



BIO-Europe Spring 2008

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Arecor



Arecor Limited was established to exploit the extensive experience of Unilever Research and the founders in the engineering of proteins for a range of applications

THE NEEDS

- ✘ Many proteins present obstacles in formulation and delivery:
 - + Drug candidates that are too unstable for development
 - + Proteins that cannot be readily formulated for new delivery strategies such as depot delivery
 - + Proteins that cannot be formulated as stable aqueous solutions for delivery



THE SOLUTION

Arecor has developed a *formulation technology* to stabilize proteins from damage or degradation by minimizing destructive events through adjustments in the ionic environment

- ✓ **Simple to implement** – *No new manufacturing steps*
- ✓ **Regulatory friendly** – *No modification of protein*
 - *Approved excipients*



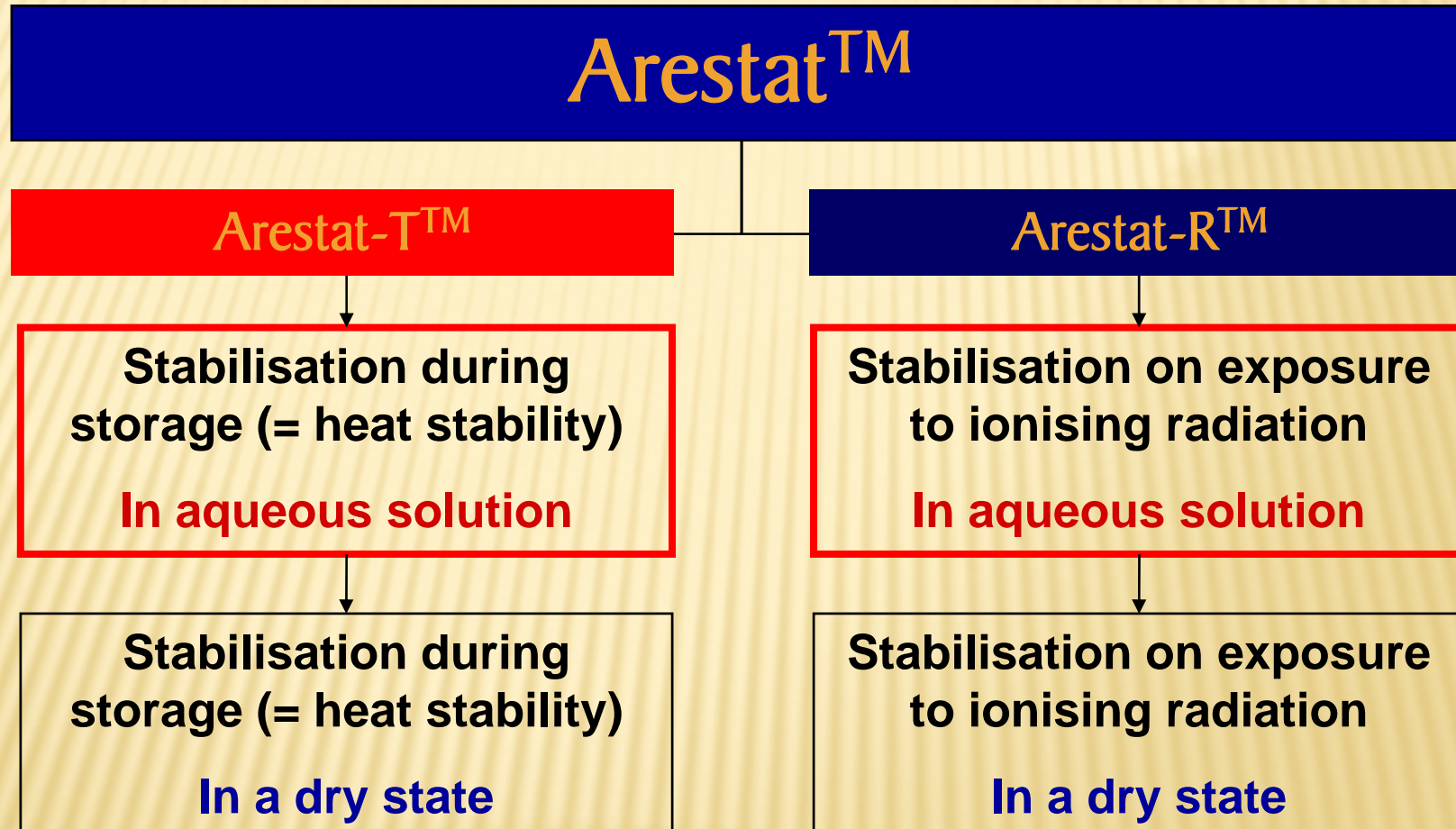
EXISTING APPROACHES

- Freeze-drying
 - ✗ costly to maintain sterility in production and limits presentation to powder
- Covalent modification of the protein
 - ✗ creating a new chemical entity with long and unpredictable regulatory hurdles
- Encapsulation technologies (e.g. glasses)
 - ✗ requiring substantial change to manufacturing practice and additional regulatory hurdles
- Excipients with no safe history of use in man
 - ✗ additional regulatory hurdles

All existing stabilization technologies carry significant limitations related to cost, regulatory approval, flexibility or ease of implementation



