Neutral Citation Number: [2009] EWHC 281 (Admin)

Case No: CO/2469/2008

**IN THE HIGH COURT OF JUSTICE**
**QUEEN'S BENCH DIVISION**
**ADMINISTRATIVE COURT**

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 19/02/2009

**Before**:

**MR JUSTICE HOLMAN**

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**Between:**

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| **THE QUEEN**<br>**on the application of**<br>**SERVIER LABORATORIES LIMITED** | **Claimant** |
| **- and -** | |
| **THE NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE** | **Defendant** |
| **and** | |
| **(1) THE ALLIANCE FOR BETTER BONE HEALTH**<br>**(2) THE NATIONAL OSTEOPOROSIS SOCIETY** | **Interested Parties** |

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**Mr Martin Chamberlain** (instructed by **Messrs. Bristows**) for the **Claimant**
**The Hon. Michael Beloff QC and Mr Daniel Stilitz** (instructed by **Messrs. Beachcroft LLP**) for the **Defendant**
**The Interested Parties were not represented**

Hearing dates: 20th, 21st and 22nd January 2009

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# Judgment

# GLOSSARY

The following glossary of acronyms is based on one prepared by Messrs Beachcroft, the solicitors for the defendant, and is reproduced with their kind permission.

| | |
|---|---|
| ACD | Appraisal Consultation Document |
| AIC | Academic in Confidence |
| BMD | Bone Mineral Density |
| CHMP | Committee for Medicinal Products for Human use (CHMP is a French acronym) |
| CI | Confidence Interval (usually, the upper and lower boundaries between which 95% of data points lie) |
| CIC | Commercial in Confidence |
| EMEA | European Medicines Evaluation Agency |
| FAD | Final Appraisal Determination |
| FRAX | An internet tool which predicts the probability of a patient with given data experiencing a fracture |
| GDG | Guideline Development Group |
| ICER | Incremental Cost Effectiveness Ratio |
| NOS | National Osteoporosis Society |
| QALY (rhymes with "jolly") | Quality Adjusted Life Year (a measure which relates length of life and quality of life to enable different diseases and treatments to be compared) |
| RCT | Random(ised) Control(led) Trial |
| RR | Relative Risk (the degree by which the risk of an event is reduced by a treatment, ranging from 1 (no effect on risk) to 0 (risk wholly eliminated)) |
| ScHARR | (Sheffield University) School of Health and Related Research |
| SD | Standard Deviation (a measure of how widely spread around the mean value a data set is) |
| SMC | Scottish Medicines Consortium |
| TAR | Technology Appraisal report |
| TROPOS | Treatment Of Peripheral Ostoeporosis (an RCT investigating the effects of strontium ranelate) |

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|---|---|
| T - score | A measure of how far a patient's bone mineral density is below the expected mean value |
| WHO | World Health Organisation |

**Mr Justice Holman:**

1. I am grateful to all three counsel for their lucid and cogent written and oral arguments in this complex case; to the National Osteoporosis Society (NOS), as an interested party, for their informed and thoughtful revised written submission; and to the solicitors for the principal parties, who each contributed greatly to the preparation of the case before and during the hearing.

**Introduction and the essential issues**

2. The demands upon the modern National Health Service are effectively unlimited. Its financial resources are very great, but they are limited and finite. Mechanisms are essential to promote, so far as possible, a distribution of those resources which is cost effective and wise, and which is fair as between all patients. In England and Wales and insofar as concerns this case, that mechanism is now provided by The National Institute for Health and Clinical Excellence (NICE) and the framework of regulations and directions within which it operates. Insofar as concerns this case, the function of NICE is thoroughly to assess health technologies, including different types of drugs, and to make recommendations and give guidance as to their use. If a particular drug is not recommended, or is only recommended for certain categories of patients, then that powerfully dissuades a clinician from prescribing the drug, or from prescribing it for categories of patient other than those for whom it is recommended. In practical terms, if a particular drug is not recommended, then much less of it will be prescribed and made available for patients, even although there may be patients who might benefit from it but for whom it is not prescribed. The tension is at once apparent. Pharmaceutical companies invest enormous sums in research and the development of drugs and, very justifiably, seek a market for them. They have a huge and legitimate commercial interest in theirs being a recommended drug. As a generalisation, patients and their doctors seek that as wide a range of drugs as possible is available, and a given patient seeks in particular the availability, financed by the NHS, of the optimum drug for his personal condition and circumstances. The task of NICE is nevertheless to encourage and influence the choice and prescription of drugs in the interests of cost effectiveness and fairness to all. NICE must have to make many tough decisions.

3. As I shall describe, NICE operates by an elaborate process of appraisals, incorporating also an appeal structure. The final outcome is a document called a Final Appraisal Determination (FAD) which incorporates the final recommendations and guidance and also records some of the underlying data and

reasoning for them. By revised FADs issued in June 2008 NICE recommended alendronate, a bisphosphonate, as the primary treatment for the prevention of osteoporotic fragility fracture in post-menopausal women. The claimants, Servier Laboratories Limited (Servier), market in the UK an alternative drug, strontium ranelate, branded under the name Protelos. Strontium ranelate is not a bisphosphonate and has a different mode of action. The prescription of strontium ranelate was only finally recommended by NICE in the revised FADs for a defined and limited group of patients. NICE say, in effect, that strontium ranelate is insufficiently effective and too expensive to justify recommending its use more widely. Servier seek a wider market for their product. Patients and patient groups seek that strontium ranelate is more widely available to NHS patients.

4. Servier, supported by NOS as interested party, claim that the revised FADs should be set aside and that NICE should reconsider them. They now rely on three grounds, which are essentially discrete and independent. I will continue to identify these as grounds (a), (c) and (e), although grounds (b) and (d) have been abandoned. Ground (a) alleges that NICE failed to act fairly and with transparency by their failure to supply or disclose to Servier and the other consultees the economic model and underlying data upon which the conclusions of NICE and the FADs are based. NICE say that they would wish to have disclosed it but were bound by an undertaking of confidence to the owner of the essential data. Ground (c) alleges that NICE failed during their appraisal properly to take into account data submitted by, and relied upon by, Servier (a post hoc analyis of the TROPOS trial) and/or that the non-acceptance by NICE of that data is insufficiently reasoned. Ground (e) alleges that the final, revised recommendations of NICE unlawfully discriminate against certain categories of disabled patient, contrary to the Disability Discrimination Act 1995.

5. The hearing was listed as a rolled up hearing. All three grounds were arguable and have been very fully argued. I thus grant permission to Servier to apply for judicial review on all three grounds still relied upon, namely (a) (c) and (e).

6. It is important to stress at the outset that NICE is the specialist, expert body, charged with making appraisals and decisions of this type. The court is not. I have neither the right, nor still less the expertise, to review the decisions as to their substance. The court can only interfere if, in one or more of the ways relied upon, NICE has acted unlawfully or irrationally.

## Osteoporosis

7. The case concerns treatments for osteoporosis. I base the following description and data on a combination of section 2 of the revised FADs, at bundle 3:39, and the first statement of Professor Timothy Spector, a consultant rheumatologist specialising amongst other things in osteoporosis, at bundle 8:20, paragraphs 4-14. Osteoporosis usually affects post-menopausal women. It is “a progressive, systemic skeletal disorder characterised by low bone mass and micro-architectural deterioration of bone tissue, with consequent increase in susceptibility to

fracture." It is estimated that more than 2 million women currently suffer from osteoporosis in England and Wales and that more than one in four women in the UK will suffer from osteoporosis during their lifetime. Osteoporotic fragility fractures occur most commonly in the vertebrae, hip and wrist, and are associated with substantial disability, pain and reduced quality of life. It is estimated that annually there are 180,000 osteoporosis-related symptomatic fractures in England and Wales, of which 70,000 are hip, 25,000 are clinical vertebral, and 41,000 are wrist fractures. After hip fractures, a high proportion of women are permanently unable to walk independently or to perform other activities of daily living and, consequently, many are unable to live independently. Hip and vertebral fractures are both also associated with increased mortality.

8. It is thus clear that osteoporosis is, as Professor Spector says, "a very serious condition." It is very prevalent. It may very seriously affect the quality of life of the patient, as well as caring family members; and it may reduce life expectancy.

9. It is not curable. The aim of drug treatment is to reduce the risk of fracture. Clinicians, and the FADs themselves, refer to "primary prevention" and "secondary prevention." Primary prevention relates to women who have not previously suffered a clinically apparent osteoporotic fragility fracture. "Secondary prevention" relates to women who have.

