NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Appraisal of the use of human growth hormone for the treatment of adults with growth hormone deficiency

Decision of the Appeal Panel

1. Introduction

1.1 An Appeal Panel was convened on 20th August 2002 to consider appeals against the Institute's guidance to the NHS on the use of human growth hormone (HGH) for the treatment of adult growth hormone (GH) deficiency.

1.2 The Appeal Panel comprised Professor Sir Michael Rawlins (chair of the Appeal Panel and chair of the Institute), Mr Frederick George and Ms Mercy Jeyasingham (non-executive directors of the Institute's Board), and Dr Robert Donnelly (industry representative).

1.3 Appeals were lodged by the following appellants:

- Eli Lilly
- Novo Nordisk
- Pharmacia
- The Society for Endocrinology and the Royal College of Physicians of London ("SoE and the RCP")
- The Society for Paediatric Endocrinology and the Royal College of Paediatrics and Child Health ("SoPE and RCPCH")
- The Pituitary Foundation

1.4 All the appellants were represented at the appeal.

1.5 In addition, the following individuals involved in the appraisal were present and answered questions from the Appeal Panel: Professor David Barnett (chair of the Appraisal Committee), Anne-Toni Rodgers (communications director and executive lead for this appraisal), Dr Carole Longson (Appraisals Programme

Director), Prof Phillip Routledge (Appraisals Committee member), Prof John Brazier (health economist ScHARR), Dr Dogan Fidan (technical lead), Janet Robinson (technical analyst), David Murray (technical team leader).

1.6 Kathleen Dalby, Technology Appraisal Project Manager at the Institute, was present. The Institute's legal advisor (Stephen Hocking, Beachcroft Wansbroughs) was also present.

1.7 The three grounds on which the Appeal Panel can hear an appeal are:

1) The Institute has failed to act fairly and in accordance with its procedures.

2) The Institute has prepared guidance which is perverse in the light of the evidence submitted.

3) The Institute has exceeded its powers.

1.8 Before the arrival of the Institute's representatives to the meeting the chairman of the Appeal Panel explained to the appellants that one member, Ms Chi Chi Iweajunwa, was unable to attend. Consequently the Appeal Panel would comprise only four members. The chairman apologised for this but indicated that it was for the appellants to decide whether they wished, nevertheless, to proceed with the appeal with a four member panel or whether they wished to seek an adjournment to enable a 5-member panel to be established at some future date. The Appeal Panel withdraw and after discussion amongst themselves the appellants expressed their unanimous wish to continue with the appeal. The Institute's representatives then joined the meeting.

2. Appeal Ground One: The Institute has failed to act fairly and in accordance with the Appraisal Procedure set out in the Institute's Interim Guidance to Manufacturers and Sponsors.

2.1 The SoE and the RCP alleged that insufficient weight had been given to the opinion of expert endocrinologists. They also expressed disappointment that, whilst they had been asked to withdraw their nominated expert (because of a perceived conflict of interest), this did not apply to the expert nominated by the Pituitary Foundation. The appellants were also disappointed that there was no endocrinologist as a full member of the Appraisal Committee.

Professor Barnett explained that the Institute, in its letter inviting the SoE and the RCP to assist in this appraisal, had indicated that persons with specific interests (i.e. those with shares in the companies, or who were in receipt of personal money from the company) were inappropriate. Professor Sheppard attended the first meeting of the Appraisal Committee and Professor Johnson attended the second meeting. Both made valuable contributions. Professor Barnett also indicated that the expert nominated by the Pituitary Foundation did not attend the relevant meetings of the Appraisal Committee.

The chairman of the Appeal Panel explained that the membership of the Appraisal Committee was fixed, and that it was not in the statutory powers of the Institute (at that time) to make additional *ad hoc* appointments.

