

### **e-Appendix 1: Measuring “big” IGF-II levels**

“Big” IGF-II levels are measured by a rather complex procedure involving acidic size-exclusion gel chromatography.<sup>1</sup> The presence of “big” IGF-II is indicated by the presence of a more diffuse peak that contains activity of a higher molecular weight. This typically elutes at fraction 34, unlike iodinated recombinant human IGF-II, which elutes at fraction 38.

Symmetrical curves are constructed around peak fractions 34 and 38, and the areas under the curves are taken to represent “big” and mature IGF-II respectively. Their serum concentrations are then calculated from total IGF-II values according to their proportion contribution. Our sample was sent to the United Kingdom and measured by Dr. J.D. Teale and Dr. G. Wark.<sup>2</sup>

<sup>1</sup>Teale JD, Marks V. Glucocorticoid therapy suppresses abnormal secretion of big IGF-II by non-islet cell tumours inducing hypoglycaemia (NICTH). *Clin Endocrinol (Oxf)* 1998;49(4):491-8.

<sup>2</sup>We thank Dr. J.D. Teale and Dr. G. Wark, Royal Surrey County Hospital, Guildford, UK, for their help in measuring IGF-II and “big” IGF-II.