**NICE and its framework**

10. Paragraphs 4 – 20 of the judgment of Dobbs J in Eisai Limited v NICE and others [2007] EWHC 1941 (Admin) contain a detailed description of the role of NICE, its legal framework, the status and effect of its guidelines, and its system of technology appraisals. In the Court of Appeal in the same case, at [2008] EWCA Civ 438, paragraphs 5 – 7 of the judgment of Richards LJ (drawing considerably from that of Dobbs J) contain a similar but shorter description. The following account, which substantially mirrors those passages, is, with their permission, drawn very considerably from the skeleton argument in the present case of The Honourable Michael Beloff QC and Mr Daniel Stilitz, counsel for NICE.

11. The function of NICE is to develop guidance covering all aspects of healthcare within the NHS. The purpose of NICE's work is to encourage: (a) best clinical practice; (b) the most efficient use of the finite resources of the NHS; and (c) consistency of treatment throughout the NHS.

12. NICE was established by the National Institute for Clinical Excellence (Establishment and Constitution) Order (SI 1999/220) ("the 1999 regulations") as a "special health authority" within the NHS with effect from April 1999.

13. By regulation 10 of the 1999 regulations, NICE is subject to the directions of the Secretary of State. Paragraph 2(1) of the current directions, "Directions and Consolidating Directions to the National Institute for Health and Clinical Excellence 2005" provides that:

"(1) The Secretary of State directs the Institute to exercise the following functions in connection with the promotion of clinical excellence and the effective use of available resources in the health service

(a) to appraise the clinical benefits and the costs of such health care interventions as may be notified by the Secretary of State and to make recommendations;

(b) to develop guidelines providing advice on good practice in the management of such diseases and conditions as may be notified by the Secretary of State …"

14. Paragraph 2(4) of the directions provides that:

"(4) In exercising the functions described in paragraphs (1) (a)-(d) …. above the Institute shall have regard to the following factors-

(a) the broad balance of clinical benefits and costs;

(b) the degree of clinical need of patients with the condition or disease under consideration;

…..

(d) the potential for long term benefits to the NHS of innovation."

**The status and effect of NICE guidance**

15. NICE guidance contains recommendations for the use of particular treatments or "health technologies". Where a treatment is recommended in clinical practice, NICE will generally give guidance as to the circumstances in which it should be used, or as to particular patient groups to whom it should be given. Guidance documents (including those to which this case relates) bear on their face the following statement:

"This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient …. "

So that is the duty "expected" of health care professionals.

16. In 2001 the Secretary of State directed that NHS Trusts must normally make the necessary funding available in respect of any treatment that is recommended by NICE. Paragraph 2 of the current, 2003, version of the "Directions to Primary Care Trusts and NHS trusts in England [I believe there are concurrent directions in Wales] concerning arrangements for the Funding of Technology Appraisal Guidance from ….NICE" provides that:

> "2. ….. a Primary Care Trust shall ….., in exercising those functions that it has been directed to exercise by the Secretary of State, apply such amounts of the sums paid to it …. as may be required to ensure that a health care intervention that is recommended by the Institute [NICE] in a Technology Appraisal Guidance is ….. normally available:
>
> (a) to be prescribed for any patient on a prescription form ….; or
>
> (b) to be supplied or administered to any patient for the purpose of his NHS treatment."

17. In April 2005 the Department of Health published the document "Standards for Better Health". Within that document the domain "Clinical and Cost Effectiveness" aims at an outcome that "Patients achieve health care benefits that meet their individual needs through health care decisions and services based on what assessed research evidence has shown provides effective clinical outcomes". It is supported by Core Standard 5 which requires, amongst other matters, that "Health care organisations ensure that (a) they conform to NICE technology appraisals and, where it is available, take into account nationally agreed guidance when planning and delivering treatment and care …. ." Core standards are ones with which health care organisations must comply (introductory paragraph 18)

18. The interrelation and effect of the language on the face of the NICE guidance documents themselves, which is directed to health care professionals, the Directions to Primary Care Trusts, made pursuant to statute, and the core standards may, in another case, require fuller consideration and analysis. For the purpose of the present case it is sufficient to note that Primary Care Trusts must ("normally") fund treatment/drugs that are recommended by NICE, but are not under a similar duty to fund treatment/drugs that have not been so recommended. Although, as Mr Beloff stresses, the overriding responsibility of the clinician is respected and emphasised, he is "expected to take [the guidance] fully into account", and Mr Beloff accepted, in a phrase which I have already used, that if a drug is not recommended that "powerfully dissuades" a clinician from prescribing it.

**The approach of NICE to technology appraisals**

19. When a particular appraisal topic has been chosen, NICE identifies those organisations which might have an interest in the outcome of the appraisal. These typically include groups representing patients and carers, bodies representing

healthcare professionals, manufacturers and research groups. Such stakeholders are divided into "consultees" and "commentators", with only consultees having a right of appeal against NICE's eventual guidance.

20. NICE works with the Department of Health to produce a scope for the appraisal. Once that scope has been finalised, the department formally instructs NICE to carry out the appraisal.

21. An independent academic assessment centre is commissioned to review and evaluate evidence on the health technology under appraisal. They produce a Technology Assessment Report (or TAR) which details their review and presents an analysis of the cost-effectiveness of the health technology. Often (as in the present case) the assessment centre will build an economic model to inform their analysis.

22. Consultees and commentators are invited to comment on the TAR and make submissions. The TAR and comments made on it are then drawn together in an Evaluation Report.

23. The appraisal is then allocated to one of NICE's appraisal committees. The appraisal committees are standing committees whose members are drawn from a wide range of backgrounds. Members of each appraisal committee include eminent clinicians, health administrators, academics, representatives of the pharmaceutical industry and lay members.

24. The appraisal committee considers the Evaluation Report. It then hears evidence from clinical experts (nominated by the consultees and commentators), patients and carers, before making initial recommendations about the use of the health technology in an Appraisal Consultation Document (ACD). Consultees and commentators may comment on the ACD. The ACD is also made available online so that members of the public, including health professionals, can comment on it.

25. The appraisal committee considers all comments that it has received on the ACD from consultees, commentators and the public. It then makes its final recommendations in a FAD.

26. The FAD is submitted to the NICE Guidance Executive for its approval. Once the FAD is approved, it is circulated to consultees and commentators. Consultees may appeal against its recommendations. If there are no appeals, or any appeals are dismissed, the final recommendations are issued as NICE Guidance. If any appeal is successful, the usual consequence is that the appraisal committee reconsiders its recommendations.

27. The approach of NICE to technology appraisals is accordingly based on conducting a thorough survey of the available evidence as to clinical effectiveness and a detailed analysis of the cost-effectiveness of the technology in question, in consultation with all relevant interested parties.

28. The key principle underlying NICE's approach to appraisals is that the limited resources of the NHS should be targeted on those treatments which provide best

value for money and, conversely, should not be used on treatments which are not cost effective. This principle is summarised at paragraph 4.1 of NICE's "Social Value Judgments – principles for the development of NICE Guidelines" (8th December 2005) as follows:

> "The Institute accepts that, for both legal and bioethical reasons, in undertaking technology appraisals and developing clinical guidelines it must take account of economic considerations. Decisions about the total resources available for healthcare are, rightly, the responsibility of parliament and inevitably compete with other demands … Within the allocations made by parliament, the resources for the NHS are finite, and the use of cost-ineffective interventions in one area of practice will deny the availability of cost-effective interventions in another. The Institute thus recognises that both it, and its advisory bodies, have a responsibility to avoid issuing guidance that would incur 'opportunity costs' that would lead to the substitution of one form of inequality by another one."

29. In determining whether particular treatments are cost-effective, NICE generally seeks to ascertain the incremental cost per quality adjusted life year (or "cost per QALY") of using a particular health technology. In broad terms, this is a standard measure of the cost of gaining a particular unit of utility through the use of the technology which can be applied across the whole spectrum of treatments appraised by NICE.

30. The general threshold for an "acceptable" cost per QALY is approximately £20,000 per QALY: see paragraph 6.2.6.10 of NICE's 'Guide to the Methods of Technology Appraisal' (April 2004). Above approximately £30,000 per QALY, technologies are not normally recommended, although there have been a small number of exceptions. Between £20,000 and £30,000 per QALY, NICE will consider whether there are specific considerations which justify recommending the technology, such as the particular needs of the relevant patient group.

31. The use of cost per QALY as the central benchmark for recommending health technologies enables NICE to make recommendations on a consistent and equitable basis in respect of the various health technologies which it is directed to appraise. Although the process is not a mechanistic one, the focus on cost per QALY means that treatments for a variety of very different conditions and illnesses can be assessed on a "level playing field" by reference to common standards of cost-effectiveness.