The Appeal Panel considered that the Appraisal Committee had taken the opportunity to consider the opinions of relevant experts both in writing and at two meetings of the committee. The panel also considered that the Institute had acted in accordance with its procedures in asking for the replacement of the SoE and RCP nominated expert who had a personal interest in the appraisal.

The Appeal Panel did not, therefore, consider that the Appraisal Committee had acted unfairly in this respect and accordingly dismissed the appeal on this point.

2.2 The SoE and RCP alleged that the Appraisal Committee was inconsistent, with respect to HGH, in comparison to some of the other technology appraisals that had undertaken.

The Appeal Panel considered that some differences in approach were inevitable in view of the range of technologies, and diseases, that the Appraisal Committee was expected to consider. The Panel did not consider that the examples quote by the SoE and the RCP constituted unjustified, or unfair, differences in approach between HGH and other pharmaceuticals.

The Appeal Panel accordingly dismissed the appeal on this point.

2.3 The SoE and RCP claimed that the Institute had unfairly adopted the "Interim Procedure", rather than the revised procedure, in its appraisal of HGH for adult growth hormone deficiency.
Professor Sir Michael Rawlins absented himself from the Panel's consideration of this point, as he had previously corresponded with the Appellants on this issue.

On 6 February 2001, the Institute's Board resolved that all appraisals initiated after that date should be carried out under a revised procedure. Appraisals initiated before that date would be carried out under the "Interim Procedure".

On 30 November 2000 the DoH and NAW wrote to the Institute to include in its work programme an appraisal of HGH in growth deficiencies and growth failure in children, and advice on the clinical and cost effectiveness of the use of HGH in adults. However this latter element was stated to be the subject of further consultation and was included in a list of topics "being considered for referral to NICE". In a letter

dated 21 February 2001 the DoH and NAW "formally notified" the Institute that HGH for adult use should be appraised as a "new topic". The remit included with that letter, however, referred to the "extension" of the appraisal of HGH in children to its use with adults.

The Panel therefore had to consider whether the letter of 21 February "initiated" an appraisal of HGH in adults. Whilst the language of the letters received by the Institute could have been more consistent, the Panel concluded that the Institute and the DoH/NAW had consistently understood the letter of 30 November 2000 to have initiated an appraisal of HGH in children and in adults, albeit that the exact terms of the adult work-stream were subject to consultation. The Panel noted evidence from Anne-Toni Rogers that "initiation" of an appraisal might occur before its "referral" and that in fact work had begun on use of HGH in adults before 6 February 2001. The Panel observed that this is consistent with the treatment of this work as one appraisal rather than two, as was the case for most of its history.

The Appeal Panel therefore rejected the appeal on this point.

2.4 The Pituitary Foundation complained that the conduct of the two Appraisal Committee meetings its representatives had attended was hostile and adversarial, and mitigated against their fair participation in the process. In particular, individual members of the committee made comments that the Foundation considered inappropriate, discussion of some points was disallowed, and the Foundation's representatives felt that they had been given insufficient time to make their points.

Professor Barnett rejected these allegations. He explained that the alleged remarks had been quoted out of context, and that the Foundation's representatives had been given adequate opportunity to sate their case. He accepted that at the first meeting of the Appraisal Committee, to consider HGH in adult

GH deficiency, there was insufficient information for the committee to draw conclusions. For this reason the committee took the unusual step of seeking a further assessment report (from ScHARR) and invited the Pituitary Foundation to the meeting at which this was considered. The Foundation had therefore been provided with two separate opportunities to make their case. Professor Sheppard, who had been present at the relevant Appraisal Committee meetings, confirmed that although the remarks complained of by the Pituitary Foundation had been made he had not considered them to be pejorative.

The chairman of the Appeal Panel indicated that the Board of the Institute expected the Appraisal Committee to treat consultees with respect and courtesy at all times. The Panel accepted that although the remarks complained of were unfortunate, they were not intended to be pejorative of either the Pituitary Foundation or the use of HGH in adults. Nor did the Panel consider that the Foundation had been given inadequate opportunity to present its case.

