

Case Study

Characterising variants in clinical grade biopharmaceuticals

The Problem

Medicinal products extracted from biological sources, called biopharmaceuticals or biologics, must be carefully produced to ensure that only high purity active material is generated. Biopharmaceutical manufacturing processes can have an impact on the amount of product-related variants in the final clinical material. Understanding and controlling amounts of these product-related variants is a major challenge in the development of biopharmaceutical products.



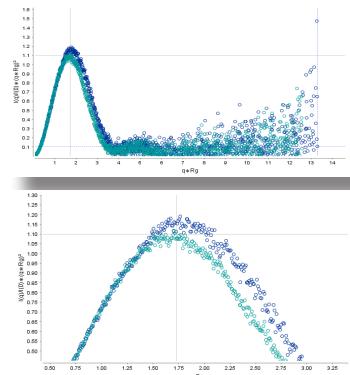
The Challenge

Erwinia chrysanthemi L-asparaginase (ErA), an enzyme commonly used in the treatment of acute lymphoblastic leukaemia, is manufactured and marketed as Erwinase® by Porton Biopharma. During biopharmaceutical development, ion-exchange HPLC is typically employed to evaluate and measure the extent of primary-sequence modifications, such as deamidation or methionine oxidation, which are important to monitor from a regulatory perspective. The ion exchange method routinely used for ErA indicates a significant proportion of material present (8-15%) is a product variant, but the method cannot identify the species present. Alternative characterisation methods were needed to gain a full understanding of the enzymatically-active, acidic variants.



The Solution

Scientists from Porton Biopharma made use of the Diamond small angle X-ray scattering (SAXS) data collection and analysis service to characterise the product variant. SAXS was used in combination with lab based techniques to prove that a conformational variant, not previously identified, was present in clinical grade ErA material. SAXS was also able to show that the conformational differences between the primary component and the variant were minor.



The Benefits

The highly-sensitive technique allowed Porton Biopharma to analyse the ErA variant in solution and provide reassurance to regulatory bodies that the subtle changes did not hinder the activity of the drug.

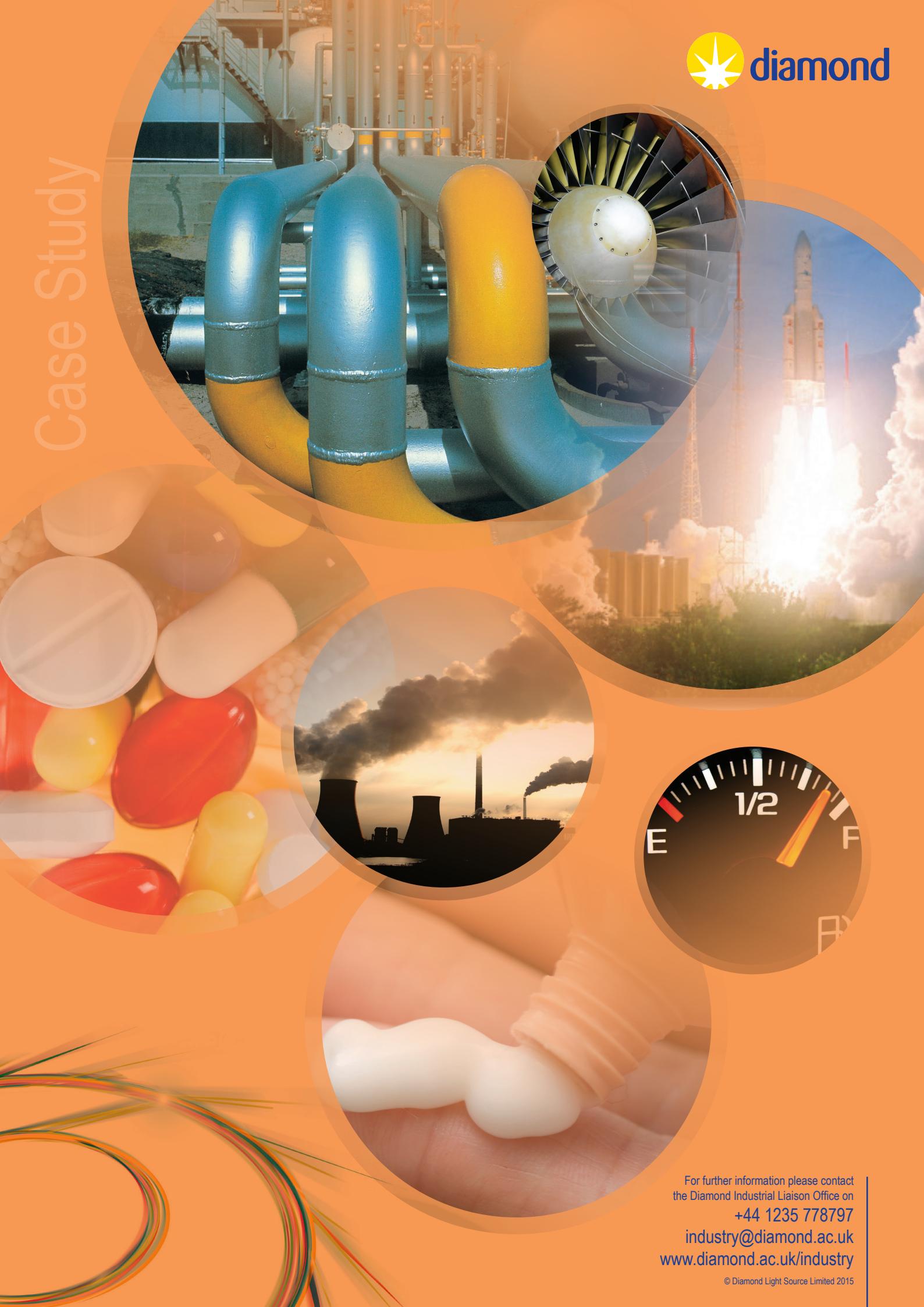


"Working with Diamond gives you access to world class experts and facilities and Diamond offers a specialist technique that isn't something many companies would have the ability to do themselves. SAXS is a very sensitive technique and it can detect tiny structural changes. No crystal was needed, so we just provided the sample in solution. We had telephone conversations before and after the study and received a detailed report of our results, which was really good. The people at Diamond were very quick to respond to our queries."

Dr Dave Gervais, Porton Biopharma

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