32. The work of NICE should have at least three principal benefits to users of the NHS:

    (a) Recommendations made applicable across the NHS tend to eliminate the so-called "postcode prescribing lottery" whereby patients in different parts of the country have historically had unequal access to particular drugs and treatments;

    (b) The use of the common standard of cost per QALY should ensure an equitable distribution of resources amongst different patient groups;

(c) Adopting a rigorous, scientific approach to technology appraisals should ensure that the highest standards are applied in assessing impartially the efficacy of various health technologies and that the most effective treatments are utilised by the NHS.

**The appraisal and appeals in this case**

33. The process began in 2004. NICE commissioned an independent assessment by Sheffield University's School of Health and Related Research (ScHARR) under the leadership of Dr Matthew Stevenson. The ScHARR assessment group produced three TARs of which that relating to strontium ranelate was published in July 2005. These TARs were then considered by one of NICE's own appraisal committees which, after considering evidence from consultees (including Servier) and commentators, produced the initial FADs in June 2007. One FAD related to primary prevention; the other to secondary prevention. Each FAD recommended alendronate (a bisphosphonate) as a treatment option for a range of women. Neither recommended strontium ranelate. Servier (and others) appealed. Their grounds included what are now grounds (a) and (c) of the present claim, namely the failure of NICE to make available the economic model and its underlying data, and the failure of NICE to take into account the post hoc analysis from the TROPOS trial. The appeal panel's decisions were issued in December 2007. The appeals were partially successful on other grounds. But insofar as the appeals related to the post hoc analysis from the TROPOS trial (now ground (c)) they were "dismissed". Insofar as the appeals related to withholding the economic model and the underlying data (now ground (a)) they were "rejected". However the appeal panel added the following important rider at paragraph 32 of its reasons (now at bundle 4:3, page 8):

> "It was evident that the appraisal committee was frustrated by the failure of the World Health Organisation (WHO) to publish its model; and the appeal panel was clear that, but for the WHO's wish for the model to remain academic-in-confidence, the appraisal committee would have offered to release it to the consultees in read-only form. The appeal panel considered that the WHO's failure to publish, for some years, data of considerable public importance was regrettable; but that, in all the circumstances, the Institute had not acted unreasonably."

34. The outcome of these, first, appeals triggered the application by Servier for judicial review by this court. But both parties agree that I should now approach the case on the basis of the facts as they now are, taking account of the subsequent developments during 2008.

35. In the period January to May 2008 staff of NICE made certain approaches, which I will later describe, to obtain permission to release the data underlying the economic model, following the rider at paragraph 32 of the appeal panel reasons. In the event, the data and the economic model never have been released. During 2008 the appraisal committee reconsidered the proposed guidance in the light of

other aspects of the decisions on appeal, and issued revised FADs on 30 June 2008. These included a recommendation for treatment by other drugs, including now strontium ranelate, but only for certain categories of patient who, exceptionally, could not be treated with alendronate.

36. Servier again appealed to the appeal panel against the revised FADs, repeating what are in effect grounds (a) and (c). The appeal panel declined to entertain these points again on the grounds that it had already done so once, and that they were now anyway the subject of the ongoing proceedings for judicial review (see email dated 21 August 2008 from Mark Taylor, appeals committee chair, now at bundle 6:43, page 580). Servier did, however, advance a further and new ground, namely that the revised FADs are disability discriminatory in their effect (what now becomes ground (e)). By its decision dated 24 October 2008 the appeal panel dismissed the appeals on the point (see paragraphs 37-51 of its reasons at bundle 3:41, pages 1196-1198.) Certain other grounds of appeal to which I need not refer were also all rejected.

37. In the upshot, the revised FADs have remained unchanged and Servier now seek that I quash the two revised FADs (one relating to primary prevention, the other to secondary prevention) dated 30 June 2008 or order NICE to reconsider them; and also quash, if it adds anything to do so, the appeal panel's decisions of 11 December 2007 (the first appeals) and 24 October 2008 (the second appeals).

## GROUND (a)

### Ground (a) Non disclosure of the economic model

38. NICE has never disclosed to Servier or any other consultee, whether in a partially ('read only') or fully executable format, the economic model which was created by the ScHARR assessment group and which underpins the FADs in this case. Indeed the model itself has not even been seen by the members of the appraisal committee or appeal panel and, as I understand it, very few people indeed apart from Dr Matthew Stevenson, who led the work of ScHARR, have ever seen it. Servier say that non disclosure of the model and its data seriously disadvantaged them in their ability to evalulate it and make submissions upon it to the appraisal committee. More generally, they argue that the effect of non disclosure was to prevent rigorous scrutiny of the model and that the resulting FADs and recommendations may be significantly flawed as a result. In this they are strongly supported by the revised written submissions of NOS. NOS say that as a result of non disclosure of the data and the model they have been unable to check the accuracy of the base case analysis, or to carry out sensitivity analysis and, generally, that "This lack of transparency is unfair; it has inevitably affected the substance and detail of the challenge stakeholders could have made to the assertions …."

39. On behalf of Servier, Mr Martin Chamberlain developed his argument on ground (a) under seven heads. These included as head (i), the significance and structure of the economic model; head (ii), the emphasis by NICE itself upon transparency;

head (iii), the lack of transparency in this case; head (iv), the history of Servier's request for access to the model; and head (vii), his response to an argument by NICE in the documents that even without access to the model, even in a read-only form, Servier had been supplied with sufficient information or material to be able to make intelligent comments during the appraisal and consultation process. This particular argument was contained within paragraphs 87-95 of the written skeleton argument of Mr Beloff and Mr Stilitz dated 13 January 2009.

40. During his later oral submissions, Mr Beloff expressly withdrew the argument to which head (vii) related, and expressly withdrew any reliance upon paragraphs 87-95 of his skeleton argument. Further, he expressly accepted the points made by Mr Chamberlain as to the significance and structure of the model (head (i)), and as to the repeated attempts by Servier to get access to it (head (iv)). He further accepted the aspiration of NICE for transparency (head (ii)) and the lack of transparency in this case (head (iii)). He stressed, however, and this is central to the argument on this part of the case, that the aspiration of transparency is, and necessarily must be, conditional on the need to respect the confidentiality of information, material or data which was supplied to NICE on an undertaking or basis of confidentiality. He submitted that insofar as there has been a lack of transparency in this case that has been due to the "confidentiality override". In the light of these concessions I propose to deal with the material in Mr Chamberlain's heads in a different order and way.

**The economic model and its importance**

41. Within the evidence in the present case there is an account by Dr Stevenson, of ScHARR, of economic modelling in general at paragraphs 10-14 of his first statement (bundle 7:12, pages 97-98). Both parties agree with the contents of those paragraphs. At the risk of over summary and simplification, a model is developed to predict the effect over a longer period of shorter term data on clinical effectiveness as reported in clinical trials. The model combines data from a number of sources so as to estimate what would happen if the treatment were used across the patient population. It compares cost/benefit outcomes for a group of patients on the alternative assumptions that they do, or do not, receive the treatment under investigation. A comparison of the results may be expressed as a cost per QALY. When developing the model itself choices have to be made as to its structure. Dr Stevenson says at paragraph 14 "It will be appreciated that health economic modelling can be a highly technical area, and almost any economic model will involve the exercise of professional judgments by the research team. ….. However, a carefully designed model will provide a reliable and robust tool to assist in assessing the cost-effectiveness of a drug."

42. The data fed into the model is patently critical to its outcomes. The key data in the present case was supplied by Professor John Kanis, to whom I will refer below. Dr Stevenson dealt with that data in his second statement (bundle 7:24). The data contained two essential elements. The first is risk equations or algorithms (the two terms are interchangeable and mean the same thing), which are based on research. These estimate or predict the risk of fracture in a given

period in populations of women with particular risk factors, such as age, bone mineral density (BMD), prior fracture, parental history, and smoking and alcohol intake. Because some of these factors may exert a greater effect on the risk of fracture than others, each risk factor was allocated by Professor Kanis a coefficient. The coefficient is the other essential element. At paragraph 8 of his second statement (bundle 7:24, page 164) Dr Stevenson says "The coefficients are integral to the WHO risk equation and are fundamental to the economic model built by the assessment group to inform the appraisal of strontium ranelate …. Without the coefficients it is impossible to properly understand what influence each risk factor exerts on the end results …." (my emphasis)

43. It is plain from this evidence that the data supplied and fed into the model, as well as the design and structure of the model itself, are fundamental to the TAR and to the resulting appraisals.

44. Quite apart from this evidence and the concessions of Mr Beloff on this point, we now have the observations of the Court of Appeal in paragraph 35 of the judgment of Richards LJ in Eisai v NICE where he said:

> "The importance of the model in the appraisal process is not in doubt. It is central to the appraisal committee's determination of a drug's cost-effectiveness and in particular to the cost per QALY and whether it comes within the threshold of acceptable cost. … The robustness or reliability of the model is therefore a key question …."

Those observations apply, in my view, with no less force to the present case.