The Appeal Panel therefore rejected the appeal on this point.

2.5 The Pituitary Foundation alleged that the evidence put before the Appraisal Committee was inadequate and misleading. In particular, the evidence relating to the use of HGH in children and adults was mixed together, the committee appeared unfamiliar with the evidence, the first assessment report failed to include important studies relevant to UK practice, the ScHARR report placed inappropriate emphasis on the “Spanish” study, and was incorrect in claiming that no study showed what happened to untreated patients.

Professor Barnett accepted that the initial assessment report relating to the use of HGH in adults provided insufficient information for the committee to reach a robust conclusion. For this reason, as outlined in paragraph 2.4 above, the committee requested a further report from ScHARR. He rejected, however,

the Foundation's claim that the committee was unfamiliar with the evidence: members were diligent in their scrutiny of all the evidence placed before them. Professor Barnett also indicated that the committee had based its conclusions on the totality of the evidence: this included both controlled clinical trials and observational studies (e.g. KIMS). He explained that the committee had given the closest attention to studies using the condition-specific quality of life measure (QoL-AGHDA) because of its potential to provide a more reliable estimate of the benefits of treatment. Professor Barnett also explained that the reference, in the ScHARR report, to the lack of data in untreated patients was in respect of the observational studies.

The Appeal Panel considered that the Appraisal Committee had acted appropriately and fairly in requesting a further assessment report (from ScHARR). The Panel also considered that the committee had given full weight to all the available evidence (including both the controlled trials and the observational studies) and that this was clearly described in the Final Appraisal Determination (FAD). Furthermore, the Panel did not consider that the Appraisal Committee had been misled by the ScHARR report in its reference to the lack of data in untreated patients.

The Appeal Panel therefore rejected the appeal on this point.

2.6 The Pituitary Foundation claimed that because its representatives had not been present when the Appraisal Committee drew its conclusions on the use of HGH in adults, it was unable to develop a reasonable refutation.

The Appeal Panel considered that the Provisional Appraisal Determination (PAD) provided a full account of the reasons for advising against the use of HGH in adults, and that the Foundation had not therefore been treated unfairly.

The Appeal Panel therefore rejected the appeal on this point.

3. Appeal Ground Two: The Institute has prepared guidance which is perverse in the light of the evidence submitted.

3.1 The SoE and the RCP alleged that the proposed guidance was at variance with accepted clinical practice and clinical opinion in the UK and internationally.

Professor Barnett explained that the Appraisal Committee had given full consideration to the views of the clinical experts who submitted evidence (both orally and in writing) to the Institute. The committee, however, was required to consider both clinical *and* cost effectiveness in its appraisals of technologies referred to it.

The Appeal Panel did not consider that the Appraisal Committee had acted perversely in proposing guidance that was at variance with accepted clinical practice and opinion.

The Appeal Panel therefore rejected the appeal on this point.

3.2 The SoE and the RCP claimed that the proposed guidance was based on the premise that all adult HGH deficient patients would be treated with HGH. The SoE and the RCP recommended that only those with severe HGH deficiency should be treated with HGH. Indeed, they alleged that this was current practice in the UK where the SoE's guidelines had been widely adopted by endocrinologists. As a consequence, the appellants estimated that only 14% of adults with GH deficiency were currently treated with HGH.

Professor Barnett explained that the Appraisal Committee had considered, most carefully, whether it

was possible to identify and treat a subgroup of patients in whom HGH therapy would be cost effective (FAD 4.3.6). It had concluded, however, that the criteria drawn up by the SoE were not appropriate to predict response.

The appellants accepted that there were no data from randomised controlled trials, using the SoE selection criteria, to enable the benefits of treatment with HGH to be assessed. The data from the KIMS data-base suggested, however, such patients did derive substantial benefit.