THE TECHNOLOGY



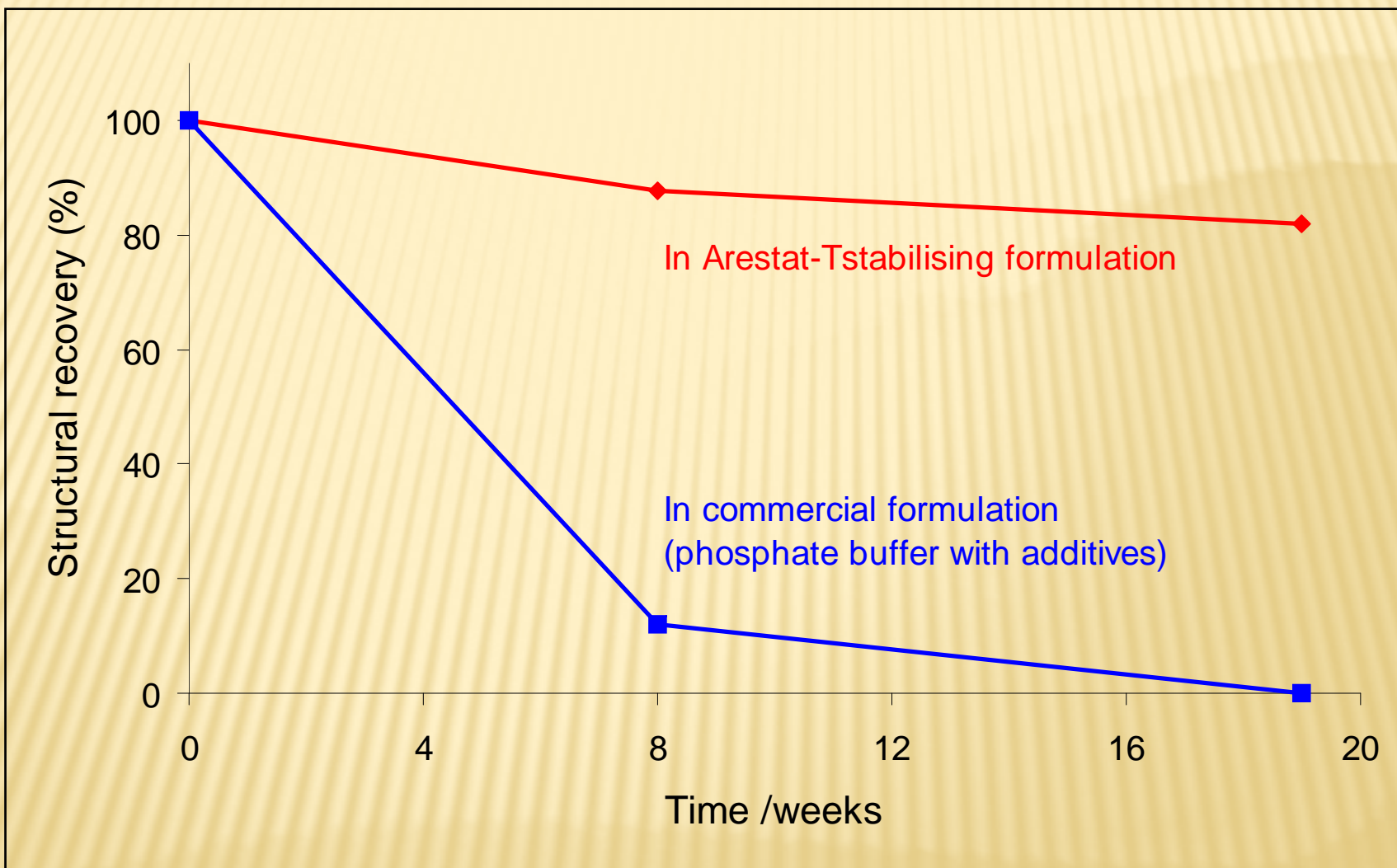
CASE STUDY – HUMAN GROWTH HORMONE

- ✘ Differentiated biosimilar
 - + Stable aqueous solution in pre-filled syringe
- ✘ Minimum specifications:
 - + Simple re-formulation with approved excipients