**Transparency and fairness**

45. NICE itself asserts the importance of transparency in its published documents. The opening paragraph of its "Guide to the Technology Appraisal Process" (the Process Guide), paragraph 1.1.1, at bundle 5:17, page 149, states:

> " ….. The purpose of this document is to describe a uniform, open and transparent process by which all technology appraisals are conducted. The process is designed to achieve robust guidance for the NHS, developed in an open and transparent way that allows maximum understanding and input from consultees and stakeholders."

46. Paragraph 3.1.1 of NICE's "Guide to the Methods of Technology Appraisal" (the Methods Guide) states:

> "….To ensure that the guidance issued by the Institute is appropriate and robust, it is essential that the evidence and analysis and their interpretation are of the highest standard and are transparent to scrutiny." (my emphasis)

47. Paragraph 3.1.3 states:

> "…. Models should also:
>
> - be replicable
> - have face validity (that is, be plausible)
> - be open to external scrutiny."

48. The chairman of NICE, Professor Sir Michael Rawlins MD FRCP, describes in paragraphs 9-12 of his statement, now at bundle 7:9, page 55, "four fundamental principles" to which NICE has always subscribed: robustness; transparency; inclusiveness; and independence. As to transparency, he says

> "The Institute …. attempts to ensure that its decisions, and the reasons for them, are placed in the public domain. This includes …. the reasoning of its advisory bodies [viz in this case, ScHARR] about the basis for the conclusions they have reached."

49. Quite apart from these published policies and statements by NICE itself, the thrust of the decision of the Court of Appeal in Eisai v NICE, to which I will later turn, is plainly that transparency and fairness require disclosure of the fully executable economic model and the data upon which it is based.

**Confidentiality**

50. NICE qualify their asserted principle of transparency, however, by asserting the need in certain circumstances for confidentiality, which Mr Beloff labels for shorthand as "the confidentiality override."

51. Within their Process Guide, now at bundle 5:17, page 155 et seq, NICE state:

> "4.2.3 To ensure that the appraisal process is as transparent as possible, the Institute considers it highly desirable that evidence pivotal to the committee's decisions should be publicly available. Ideally, all the evidence seen by the appraisal committee should be available to all consultees and commentators. Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence').
>
> 4.2.4 The Institute expects consultees to keep confidential material within a submission to an absolute minimum. When a consultee believes that part of

a submission needs to be treated as confidential, the rationale for doing so should be clearly stated and should be consistent with the principles set out below.

- Information that has been put into the public domain, anywhere in the world, may not be marked as confidential.

- The results of clinical trials submitted for appraisal that relate to products that have received regulatory approval should be available for scrutiny …

- The same principles apply to the release of information submitted in the form of economic models. The full economic model, in electronic format, should be available for scrutiny by the Institute and the assessment group. A structured abstract of economic models submitted by consultees should, as a minimum, be made available for public disclosure.

4.2.5. The Institute asks consultees to reconsider restrictions on release of data when either there appears to be no obvious reason for the restrictions, or such restrictions would make it difficult or impossible for the Institute to show the evidential basis for its guidance."

52. Paragraph 4.4.1.9 of the Process Guide, now at bundle 5:17, page 162, states that:

"The assessment group may produce an economic model in support of the assessment report. If the model does not contain information that was designated as confidential in the submission, the Institute offers consultees and commentators the opportunity to receive by email a read-only version of the model, for information only. Requests for the model must be made in writing, and it is supplied on the basis that the consultee or commentator agrees, in writing, to the following conditions for its use …." (emphasis added - see below).

53. The conditions for its use which follow are conditions designed to respect the intellectual property in the model and to limit its use by consultees and commentators to informing their understanding of the assessment report.

54. Mr Beloff says that following the decision of the Court of Appeal in Eisai v NICE the practice of NICE under paragraph 4.4.1.9 has now been altered to extend to offering a fully executable and not merely a read-only version of the model. He stresses that in all other respects paragraph 4.4.1.9 remains unchanged and, in particular, that it remains subject to the conditional clause that I have underlined and emphasised in the above quote.

55. Paragraph 4.2.4.1 of the Methods Guide, now at 5:18, page 201, states that:

"Under exceptional circumstances, the Institute will accept unpublished evidence under agreement of confidentiality – for example, if the information

is commercially sensitive ('commercial in confidence') or if its use might adversely affect future publication rights ('academic in confidence'). To ensure that the appraisal process is as transparent as possible, it is highly desirable that evidence pivotal to the committee's decisions should be available publicly. Ideally, all the evidence seen by the appraisal committee should be available to all consultees and commentators. Manufacturers and sponsors (as well as all others submitting evidence) are therefore required to keep 'in confidence' restrictions to a minimum, provide the rationale for submitting material as confidential and permit the Institute to acknowledge that it exists."

56. Professor Sir Michael Rawlins says at paragraph 13 of his statement, now at bundle 7:9, page 55:

> "13. There are tensions between some of these principles, in particular, between robustness and transparency …. do we design a process which maximises our access to relevant material (some of which may be confidential and not released) or do we design a process which maximises transparency (at the price that holders of confidential information will or may not deny to us because it would be published)." [sic, but his sense is clear]

57. After describing the, largely self evident, distinction between commercial in confidence (CIC) and academic in confidence (AIC), Professor Sir Michael Rawlins continues at paragraph 17:

> "…. NICE has to operate within an environment where those who have data that it needs may be able to claim that some of that data is confidential. This confidentiality is not for the Institute's benefit.
>
> 18. From the outset, NICE has had to grapple with the tension between developing robust guidance (which requires using confidential material where this is necessary) and the interests of transparency. Although the Institute makes considerable effort to persuade holders of confidential information to allow its guidance to quote from confidential material where necessary, and/or otherwise to allow the confidential material to have some visibility in the assessment process" [which, I interpose, disclosure of the economic model in this case would do] "it is not invariably successful. We have no power to compel disclosure. In these circumstances NICE has two options: either to accept confidential information and abide by the undertakings that the Institute has given; or refuse to accept evidence submitted as confidential ….
>
> 19. A policy of refusing to accept confidential information would be detrimental to patients as well as for the reputation of - and confidence in - the Institute. Confidential information may include critical information about efficacy and safety, as well crucial information about the proposed acquisition cost of a product. This latter information is often not published until shortly before the product is marketed. If NICE did not have access to such confidential data its guidance function would be so severely compromised as

to make it impossible for the Institute to fulfil its responsibility to the NHS, patients, the public or Parliament. In particular, for products that have only recently reached the market, or have yet to be licensed, the published information is slender. Systematic reviews that ignored unpublished, or confidential data, would be of limited value. If it is to develop robust guidance, the Institute must have access to similar information on the efficacy and safety of new products that is provided (in confidence) to drug regulatory authorities … The Medicines and Healthcare Products Regulatory Agency, as well as the European Medicines Regulatory Agency and the Food and Drugs Administration in the US, all necessarily accept confidential data for the same reasons as NICE. To do otherwise would unquestionably harm patients either by denying them access to effective and cost effective products, or by exposing them to dangerous or cost ineffective ones …."

58. As well as the "two options" referred to in paragraph 18 quoted above, Professor Sir Michael Rawlins does make reference in his statement to a theoretical "third option", namely to accept confidential information but then to ignore the undertakings given and simply to publish or disclose the information in breach of the confidence and any undertakings. In paragraph 34 he describes such a course as being "ethically very unappealing" and says that if NICE were to do it "I have little doubt the consequence would be that we would never be offered confidential information." He says at paragraph 35 that were NICE simply to breach confidentiality undertakings that it had given, "…. there is no doubt that researchers …. would decline to accept the Institute's assurances in the future; and the adverse publicity thus generated would …. irreparably ruin the Institute's reputation for probity. Again I have no doubt that the consequence would be that we would never be offered confidential information from any source."

59. It was no part of the submissions of Mr Chamberlain in the present case that NICE could indeed have resorted to the "third option" and simply disclosed without permission information and data which it had received in confidence. In my judgment (and *pace* the last sentence of paragraph 59, to which I will later refer, of the judgment of Richards LJ in Eisai v NICE) the "third option" is indeed simply not an option at all, for the very reasons given by Professor Sir Michael Rawlins. NICE is a public body, established by statutory instrument. High standards of probity are patently required and expected of it. To breach an undertaking of confidentiality (except, perhaps, in obedience to an unequivocal court order) would be unethical and lack all probity and, as Sir Michael explains, would be disastrous to NICE, its standing and its future efficacy.

**Professor Kanis and the confidentiality in this case**

60. Professor John Kanis MD FRCP, is a physician and Professor Emeritus in metabolic bone diseases at the University of Sheffield Medical School, and also director of the WHO collaborating centre for metabolic bone diseases at the University of Sheffield. His research interests encompass benign and malignant bone disease, including osteoporosis. It is evident from his CV that his

experience and distinction in this field is very great. The fact that he is based at Sheffield University is, as I understand it, entirely coincidental. He was not a part of the ScHARR assessment group in this case.