The Appeal Panel fully accepted that the Appraisal Committee had attempted, in good faith, to identify a subgroup of adult GH deficient patients in whom treatment with HGH might be clinically and cost effective using the SoE criteria. The Appeal Panel was disappointed with the quality of data on the clinical and cost effectiveness of treatment with HGH in adult GH deficiency, and with the paucity of data to support current UK practice. Nevertheless, the Appeal Panel was concerned that there might exist a group of patients with adult GH deficiency in whom HGH was clinically and cost effective. Indeed, there were suggestions in the ScHARR report to support this possibility (pages 39 to 41).

The Appeal Panel therefore upheld the appeal on this point. The Institute should undertake further discussions with consultees aimed at defining, with greater precision, appropriate selection criteria for patients with adult GH deficiency in whom treatment with HGH might be clinically and cost effective. Such selection criteria should not, necessarily, preclude the consistent use of a single, specific, validated measure of quality of life (e.g. QoL-AGHDA). These discussions should also entertain the possibility of identifying patients who, after a predefined period of treatment, respond inadequately and in whom therapy with HGH should be withdrawn. The Appraisal Committee should be asked to review its guidance in the light of these discussions.

3.3 Eli Lilly alleged that the Appraisal Committee had been inconsistent in its appraisals of HGH therapy in children and adults. Whilst the committee had recommended use in children on the basis of limited evidence from randomised controlled trials, it had declined to recommend use in adults despite the existence of substantive data from both randomised controlled trials and observational studies.

Professor Barnett explained that the quality of data available to the committee, in its appraisal of HGH in adults with GH deficiency, was of generally poor quality and that this problem had been discussed in the guidance (FAD 4.1.10, 4.3.5).

The Appeal Panel considered that the Appraisal Committee was required to consider each appraisal on its merits; and that it was expected to make judgements about the balance between clinical and cost effectiveness on a case-by-case basis. The Appeal Panel did not, in this instance, consider that the Appraisal Committee had acted shown any fundamental inconsistency or had acted perversely.

The Appeal Panel therefore rejected the appeal on this point.

3.4 Eli Lilly alleged that the Appraisal Committee did not give thought to the implementation of an adequate selection process in its appraisal of HGH for adults with GH deficiency.

Professor Barnett pointed out that the committee (FAD 4.3.6) indeed considered this but rejected it.

The Appeal Panel considered that the Appraisal Committee had indeed clearly given thought to this issue. Nevertheless, as discussed in paragraph 3.2 above the, Panel considers further steps should be taken to investigate the possibility that HGH treatment may be cost effective under certain circumstances.

The Appeal Panel therefore upheld the appeal on this point.

3.5 Eli Lilly alleged that quality of life data using QLS-H had been ignored in both the assessment reports.

Professor Barnett confirmed that the Appraisal Committee had, indeed, given consideration to studies using QLS-H as a measure of patients' quality of life but did not regard these as contributing further to the evidential base.

The Appeal Panel therefore rejected the appeal on this point.

3.6 Eli Lilly alleged that the guidance (FAD 4.3.3) discounted the effect of HGH treatment using the Nottingham Health Profile (NHP) on the grounds of possible biased reporting.

Professor Barnett explained that there were several problems with the use of the NHP in assessing the changes in quality of life associated with HGH treatment. In particular, pooled analyses could only be undertaken from those studies reporting results in full. The results from other studies were necessarily excluded and the possibility of bias was therefore real.

The Appeal Panel recognised that pooled results from a partial data-set inevitably lead to concerns of bias. It did not therefore consider that the Appraisal Committee had acted perversely.

The Appeal Panel therefore rejected the appeal on this point.

3.7 Eli Lilly alleged that the Appraisal Committee had ignored the effects of HG on body composition, bone mineral density and cardiovascular risk.