 - + Shelf life: 2 to 3 years at 2-8°C ; 3 months at 25°C
- ✘ Stability studies ongoing



Application of Arestat-T™

Human growth hormone at 25°C



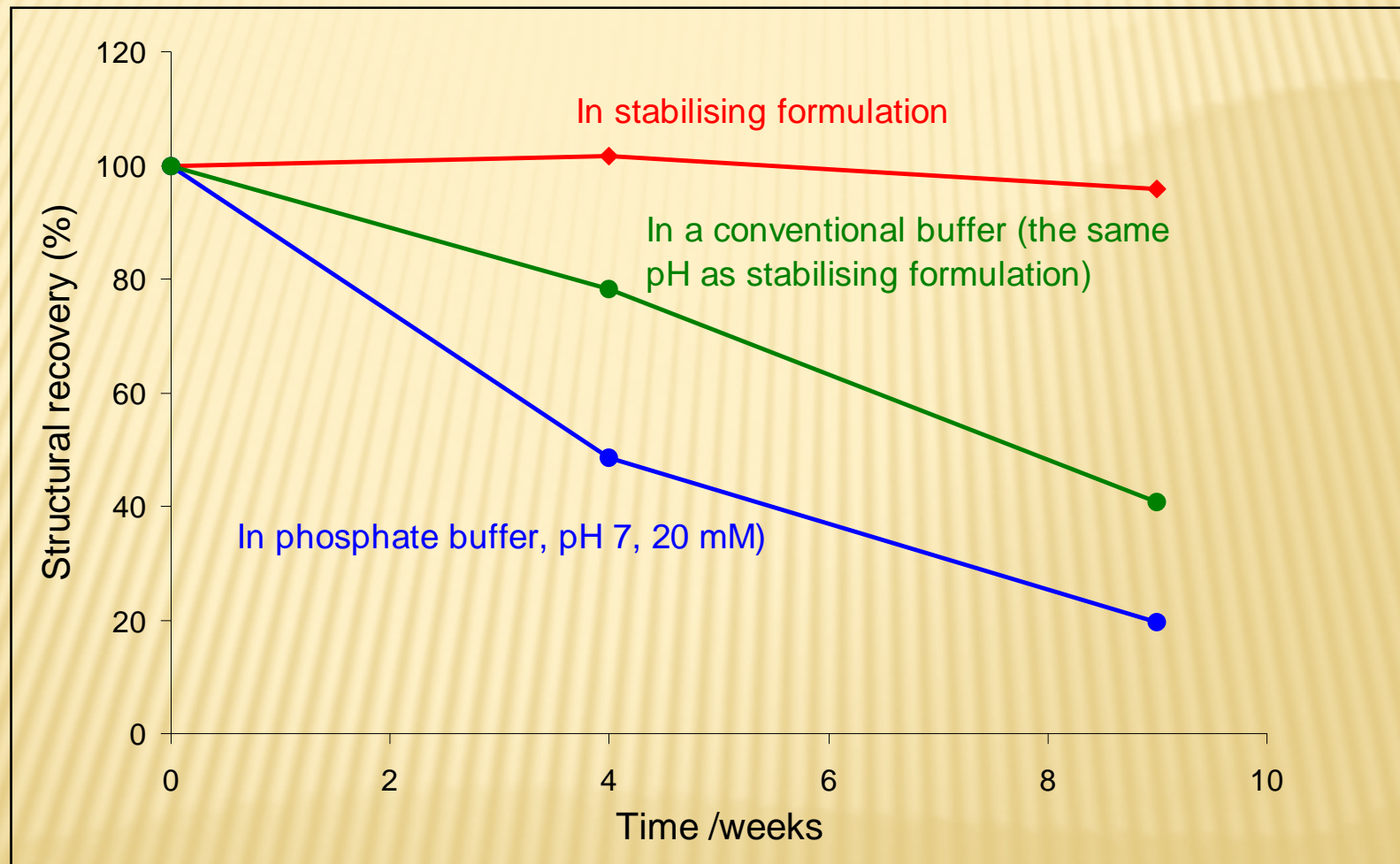
Pharmacopoeia RP-HPLC method used to assess structural stability