61. The risk algorithms and coefficients which underpin the economic model in this case were supplied by Professor Kanis to Dr Stevenson. Although Professor Kanis had researched and developed these algorithms and coefficients in the course of his work for the WHO, it is common ground that the intellectual property in them belongs to Professor Kanis personally and they have never been published. I infer that they have commercial as well as academic value to Professor Kanis. He says at paragraph 14 of his first statement, now at bundle 8:1, page 5, "Both the risk equations and the coefficients are highly confidential and represent a significant body of work."

62. It is also common ground in this case that Professor Kanis supplied the algorithms, coefficients and other data to Dr Stevenson on an unqualified academic in confidence undertaking for so long as the data remained unpublished. Dr Stevenson says at paragraph 24 of his first statement, now at bundle 7:12, page 100:

> "Although commissioned by the WHO, it is the lead researcher, Professor Kanis, who owns the intellectual property rights to the products of that work ….. Professor Kanis agreed to provide me personally with the risk equations that were developed to calculate the risk of fracture. He did this on condition that I sign and return a confidentiality agreement restricting the disclosure of the information to colleagues of mine at the assessment group working on the appraisal and the development of the guideline."

63. Rather bizarrely, neither Professor Kanis nor Dr Stevenson can now locate their copy of the signed undertaking, so I have been unable to study its precise language and terms. They both agree, however, that it was signed and is to the effect described by Dr Stevenson.

64. Dr Stevenson says at paragraphs 29 and 33:

> "29. The assessment group provided NICE with a fully executable version of the new model on the strict basis that it would not be circulated beyond NICE. This was because I considered that if the model – in any format – were made available to anyone other than NICE then I would be in breach of the confidentiality I had given personally to Professor Kanis.
>
> 33. The risk equations and epidemiological data that Professor Kanis provided to me in confidence remain unpublished …. and therefore my confidentiality agreement with him, and NICE's confidentiality undertaking to me, will remain in place for the foreseeable future."

65. As I have already said, NICE has not disclosed the data even to the members of its own appraisal committee and I understand that apart from Dr Stevenson only a very small number of people have seen it.

66. Dr Stevenson also makes clear at paragraph 27 of his statement, now at bundle 7:12, page 101, that in this case it is impossible to supply even a read-only version of the economic model while maintaining the confidence of the data:

> "As full a description as possible (given the confidentiality undertakings) is provided in the strontium ranelate TAR. Unfortunately (and unusually) it was not possible to redact the model to hide the confidential information, while still leaving meaningful information available for consultees to examine. Even if the WHO risk equations were entirely invisible, it would still have been possible to backward-engineer the risk equations from the results in the various cells. This would have been a breach of the confidentiality undertaking I gave ….. to Professor Kanis."

**The approach to Professor Kanis to release confidentiality and permit disclosure**

67. Even when data has been supplied and accepted in confidence, NICE may later seek to persuade the owner and supplier of it to relax the confidentiality. In paragraph 4.2.5 of its Process Guide, quoted above, NICE state "The Institute asks consultees to reconsider restrictions on release of data when …. such restrictions would make it difficult or impossible for the Institute to show the evidential basis for its guidance."

68. At paragraph 18 of his statement, also quoted above, Professor Sir Michael Rawlins says:

> "…. Although the Institute makes considerable effort to persuade holders of confidential information to allow its guidance to quote from confidential material … and/or otherwise to allow the confidential material to have some visibility in the assessment process, it is not invariably successful…."

69. NICE makes clear, in my view appropriately and correctly, that it has to be even handed to all consultees, so it cannot disclose some data to one consultee but not to another. Subject to that, NICE may explore the possibility of the release of data to named individuals within, and on behalf of, any given consultee organisation, and on express terms as to confidentiality and the way in which the disclosed data may be used.

70. It will be recalled that the first appeal panel in December 2007 added a rider at paragraph 32 of its reasons to the effect that the failure of the WHO (but in fact the owner of the data was not the WHO but Professor Kanis) to publish data of considerable public importance was "regrettable". The staff of NICE interpreted this as a "recommendation" that the appraisal committee should seek permission from Professor Kanis to release the confidential information (see paragraph 17 of

the first statement of Dr Elisabeth George, employed by NICE and the associate director in the appraisal programme, now at bundle 7:1, page 5).

71. So, in the first part of 2008 NICE began a course of communication with Professor Kanis in which NICE sought release from the confidentiality and permission to disclose data. So far as I am aware, that course of communication consisted entirely of emails, with the exception of one, unfruitful, telephone conversation and one undelivered letter to which I will later refer.

72. Very recently, in preparation for the final hearing of these proceedings, each party has filed statements in explanation or elaboration of what the respective writer intended by each email. On behalf of NICE, that evidence is contained in the statements of Dr Elisabeth George. On behalf of Servier, it is contained in the statements of Professor Kanis himself who seems (not least, from his physical position in the courtroom throughout the hearing and the assistance he gave from time to time to Mr Chamberlain) now to ally himself with Servier.

73. I agree with Mr Beloff, however, that on an issue such as this it is not permissible or appropriate for the court, in judicial review, to take into account later statements by a writer as to what he meant or intended by what he wrote at the time. The recipient saw only the words on the paper (the emails). In assessing NICE's reaction to the communications from Professor Kanis I must leave out of account his later (and very recent) statements as to what he meant by them. At this stage of this judgment I will accordingly set out the essential parts of the exchanges with little comment from myself upon them. The emails and one published editorial are now conveniently gathered together in chronological order in bundle X:1.

74. On 23 January 2008 Dr George wrote to Professor Kanis:

> "…As you may … be aware, the appeal panel has requested [viz by its rider at paragraph 32] to seek permission from the WHO to release the Institute from its undertakings relating to academic-in-confidence data used to populate the economic model underpinning this appraisal. This request relates to the key epidemiological data on fracture risk which you provided under an academic-in-confidence agreement to the economic modeller at ScHARR early in 2005.
>
> I understand that you are the originator of this data and therefore seek permission that this data can be released from the academic-in-confidence agreement. We would appreciate if you could let us know by 21 February 2008 if you agree to this request."

75. Professor Kanis replied to Dr George on 7 February 2008:

> "Thank you for your letter of the 23rd January concerning the confidential data used to populate the health economic model for the appraisals on osteoporosis. I have now had the opportunity of discussing this internally, and we recognise the needs of NICE for transparency. For this reason, I am pleased to inform you that in principle the Collaborating Centre can make the probability algorithms (FRAX) available to NICE. I would be pleased to

meet Dr Andrew Dillon at a mutually convenient time to discuss the principles on which this might be based.

Please note that this offer of transparency does not release you or ScHARR from the obligation to keep in confidence the information previously provided.

You may be interested to know the manner in which the FRAX tool is intended for use, and I attach a prepublication preprint for your internal use."

Mr Andrew Dillon (he is not actually a doctor) is the Chief Executive of NICE.

76. Dr George then sent an internal email dated 22 February 2008 to staff at NICE, including Mr Dillon. It attached the above email from Professor Kanis, and said:

"After my request to John Kanis to release the confidential status of the WHO data (a request from the Appeal Panel) I received the message below…

It appears that the fracture algorithm developed by Prof Kanis has now been accepted for publication (see attached preprint), but that he is still not willing to lift the AIC status of the information that has fed into the model in 2005. I am not sure what 'principles' Prof Kanis has in mind that he wishes to discuss with you, Andrew, [viz Mr Dillon] related to the probability algorithms. These algorithms are the basis of Prof Kanis' fracture prediction tool (FRAX) which is now available on the internet.

I have looked at this FRAX tool briefly. There is no indication that it has been 'approved officially' by the WHO, but I don't know if that is possible anyway. The tool seems to be functioning well, but I cannot establish at the moment if, together with the above paper, the inputs in our economic model can be back-calculated. Which means that I do not know at the moment, if the availability of the paper and the internet tool automatically makes the AIC status invalid.

I have not had time to check if the data that the tool produces are the same as the data that the model produces. I will ask the technical lead to do that next week.

I need your advice as to how to proceed with this.

- Option 1: Acknowledge the e-mail and re-iterate that our request was about the release of the AIC status of the model, that once the data is available in published form (which it seems to be), we cannot see any justification for a continuation of the AIC status can be justified. I don't think this is going to be successful, but formally we would have done 'our duty' of requesting the information to be released, and leave it there. If C & C [consultees and commentators] keep requesting the model, we can state that Prof Kanis is not allowing us to do so.

