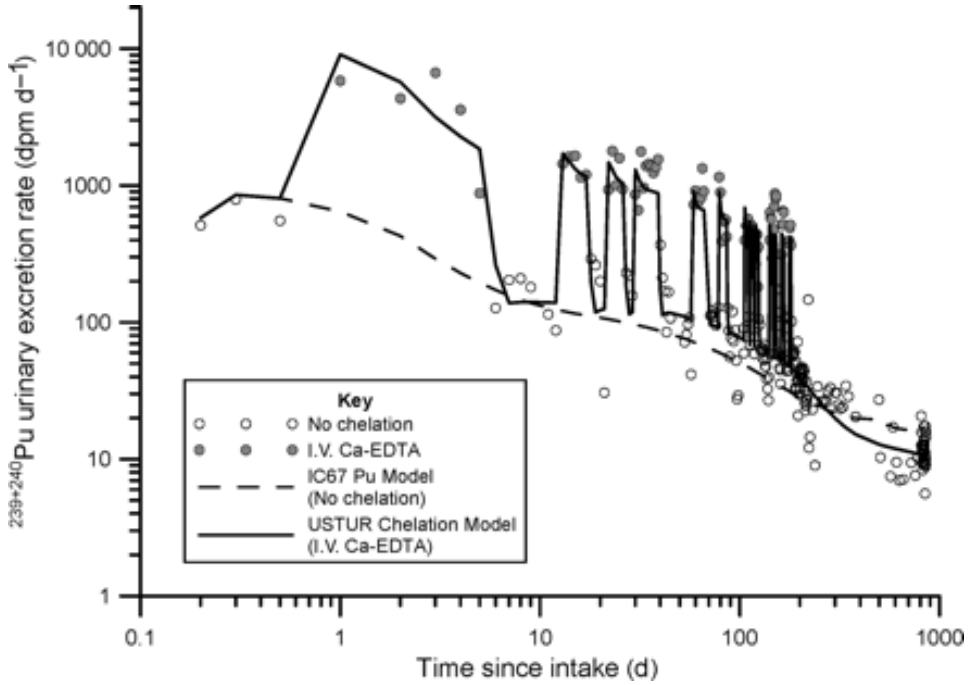


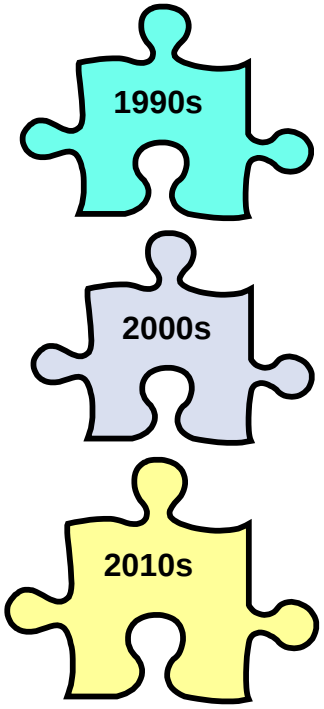


Taken from: T. La Bone „A comparison of Methods Used to Evaluate Intakes of Transuranics Influenced by Chelation Therapy, HPS Summer School 2002

DTPA – still puzzling after all these years

- Models of DTPA-decorporation therapy
  - Modification of existing compartmental models
    - Mostly case specific modeling
      - Additional compartments representing DTPA/Pu-DTPA
      - Multiplication factors for transfer rates

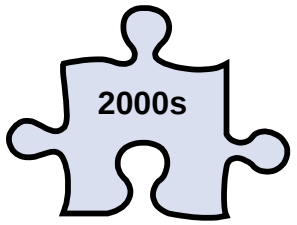


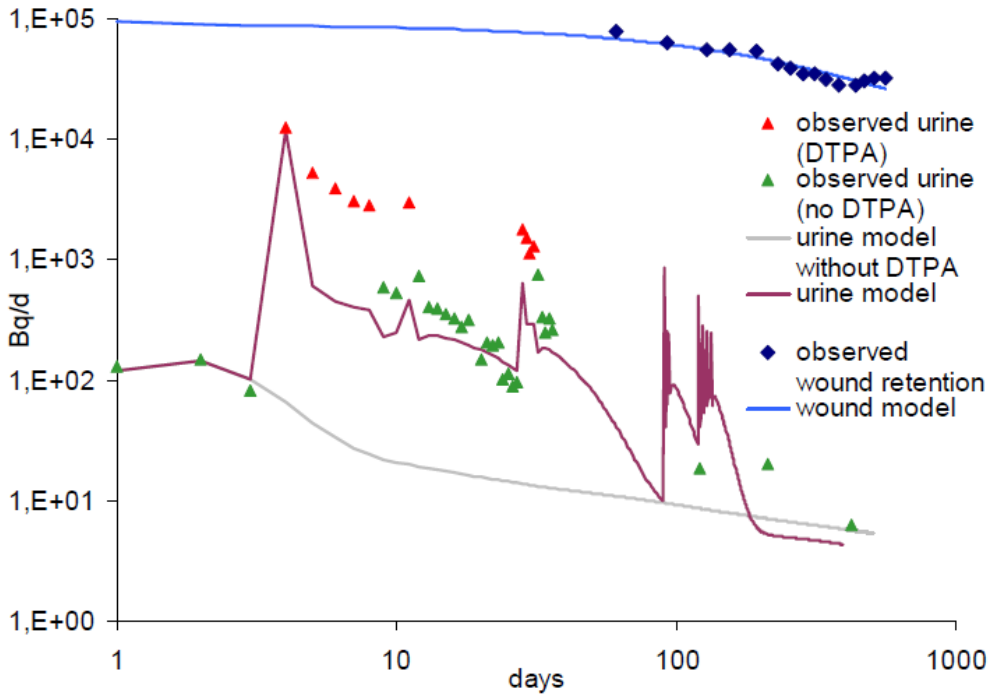


Taken from: James, AC et al. , Radiation Protection Dosimetry, 127(1-4), 449-455, 2007.

DTPA – still puzzling after all these years

- Models of DTPA-decorporation therapy
  - Expilict consideration of in-vivo chelation process
    - Coupling of Pu-model and DTPA-model
      - 2nd order kinetics





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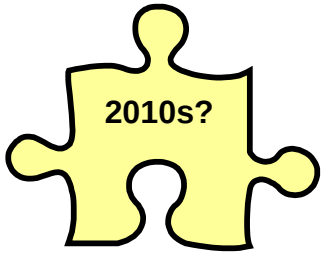
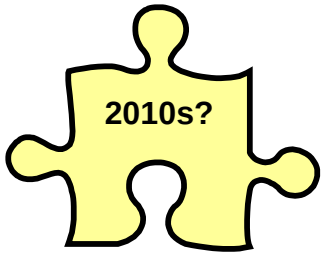
- Some open questions about DTPA decorporation
  - Where does the chelation take place?
    - Distribution volume of DTPA?
    - Which parts of the models are affected?



  - In-vivo chemistry of chelation?
    - Competitors for reactands?
      - Bio-ligands (e.g. Transferrin, Citrate)
      - Metal-ions (e.g. Zn-DTPA vs. Ca-DTPA)
    - Transfer of results from in-vitro studies → in-vivo
      - Influence of environment at location of chelation



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