Professor Barnett indicated that the Appraisal Committee had indeed considered these potential benefits of HGH therapy. The committee had

concluded that the effects on body composition were best reflected from quality of life data. Professor Brazier stated that the other clinical data had also been incorporated into the ScHARR cost effectiveness model.

The Appeal Panel considered that the Appraisal Committee had, indeed, taken account of these clinical benefits and had not acted perversely.

The Appeal Panel therefore rejected the appeal on this point.

3.8 Eli Lilly claimed that the guidance failed to provide advice for children with growth failure with GH deficiency making the transition to adult life. The company's representatives pointed out that in the published guidance for children with GH deficiency (Technology Appraisal Guidance - No 42) it states (paragraph 7.3) "The decision to stop treatment is made by the paediatrician with special expertise in the management of GH disorders in consultation with the patient and carers or therapy is continued until re-evaluation by an adult endocrinologist has been undertaken". The proposed guidance for adults with GH deficiency provided no clear advice in these circumstances.

Professor Barnett accepted that the guidance, as constructed, considered only patients with GH deficiency acquired in adulthood.

The Appeal Panel noted that the referral from the Department of Health and the Welsh Assembly Government requested the Institute to advise on "the clinical and cost effectiveness of the use of human growth hormone in its licensed indications for adults". The Appeal Panel therefore considered that the Appraisal Committee had acted perversely in not providing guidance on the use of HGH in adults previously treated for growth failure as children.

The Appeal Panel therefore upheld the appeal on this point. The Appraisal Committee should prepare revised guidance that included advice to the NHS on this matter.

3.9 Eli Lilly claimed that attempts should be made to identify patients likely to achieve the greatest benefit from treatment.

The Appeal Panel, noting the comments of Professor Barnet, as well as its conclusions and recommendations in paragraphs 3.2 and 3.4 above, accepted this.

The Appeal Panel therefore upheld the appeal on this point.

3.10 Eli Lilly claimed that the initial 3 months treatment with HGH, usually provided free of charge by manufacturers, had not been considered in the estimates of cost effectiveness provided in the ScHARR report.

Professor Brazier confirmed that this was correct but indicated that including this in the ScHARR model reduced the cost per quality adjusted life year (QALY) by only £2,000.

The Appeal Panel accepted that this would have made little difference to the Appraisal Committee's conclusions about the cost effectiveness of HGH in treatment of adult GH deficiency. It did not consider, therefore, that the guidance was perverse.

The Appeal Panel therefore rejected the appeal on this point.

3.11 Novo Nordisk claimed that the guidance failed to consider the needs of survivors of childhood cancer with iatrogenic pituitary failure.

Professor Barnett accepted that the guidance did not cover this group of patients.

The Appeal Panel, noting its conclusions in paragraph 3.8 above considered that the guidance was perverse in failing to consider the use of HGH in this patient subgroup.
The Appeal Panel therefore upheld the appeal on this point.

3.12 Pharmacia alleged that, in focusing on quality of life, the Appraisal Committee had ignored significant clinical data. In particular, the ScHARR report made no reference to the beneficial effects of treatment other than quality of life; the Appraisal Committee appeared to have ignored the reduction in the Standard Mortality Ratio of GH patients treated with HGH; and that the ScHARR report made unfounded assumptions about changes in quality of life amongst treated and untreated patients.

Professor Barnett explained that the ScHARR economic model had taken potential clinical benefits into account and Professor Brazier confirmed this. Professor Barnett also confirmed that the Appraisal Committee had considered the effects of HGH treatment on the Standard Mortality Ratio but regarded these as being more reliably subsumed within the estimates of cost effectiveness as determined from the ScHARR economic model. Professor Barnett indicated that the Appraisal Committee also took full account, where provided, of the evidence on the clinical effectiveness of treatment with HGH in both treated and untreated patients.

The Appeal Panel considered that the Appraisal Committee had taken all these matters into account when drawing up its guidance, and that it had not acted perversely.