- Option 2: We find out what he wants and offer a meeting. I am not sure what this could achieve technically, but you may have a preference for this for other reasons.

Please let me know how you want me to proceed. Many thanks."

77. Mr Dillon reacted to that email by asking Professor Peter Littlejohns, Clinical and Public Health Director of NICE, to telephone Professor Kanis to clarify the basis upon which NICE could use the FRAX tool to which Professor Kanis had referred in his email of 7 February. There is no filed evidence from Professor Littlejohns, but according to paragraph 22 of the statement of Dr George, now at bundle 7:1, page 7, "… Professor Littlejohns informed me that he spoke briefly with Professor Kanis by telephone, but Professor Kanis refused to go into the detail of the matter with anyone other than Mr Dillon." At paragraph 22 of his first statement, now at bundle 8:1, page 9, Professor Kanis agrees that Professor Littlejohns did telephone him and that "… during this call I explained to Professor Littlejohns that I would prefer to speak on the matter to Dr [sic] Dillon … The call was terminated at that point and there were no further discussions with Professor Littlejohns." The actual date of the telephone conversation is not evidenced but it must have been between 24 February (see bundle X:1, page 9) and 5 March (see bundle X:1, page 11).

78. On or about 5 March 2008 Mr Dillon sent to Professor Kanis a letter. Professor Kanis says that he only first received or saw that letter at or after about 18.00 on 28 April 2008 when, having not meantime received any reply, Mr Dillon re-sent it to Professor Kanis as an email attachment.

79. In these proceedings Servier, for their part, accept that Mr Dillon did first send the letter on or about 5 March. NICE, for its part, accepts that Professor Kanis never received the mailed letter and only first saw it in email form at or after about 18.00 on 28 April. This unfortunate twist, for which neither party can be blamed, had a somewhat bizarre consequence as I will shortly explain.

80. This judicial review involves a challenge to the acts and omissions and decisions of NICE, so I will next quote the letter of 5 March since, from the perspective of Mr Dillon and NICE, that is when he sent it and it then remained unanswered. Mr Dillon wrote:

> "I am writing with reference to you correspondence with Elisabeth George and also to your recent telephone conversation with Peter Littlejohns. Elisabeth George wrote to you on 23 January 2008, asking you for release of the data used to populate the economic model which is being used in these appraisals, which you provided under an academic-in-confidence agreement with ScHARR in 2005. We understand that the data is now publicly available through the FRAX website and is to be published in Osteoporosis International. I appreciate that you have views about how the technology appraisal and the clinical guidelines have been developed and that you would like to talk to me about them. However, our guidance development processes follow open and structured methods for engaging with those who have an interest in what we do. Unless there is a specific point about our request for

> the release of data, referred to above, I would prefer our engagement with you to use our normal consultations arrangements. My direct line telephone number, if you do need to speak to me about our request, is [a number is then given]."

81. As that letter evidences, Mr Dillon knew that there had been the recent telephone conversation with Professor Littlejohns. Mr Dillon gave his own direct line telephone number "if you do need to speak to me about our request." Professor Kanis (who, unbeknown to Mr Dillon, did not receive the letter) did not ring him.

82. From the perspective of Professor Kanis, he had not received any written response from NICE to his email dated 7 February 2008. He had been telephoned by Professor Littlejohns in late February/early March but had told him, in the words of Professor Kanis himself at paragraph 22 of his first statement, "that I would prefer to speak on the matter to Mr Dillon."

83. What followed next is bizarre. On 28 April 2008 an academic journal, "Osteoporosis International", received from Professor Kanis (and a co-author) an editorial which it "accepted" on 6 May and published on 5 June. It appears from the last, unnumbered, footnote to the editorial (now at bundle X:1, page 18) that it followed "a debate on NICE guidelines" at a European Congress on clinical and economic aspects of osteoporosis at Istanbul on 9-12 April 2008. Since the editorial was "received" on 28 April, and the email of Mr Dillon only sent at 18.03 on 28 April, I assume that Professor Kanis had already both written and submitted the editorial before he received Mr Dillon's email and, with it, the letter of 5 March. Since both Mr Chamberlain and Mr Beloff each place some reliance upon this editorial in the sequence of the correspondence, and since Professor Kanis later attached it to his email to Mr Dillon of 1 May 2008 (see below), I will briefly quote from it.

84. The editorial is headed "NICE continues to muddy the waters on osteoporosis." It begins that "The storm generated by NICE over the appraisal of osteoporosis treatments in the UK continues unabated." It implies that the effect of the appraisals in this case (referring at that date to the first, unrevised, FADs) is "disastrous." It then makes some comments critical of the NICE model, saying that "Some of these problems could readily be resolved by greater transparency of the model used by NICE." The editorial continues:

> "According to the NICE website, an approach was made in January 2008 to obtain from the WHO access to the algorithms used in the construction of the FRAX, but it is stated in the consultation documents that the committee [viz the appraisal committee] did not have access to these algorithms."

That would appear to be a reference to the letter from Dr George to Professor Kanis of 23 January 2008. The editorial continues:

> "This is at best misleading, since full access to FRAX was offered and a response from NICE is still awaited (J.A. Kanis, personal communication, 28 April 2008)."

85. The offer of "full access to FRAX" appears to be a reference to Professor Kanis' email letter to Dr George of 7 February 2008. Professor Kanis was able to write "a response from NICE is still awaited" since at that point he had not received the letter from Mr Dillon of 5 March 2008. The editorial continues by referring to "the dysfunctional consultation process" of NICE and is, generally, critical of the then FADs and recommendations.

86. Mr Dillon's email of 28 April attached the letter of 5 March and simply asked:

> "I wonder if you have yet had a chance to consider the attached letter, which I sent to you at the beginning of March?"

87. Professor Kanis replied on 1 May 2008 as follows:

> "Thank you for your letter dated 5th March 2008 that I received on 28th April. I had thought that my reply of 7th February was clear as was my later conversation with Peter Littlejohns.
>
> As you surmise, I do have concerns with the appraisals, but these have been persistently articulated through the Guideline Development Group, at least up to the time of my removal. In the absence of a formal route to NICE, I have thereafter voiced my concerns in the literature (see attachments).
>
> My reason for writing was not, however, to have a private voice on these matters, but to offer greater transparency of the FRAX tools to NICE. If you judge that this has been served by the availability since February 21st of the tools on the web, and our recent publications on FRAX, then the matter is closed. If not, then my offer to NICE still stands."

One of the attached items of literature was the (at that stage unpublished) editorial in Osteoporosis International.

88. Mr Dillon replied on 13 May 2008:

> "Thank you. I take it that you are now content for us to release to our consultees the data used to populate the economic model used in these appraisals, which you provided under an academic-in-confidence agreement with ScHARR in 2005."

89. Professor Kanis replied on 19 May 2008:

> "Thank you for your letter of 13th May, which I find somewhat disingenuous. The offer is clearly articulated in my letter to Elizabeth George of the 7th February (see copy pasted below). It does not 'clear' you or ScHARR from the obligation to keep in confidence the information previously provided."

The letter of 7 February clearly appears immediately below.

90. Mr Dillon replied on 19 May 2008:

> "Thank you. Your position is, finally, made clear."

91. The correspondence there ended and, so far as I am aware, there has been no subsequent communication between NICE and Professor Kanis. The continuing position of NICE is, in a sentence, that Professor Kanis has not released it from the undertaking of confidentiality, despite its approach and request to him, and that NICE is bound by the "confidentiality override."

## Eisai v NICE and the law

92. The decision of the Court of Appeal in Eisai v NICE clearly occupies the same territory as the present case. In that case, which related to the appraisal of drugs for the treatment of Alzheimer's disease, NICE disclosed to consultees a read-only, but not a full version of its economic model. NICE argued that it had disclosed enough to meet the requirements of fairness, and that confidentiality and other administrative considerations precluded disclosure of the fully executable version. The Court of Appeal held that fairness required disclosure of the full model and that "the argument concerning confidentiality is not one to which I would attach any weight." (Richards LJ at paragraph 59).

93. It is clear that the Court of Appeal did not regard their decision and reasoning as wholly fact-specific, for at paragraph 67 Richards LJ said:

> "Strictly, I should express myself in the past tense, by reference to the particular circumstances of the appraisal process to which the challenge relates. The reality, however, is that much of the argument has been advanced in wider terms, by reference to NICE's general policy and the general implications for its work of appraisal if it is required to release fully executable versions of its economic models to consultees. I have borne firmly in mind, in reaching my conclusion, the wider significance of the court's decision in this case."