CASE STUDY – MONOMERIC INSULIN

- ✘ Company seeks new depot delivery of insulin
- ✘ Monomeric human insulin unstable – typically modified or converted to hexamer
- ✘ Minimum specifications:
 - + Stable formulation of monomeric human insulin stable at 25⁰C for 2 years /40⁰C for 12 weeks
- ✘ Stability studies ongoing



Application of Arestat-T™ Monomeric Human Insulin at 40 °C (structural stability)



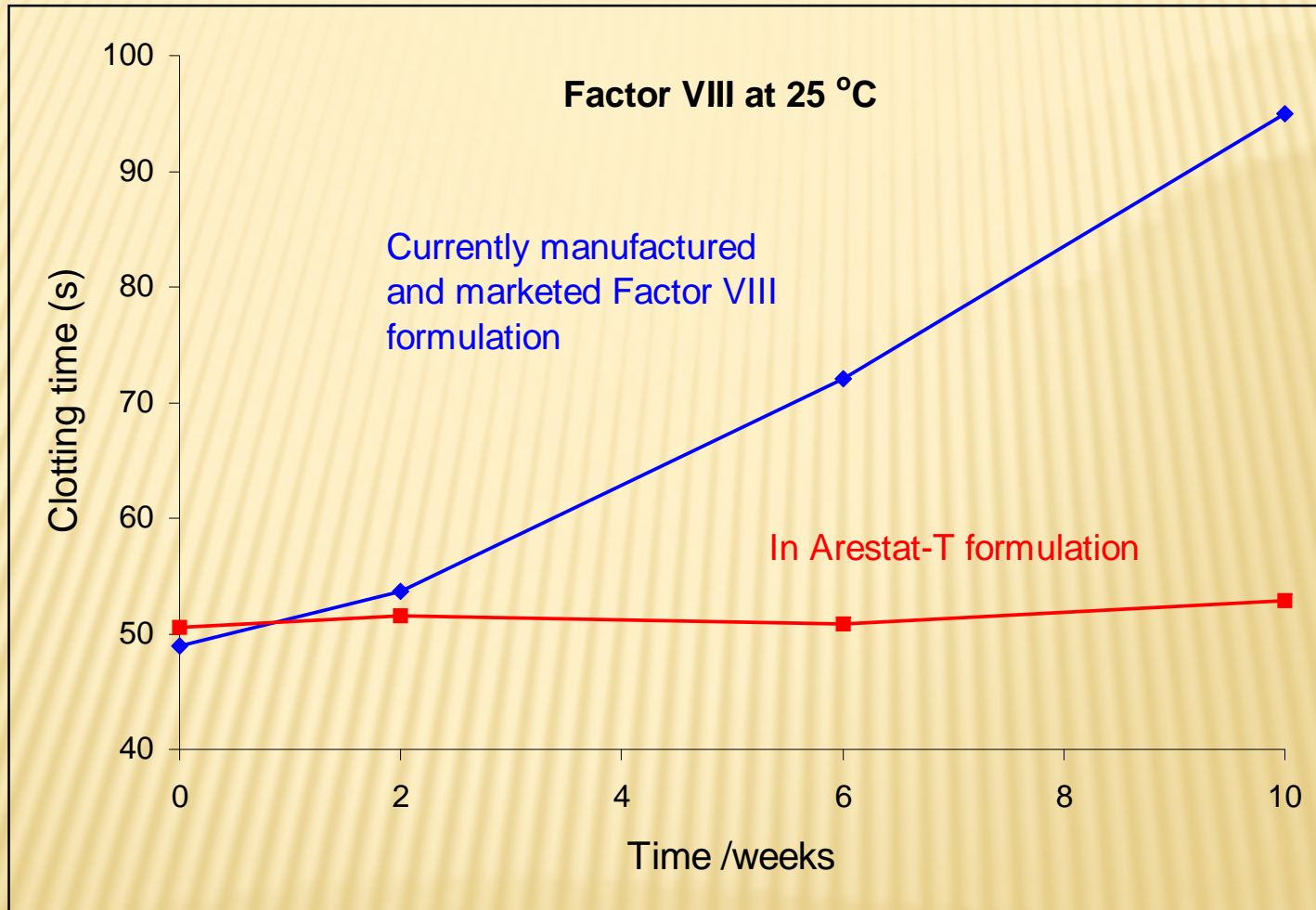
Pharmacopoeia RP-HPLC method used to assess structural stability