The Appeal Panel therefore rejected the appeal on this point.

3.13 Pharmacia claimed that the guidance was based on the assumption, by the Appraisal Committee, that it was not possible to identify a subset of patients more likely to respond favourably to treatment with HGH. Current clinical practice does, however, target patients who are most likely to benefit from treatment.

The Appeal Panel, noting the comments of Professor Barnett as well as its own conclusions and recommendations in paragraphs 3.2 and 3.4 above, accepted this.

The Appeal Panel therefore upheld the appeal on this point.

3.14 Pharmacia claimed that the Appraisal Committee should have given little weight to those trials of poor quality and especially those recruiting patients with largely normal quality of life and different dosing schedules than now used in routine UK practice.

Professor Barnett explained that the Appraisal Committee had, indeed, placed lesser weight on studies such as these, and emphasised that its conclusions on the clinical and cost effectiveness of HGH in adult GH deficiency was based primarily on data most closely replicating current UK practice.

The Appeal Panel considered that the Appraisal Committee's had given appropriate weight to the totality of the available evidence, and had not been perverse.

The Appeal Panel therefore rejected the appeal on this point.

3.15 Pharmacia claimed that the KIMS data-base had not been adequately considered, and that too little weight had been given to its findings. Moreover, the fact that 92% of patients remained on treatment after two years mitigated against a placebo effect.

Professor Barnett explained that the Appraisal Committee considered the KIMS data most carefully, and that its findings made a significant contribution to the economic evaluation of HGH treatment in adult GH deficiency. The committee, however, had been conscious of the limitations of such observational data which tended, in general, to over-estimate effect sizes. For this reason the Appraisal Committee had been circumspect in its evaluation of the data.

The Appeal Panel considered that the Appraisal Committee had made a reasoned judgement about the value of the KIMS data and had not acted perversely.

The Appeal Panel therefore rejected the appeal on this point.

3.16 Pharmacia alleged that the cost effectiveness analysis was flawed; that the wording of the guidance when compared to the PAD, in respect of the regression analysis, would lead to unwarranted inferences about the quality of the data; and that the economic evaluation had assumed 100% compliance.

Professor Barnett indicated that, overall, the quality of the data was indeed poor and that this problem was discussed in the guidance. The Appraisal Committee had been aware of the implications of non-compliance but had nevertheless concluded that HGH was not clearly cost effective in the treatment of adult GH deficiency.

The Appeal Panel noted that the wording relating to the use of regression analysis in the PAD and FAD were similar (paragraphs 4.2.8). It sympathised with the Appraisal Committee's problems in appraising the heterogeneous data available to it. And it considered that the committee had not acted perversely in its evaluation and interpretation of the available evidence.

The Appeal Panel therefore rejected the appeal on this point.

3.17 Pharmacia claimed the comment that a small change in the price of HGH would significantly alter treatment costs was mistaken: a 10% price reduction would only save £600,000 per annum.

Professor Brazier explained that the cost of HGH was the main "driver" of its cost effectiveness.

The Appeal Panel accepted that the budgetary impact of NICE guidance was no business of the Appraisal Committee or the Institute. The Panel accepted, however, that the acquisition costs of HGH were a major determinant of its cost effectiveness. The Appraisal Committee had not, therefore, acted perversely in its consideration of this matter.

The Appeal Panel therefore rejected the appeal on this point.

3.18 Pharmacia claimed that the recommendations for further research were perverse because patient selection is established in clinical practice.

Professor Barnett explained that the Appraisal Committee's advice on further research (FAD 6.1) was predicated on its conclusions about the clinical and cost effectiveness of HGH treatment for patients with adult GH deficiency.

The Appeal Panel, noting its conclusions in paragraphs 3.2, 3.4, 3.8 and 3.11 above, considered that the guidance was perverse in this respect.