94. Mr Chamberlain thus submits, in effect, that in Eisai the Court of Appeal intended to, and did, lay down a general principle that NICE must always disclose its full economic model to consultees (at any rate, if they request to see it). If the Court of Appeal did lay down such a principle that is, of course, binding upon me and determinative of ground (a) in this case. At paragraph 57 of his skeleton argument Mr Chamberlain put the proposition thus:

> "Eisai plainly establishes that, in the light of the centrality of the economic model, natural justice requires the disclosure of the model; and that confidentiality concerns generally are of insufficient weight to justify non-disclosure."

95. In my view, however, the decision of the Court of Appeal was more fact specific and its true scope requires careful analysis. Richards LJ said that he had "borne firmly in mind… the wider significance" of the court's decision. He did not express that he was laying down a general principle that confidentiality can never justify non disclosure of the full model.

96. The overriding requirement is "fairness". But what fairness requires is itself fact-specific: see Richards LJ at paragraph 27:

> "What fairness requires depends on the context and the particular circumstances …. Simon Brown LJ emphasised the need to avoid a mechanistic approach to the requirements of consultation."

97. Eisai plainly establishes in paragraphs 34-53 the very high importance of consultees being able to see the fully executable version of the economic model. Although the science in the two cases is different, there is no less importance in the present case as I have explained in paragraphs 41 - 44 above.

98. Richards LJ then turned at paragraph 55 to consider the reasons relied upon by NICE as outweighing disclosure, of which the first was confidentiality. I need say nothing about the second reason, "adverse practical consequences for the appraisal process" (see paragraphs 61-65), since such reasons are not advanced in the present case.

99. Richards LJ described at paragraph 55 the legal and factual basis of the claim for confidentiality in that case. The claim was as to the confidentiality of the model itself. The model had been commissioned from a university (SHTAC) by the Secretary of State for the purpose of the appraisal process. The director of SHTAC (who corresponds to Dr Stevenson, as head of the ScHARR assessment group in the present case) considered that the model was confidential, and could not be released without the agreement of SHTAC (see Richards LJ paragraph 55). Richards LJ continued at paragraph 56:

> "That all goes to explain why, as a practical matter, NICE treats the model as subject to obligations of confidentiality and is unwilling for that reason to volunteer disclosure of the fully executable version."

100. I stress in that quote the words "as a practical matter". It seems that at that stage, consistent with paragraph 4.4.1.9 of the Process Guide quoted above, NICE was operating, "as a practical matter," a policy of treating the fully executable version as confidential.

101. Richards LJ continued at paragraph 56: "In legal terms, however, the explanation does not withstand scrutiny." He then examined the terms of the actual research contract in that case between the Secretary of State for Health and the university and concluded that, under that contract:

> "There is no express duty of confidentiality restricting the use or disclosure of the model, and there is no reason why, in the circumstances, such an

> obligation might be implied so as to prevent the disclosure that Eisai seeks. It would … be very surprising if a model commissioned and paid for by the Secretary of State for the purpose of NICE's appraisal process were subject to obligations of confidentiality preventing disclosure of the fully executable version to consultees."

102. Pausing there, I stress the words "no reason why, in the circumstances, such an obligation might be implied so as to prevent the disclosure." The relevant circumstances were the contractual arrangement between the Secretary of State and the university, and the fact that the subject matter of the claimed confidentiality, namely the model itself, had been commissioned and paid for by the Secretary of State for the very appraisal in question. Further, Richards LJ plainly contemplated, in the words which I have stressed, that there may be other circumstances in which an objection of confidentiality may be implied so as to prevent disclosure.

103. The whole argument and issue in the Eisai case was as to disclosure of the fully executable model. Disclosure of the read-only version was not, in that case (nor usually), in issue. But Richards LJ described at paragraph 57 that as "all the relevant information" could in any event be found in the read-only version it was "difficult to see how release of the fully executable version can be subject to objection on the ground of confidentiality."

104. At paragraph 58, to which I will later return, Richards LJ referred to the possibility of NICE seeking permission from the SHTAC to disclose. He then concluded at paragraph 59:

> "Accordingly, the argument concerning confidentiality is not one to which I would attach any weight." (my emphasis).

105. The conclusion in that case that the argument concerning confidentiality does not carry any weight, plainly follows from the earlier conclusion that the legal basis of the claim does not withstand scrutiny. So in his summary at paragraph 66, "pulling the various strands together", Richards LJ described the reasons put forward for refusal to release the fully executable version as "in part unsound" and "in any event of insufficient weight to justify NICE's position". The reason based on confidentiality had been shown in paragraph 56 to be unsound, with the result that, at paragraph 59, it did not carry any weight. The reference in paragraph 66 to being "in any event of insufficient weight" must ultimately, therefore, relate to the second reason of "adverse practical consequences" to which I need not refer.

106. The entire argument in Eisai related to provision of the fully executable version of the model in circumstances in which the read-only version was in any event provided. Richards LJ concluded paragraph 57 by saying:

> "If [my emphasis] provision of the read-only version gives rise to no issue of confidentiality, …. it is difficult to see how release of the fully executable version can be subject to objection on grounds of confidentiality."

In the present case, provision even of the read-only version does indeed give rise to a serious issue as to confidentiality.

107. In my judgment, the claim to confidentiality in the present case is founded on a totally different basis to that in Eisai. Although NICE has declined to disclose the model at all, whether in fully or even only partially executable form, it is not actually the confidentiality of the model itself that it seeks to protect; rather, it is the algorithms, coefficients and other data which were supplied by Professor Kanis and which disclosure of the model would reveal.

108. In contrast to Eisai, there is no claim to any confidentiality based on the written contract with ScHARR which commissioned the appraisal. The claim is firmly based on the undertaking of confidentiality that was given by Dr Stevenson to Professor Kanis. If a contract is constructed as to the supply of the data by Professor Kanis to Dr Stevenson, then the promise of confidentiality was an express and fundamental term of that contract. NICE in turn gave an undertaking as to confidentiality to Dr Stevenson (see paragraph 64 above). In the present case, in my view, there is an express duty of confidence upon each of Dr Stevenson to Professor Kanis, and NICE to Dr Stevenson, by which they are bound and to which some weight must be given.

109. At paragraph 59 of his judgment in Eisai v NICE, Richards LJ said:

> "I should add, though I do not think it arises, that even if disclosure were prima facie a breach of confidence, [leading counsel for NICE] conceded that NICE would have a public interest defence available to it if disclosure were necessary in order to meet the requirements of procedural fairness."

This refers, in effect, to Professor Sir Michael Rawlins' "third option" to which I have referred in paragraphs 58 and 59 above.

110. Strictly, that sentence by Richards LJ is no more than a recording of a concession made, and does not express any considered view of the court. In any event it is patently obiter ("though I do not think it arises"). Further, the terms of the concession (and any implied opinion of the Court of Appeal as to the correctness of the concession) are not clear. To concede that there is a public interest defence "available" may be to concede no more than that such a defence might reasonably be deployed. It is not necessarily to concede that such a defence would prevail.

111. In my view, whether or not a public interest defence might be "available", the third option of breaking the confidence is simply not an option at all for ethical and policy reasons that I have described in paragraphs 58 and 59 above and will not repeat.

112. NICE is inevitably faced, therefore, with the two options described by Professor Sir Michael Rawlins in his statement and quoted in paragraph 57 above. Whilst there is a very high duty of procedural fairness, it is not the only duty in play. The overall duties upon NICE are those imposed by the statutory instrument by which it was founded and exists, and any lawful directions to it from the Secretary of State. In general terms, it also has high duties to all patients of the NHS, to the taxpayer, and to the public generally. If it is to discharge all

those duties, then there may, I stress may, be some circumstances in which it has no effective alternative than to give a confidentiality undertaking for the reasons described by Professor Sir Michael Rawlins.

113. For these reasons it cannot, in my view, be the law that NICE must always and without exception disclose the economic model such that it is invariably driven into Professor Sir Michael Rawlins' second option and can never accept confidential material no matter how important that material nor how hard it has tried to obtain release from the confidentiality.

114. In other areas of the law, the law recognises that a balance may need to be struck, having regard to the importance of the context, between the imperative and duty of transparency/fairness/disclosure, and any imperative and duty of confidentiality. I instance the law in relation to public interest immunity; and the recognition by the law that, very exceptionally, the overarching welfare of a child may require and justify non-disclosure of a document even if (very exceptionally) it is seen by the court. Of course these are very different legal situations with different values and different statutory and other legal principles in play. I do not suggest there is any analogy; but only that they are examples of a balancing process.

115. In general terms the principle is, in my view, as follows. NICE is always under a duty and imperative of transparency and fairness which normally requires full disclosure of its fully executable economic model and the data upon which it is based. It should not, therefore, normally give (or permit its assessment groups to give) undertakings as to confidentiality. Exceptionally, it may do so if the importance of the material to the quality and robustness of the appraisal is sufficiently great; and if it has tried sufficiently hard to obtain permission to disclose, but has failed. Further, the ambit of any confidentiality undertaking should be as restricted as possible. For convenience I will call this "the exceptional imperative of confidentiality."