CASE STUDY – FACTOR VIII

- ✘ Grant funded project to improve stabilization of blood clotting factors in process and storage
- ✘ Large unstable protein requiring re-constitution
- ✘ Minimum specifications:
 - + Stable aqueous solution for 2 years at 2-8°C/6 months at 25°C
- ✘ Development ongoing



Application of Arestat-T Factor VIII at 25 °C



Measured by clotting time assay

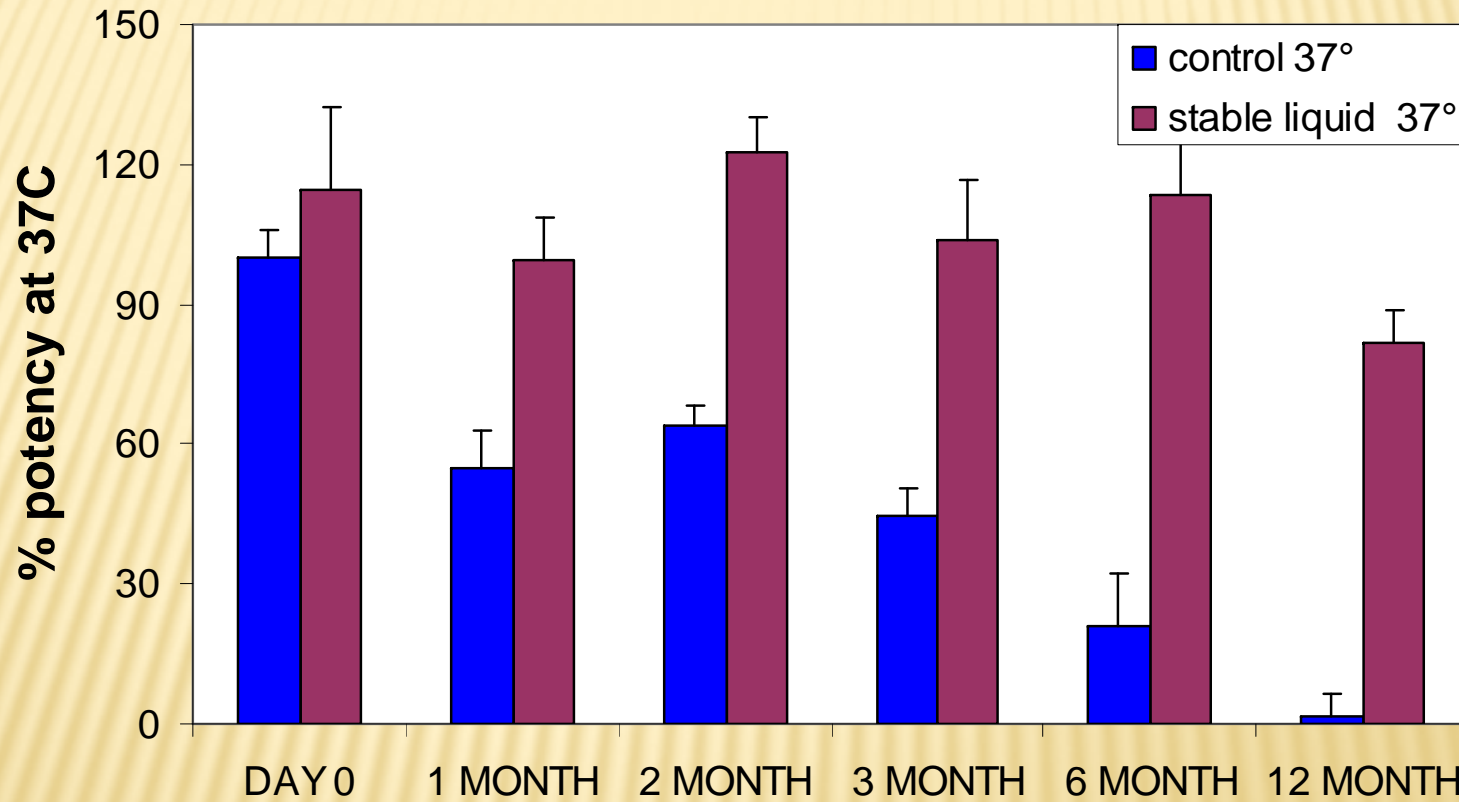


CASE STUDY:

A THERMOSTABLE HEPATITIS B VACCINE

- ✘ Joint program with PATH
- ✘ Combine ARESTAT with PATH's freeze protection
- ✘ Current shelf life: 2 to 3 years at 2°-8°C
- ✘ Minimum specifications:
 - + Freeze stability:
 - ✘ Does not freeze at -10°C or above?
 - ✘ May freeze, but is not damaged at temperatures as low as minus 20°C.
 - + Heat stability: 45°C for 6 months
- ✘ Negotiating non-exclusive licenses

HEAT-STABLE HEPATITIS B LIQUID VACCINE

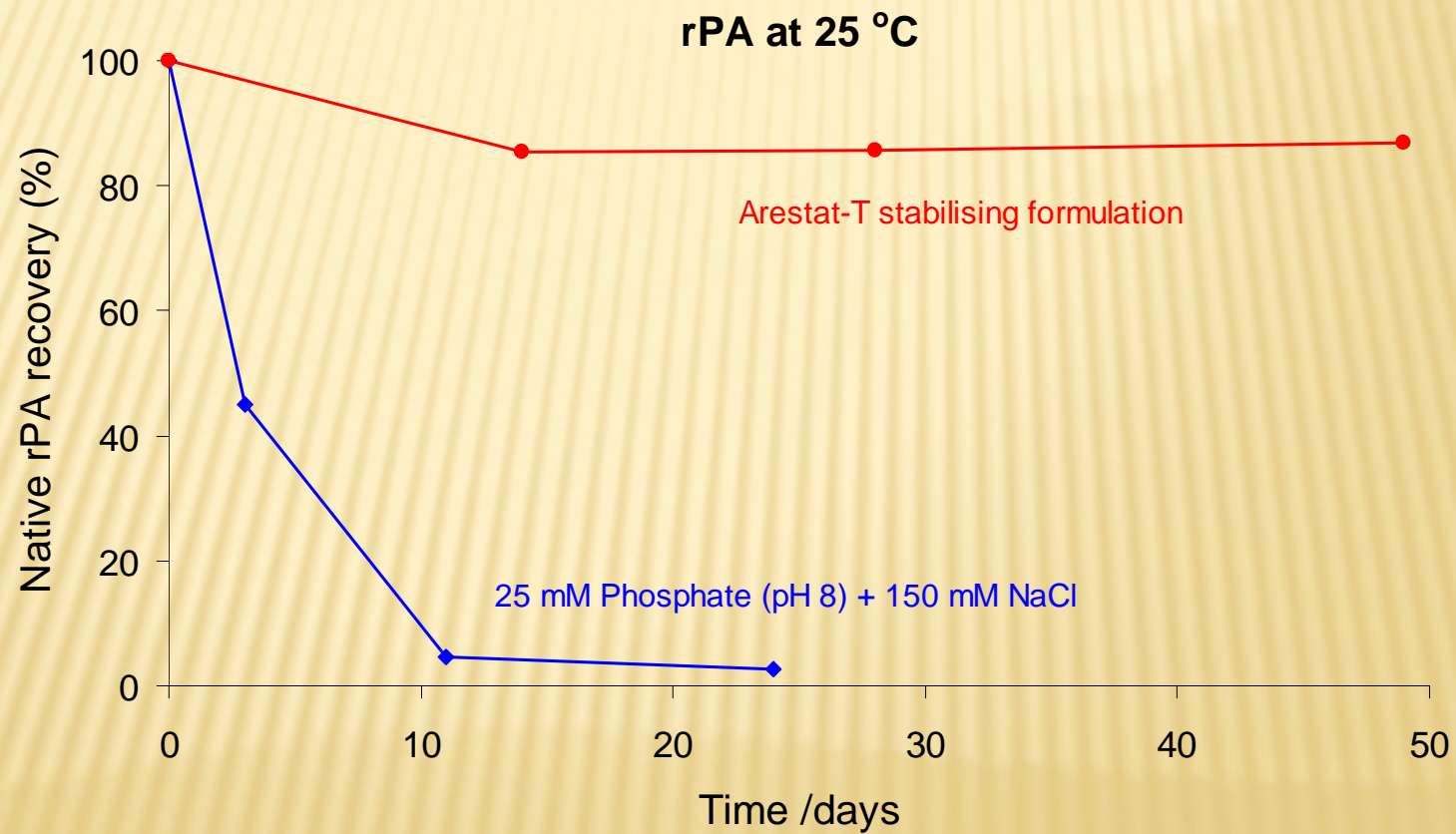


CASE STUDY: A THERMOSTABLE ANTHRAX RECOMBINANT PROTECTIVE ANTIGEN

- ✘ Program with the UK Health Protection Agency
- ✘ Minimum Specifications:
 - + Ready to use stable aqueous solution at 25°C
- ✘ Completed first phase indicating structural stability of native protein
- ✘ Stability of adjuvanted protein (alum) confirmed by polyclonal and monoclonal assays
- ✘ In vivo studies arranged