The Appeal Panel therefore upheld the appeal on this point and recommend that the Appraisal Committee reconsider this section of its guidance in the light of its conclusions in relation to the relevant paragraphs in the guidance.

3.19 The SoPE and the RCPCH expressed broad disagreement with the proposed guidance. In particular, the appellants alleged that the conclusions

were perverse because, despite the small improvement in patient's quality of life, the use of HGH in the treatment of adult GH deficiency was advocated by both patient and professional groups.

The Appeal Panel considered that, whilst the contributions of patient and professional organisations represented a critical component of the appraisal process, their advocacy, alone, was an insufficient basis for recommending treatments to the NHS.

The Appeal Panel therefore rejected the appeal on this point.

3.20 The SoPE and the RCPCH expressed concern about the continuity of HGH treatment between childhood and adulthood in the light of the guidance.

The Appeal Panel, noting its comments and conclusions in paragraph 3.8 above, considered that the Appraisal Committee had been perverse in failing to provide guidance appropriate for such clinical circumstances.

The Appeal Panel therefore upheld the appeal on this point.

3.21 The Pituitary Foundation claimed that the use of QALYs was suspect. In particular, the Foundation claimed that the study used to estimate QALYs did not embody UK clinical practice where only a subgroup of adult GH deficient patients are selected for treatment.

Professor Barnett explained that the Appraisal Committee frequently undertook its economic evaluations using QALY data. In its appraisal of HGH for adult GH deficiency the Appraisal Committee had utilised all the available data. It had considered the possibility of targeting treatment in a subgroup of patients but had not been able to identify appropriate criteria (FAD 4.3.6).

The Appeal Panel considered that the use of QALYs in this context was appropriate and that the Appraisal Committee had not been perverse. Nevertheless, noting its comments and conclusions in paragraphs 3.2 and 3.4 above, the Panel was concerned that there might exist a group of patients with adult GH deficiency in whom HGH was clinically and cost effective. Indeed, there were suggestions in the ScHARR report to support this possibility (pages 39 to 41).

The Appeal Panel therefore partially upheld this point.

3.22 The Pituitary Foundation considered that there were inconsistencies between the approach used in the appraisal of HGH in adult GH deficiency, and that adopted by the Appraisal Committee for other technologies. In particular, some appraisals used different measures of health gain; failure to accept patients' views; targeting therapy to those most likely to benefit; differences between advice on the use of GH in adults and children; and inconsistencies between the ScHARR reports.

The Appeal Panel again (see paragraph 2.2 above) considered that some differences in approach were inevitable in view of the range of technologies, and diseases, that the Appraisal Committee was expected to consider. The Panel did not consider that the examples quoted by the appellants constituted unjustified, or unfair, differences in approach between the appraisal of HGH and other technologies.

The Appeal Panel therefore rejected the appeal on this point.

3.23 The Pituitary Foundation claimed that deliberately withholding a naturally occurring substance that the body needs is to deliberately cause injury to the body.

The Appeal Panel did not accept that a failure to provide a treatment, even where the treatment is the supply of a naturally occurring substance, is the same as deliberately causing harm. In any case such a

contention begged the question whether HGH is clinically effective in all patient groups, an important aspect of the appraisal. The Appeal Panel also reminded the appellants that the Institute has a responsibility to advise the NHS on the clinical and cost effectiveness of the technologies it is asked to appraise. It considered that the Appraisal Committee had not acted perversely in considering both the benefits, and the costs, of treating adult GH deficiency with HGH.

The Appeal Panel therefore rejected the appeal on this point.

4. Appeal Ground Three: The Institute has exceeded its powers.

4.1 There were no allowable grounds of appeal under Ground 3.

5. Conclusions

5.1 The Appeal Panel upholds this appeal (see paragraphs 3.2, 3.4, 3.8, 3.11, 3.13, 3.18 and 3.21 above). The Panel recommends that the Guidance Executive institutes the measures described above including referral back to the Appraisal Committee.