Recombinant Anthrax Vaccine (rPA) Stability at 25 °C



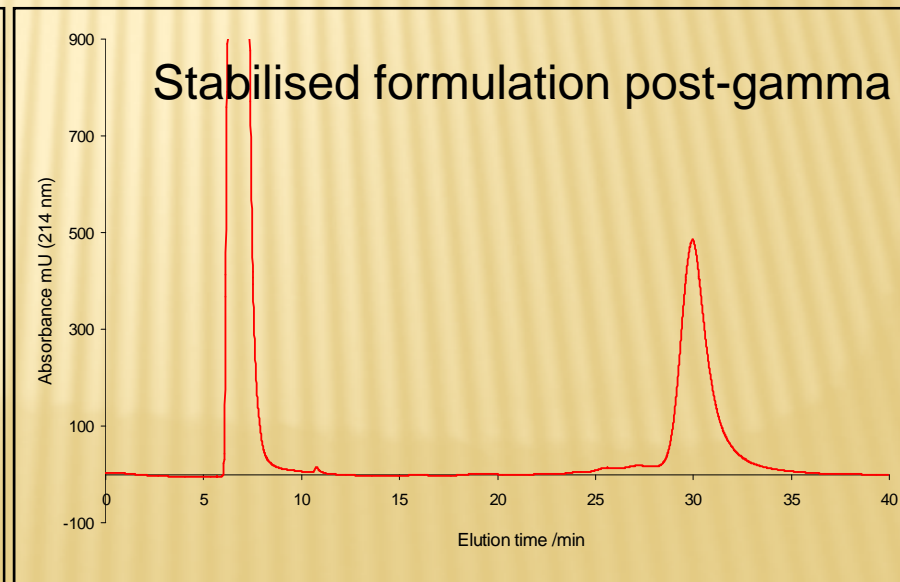
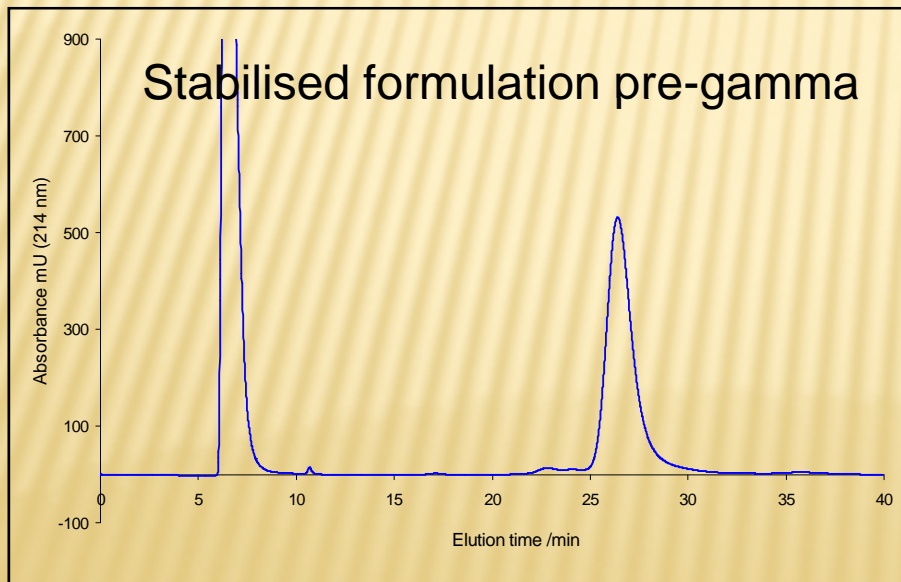
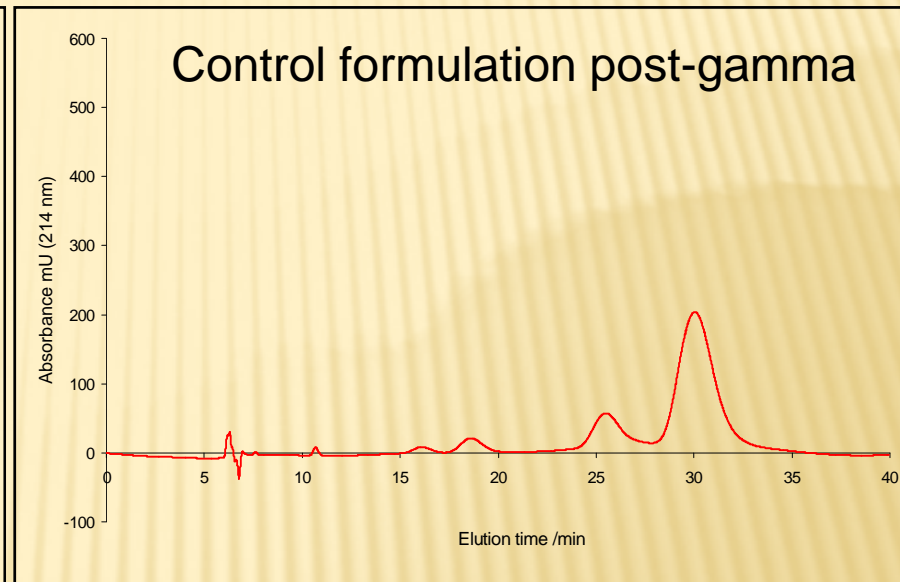
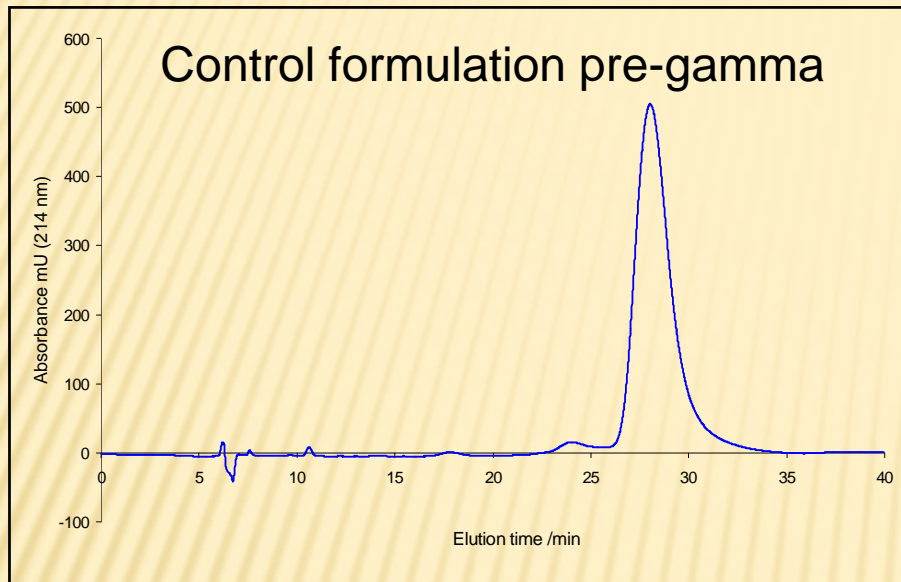
CASE STUDY – ARESTAT-R™

- × A drug delivery company wants to formulate human growth hormone for subcutaneous delivery injection as a solid depot
- × Aseptic sterilization is not practical; seeking option of terminal sterilization
- × Minimum specifications:
 - + >98% recovery product in the presence of 25kGy gamma radiation
- × Structural integrity confirmed by partner



Application of Arestat-R™

Dry hGH sterilised by gamma



APPLICATIONS FOR ARESTAT™

- ✘ *Unstable proteins in clinical development*
- ✘ *Ambient stable aqueous formulations*
- ✘ *Extended product shelf life*
- ✘ *Reduced production costs/increased yields*
- ✘ *Terminal sterilization of solid preparations*
- ✘ *Stable protein depot formulations*
- ✘ *Patent extension for proprietary proteins*



FOR FURTHER INFORMATION:

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