116. Plainly it is NICE which must, in the first instance, make a judgment and decision as to whether there is an exceptional imperative of confidentiality such that it, or its assessment group, must give a confidentiality undertaking, and if so, its ambit or scope. Such judgments and decisions by NICE are reviewable by a court in judicial review and NICE must be prepared to justify them.

117. For present purposes I am prepared to assume, without deciding, that NICE (or Dr Stevenson) were justified in deciding that the exceptional imperative of confidentiality applied in this case, and were justified in giving the undertaking to Professor Kanis. His own evidence indicates (and Servier do not dispute) that he simply would not, in 2004/2005, have supplied the algorithms and coefficients except on an undertaking as to confidentiality.

118. That, however, is not the end of the matter. The fact that an undertaking as to confidentiality has been given does not release NICE from any further obligation to seek that permission is later granted to disclose.

119. That follows, first, from NICE's own published position: see paragraph 4.2.5 of its Process Guide, quoted to in paragraph 51 above; and its practice: see paragraph 18 of the statement of Professor Sir Michael Rawlins, quoted in paragraph 57 above.

120. It also plainly follows from part of the reasons and reasoning of the Court of Appeal in Eisai v NICE. One of the reasons why the court considered no weight attached to confidentiality in that case appears in paragraph 58 of the judgment of Richards LJ where he said:

> "…. there is nothing to show that, if it had wanted to disclose [the fully executable] version (on appropriate undertakings) during this appraisal and had sought the consent of SHTAC for the purpose, such consent would not have been given. The evidence is that SHTAC did not in fact agree to disclosure; but it is not said that SHTAC would have withheld its agreement …..if it had been pressed on the point by NICE."(my emphasis)

121. In my view that passage, and in particular the words I have emphasised, clearly indicates that even when NICE is (or, as in that case, believes itself to be) under a duty of confidence, it is also under some duty to "press". The Court of Appeal did not further elaborate on that duty nor the extent of it. However during the course of his submissions Mr Beloff said (see verbatim transcript of the proceedings, Day 3, 22 January 2009, page 321, line 23 – page 322, line 6):

> "We would be prepared to proceed on the basis of this, but go no further, that as a subset of our obligation of procedural fairness, and in order to see whether or not we could grant a consultee access to that which he or it properly wishes, where there is a confidentiality inhibition, we ought to take reasonable steps, and I emphasise that, reasonable steps, to obtain permission to disclose the confidential information."

122. In the ensuing passage at pages 323-327, in dialogue with myself, Mr Beloff accepted (see page 324, line 9) that what amounts to reasonable steps is context specific; but stressed that the court in judicial review must allow a margin of appreciation to NICE in NICE's judgment as to what amount to reasonable steps; and that the court may only impugn NICE's judgment if it considers that it was a perverse judgment (page 323, lines 1-13).

123. I broadly accept those submissions. At any rate for the purpose of this case, I formulate the duties upon NICE, and the powers of this court, as follows: Even after a confidentiality undertaking has been justifiably given, NICE remains under a positive duty, at appropriate stages in the process, to take all reasonable steps to obtain permission to disclose the information. In deciding what are reasonable steps it must keep firmly in mind the high importance of fairness and transparency, and the importance of the respective information to understanding the appraisal. Having regard to the decision of the Court of Appeal in Eisai v NICE, it must particularly strive to seek permission to disclose the economic model and /or the data contained therein. In proceedings for judicial review, the court should afford due weight to the decision of NICE as to what amount to reasonable steps, but may grant relief if the court considers that NICE has not taken such steps as are reasonable in all the circumstances of the case.

**The steps taken by NICE in this case**

124. I now apply that test to the correspondence and events described in paragraphs 71 - 91 above.

125. It is part of the background of this case that there had earlier been some falling out between Professor Kanis and NICE. Since 2001 he, with his great expertise in this field, had been part of the original Guideline Development Group (GDG) for this appraisal. Several years later, in late 2006, NICE removed him from the GDG because of perceived conflicts of interest, although Professor Kanis had declared all the relevant interests at the outset. By his later letter dated 15 March 2007, now at bundle 8:3, page 136, Mr Dillon effectively accepted (and apologised) that he, Mr Dillon, had been at fault in permitting Professor Kanis to become a member of the GDG in the first place. Professor Kanis frankly says at paragraph 11 of his first statement, now at bundle 8:1, page 4, that he "was upset to have been removed from such an important project without what I considered to be a good reason." Mr Beloff suggested in his skeleton argument that Professor Kanis "appears to harbour a grudge against NICE." I am not prepared to impute or assume that Professor Kanis has been motivated in anything he has said or done by "a grudge". But I do bear in mind in a general way that Mr Dillon had removed him from the GDG. Mr Dillon felt that he, Mr Dillon, had erred and owed an apology to Professor Kanis. Professor Kanis was upset. So relations between the two men may have been strained, and that seems to be part of the background to the somewhat obtuse correspondence between them.

126. Mr Beloff submitted that NICE had asked Professor Kanis altogether five times to release the confidentiality. This counted in the unreceived letter of 5 March and its resending on 28 April as two times; but Mr Beloff submitted that, from the perspective of NICE, they did still ask five times. He subjected the correspondence and in particular Professor Kanis' replies to detailed textual analysis. He submitted that NICE were not being obtuse but that Professor Kanis was being obscure and even obstructive and playing hard to get.

127. It must, however, be borne very firmly in mind that the duty was upon NICE. There was no duty upon Professor Kanis.

128. I agree that there is some confusion in the first paragraph of Professor Kanis' letter of 7 February by the juxtaposition in the phrase "make the probability algorithms (FRAX) available." Professor Kanis', now published, FRAX tool is based upon his algorithms and coefficients but does not reveal them. There is ambiguity in the letter as to whether what he is offering is simply the FRAX, or the algorithms themselves. I agree, too, that the letter does not make any express reference to the coefficients.

129. Mr Beloff was critical that the letter made an offer "in principle" only and that meantime it reiterated and stressed in the second paragraph the existing confidentiality. I do not see how there is anything obscure, obstructive, or hard to get about that. It must have been obvious to NICE that release of the

confidentiality would be a very significant step for Professor Kanis to take. In his first response they could hardly have expected him to go further than an in principle offer, reiterating the confidentiality until the details had been negotiated. To my mind the key sentence is the very clear offer to meet Mr Dillon: "I would be pleased to meet Dr Andrew Dillon at a mutually convenient time to discuss the principles on which this might be based." That is a clear offer to meet, specifically in order to discuss the principles of disclosure. There is no hint or suggestion in it of meeting to discuss the content of the technology appraisals (i.e. the then FADs) themselves.

130. The internal email of Dr George dated 22 February suggested two options to Mr Dillon. The first was to do no more than go through the motions so that NICE had "done 'our duty'", which would plainly be an inadequate response. The second was to find out what he wants and offer a meeting. The meeting which Professor Kanis had requested was, of course, with Mr Dillon, as chief executive. Why Mr Dillon then suggested in his internal email of 24 February that Professor Littlejohns, rather than he himself, should give Professor Kanis a call is obscure. At all events, it is common ground that that telephone call was short and unproductive; but, and this is crucial, that Professor Kanis repeated (consistent with his email of 7 February) that he would prefer to deal with Mr Dillon.

131. I find it hard to understand why, in these circumstances, Mr Dillon did not, as a minimum, telephone Professor Kanis himself and (subject to the content of any telephone conversation) offer a meeting. Instead, the letter dated 5 March is, frankly, obtuse. It stated in the first main paragraph that "We understand that the data is now publicly available through the FRAX website …." That was not the understanding at any rate of Dr George, for her email of 22 February very clearly indicates her uncertainty whether publication of the FRAX reveals the data: "…. I cannot establish …. if … the inputs in our economic model can be back-calculated …. I do not know … if the availability of the internet tool automatically makes the AIC status invalid." If NICE had enquired of its own experts, e.g. Dr Stevenson, it would soon have established that it did not.

132. The last paragraph began by a confusing reference to Professor Kanis talking to Mr Dillon about the appraisal itself. As to direct communication between them about the request for the release of data, Mr Dillon merely gave his telephone number and left the initiative entirely to Professor Kanis. I repeat, however, that the duty was not on Professor Kanis but on NICE.

133. It was no fault of NICE that that letter was not received, but the fact that NICE then took no further step or action at all between 5 March and 28 April suggests to me that they were not being at all active or exigent in their attempt to discharge the duty to seek permission to disclose.

134. The next event was submission by Professor Kanis of his editorial. I personally find the part which I have quoted from that editorial bizarre. If, from his perspective, Professor Kanis was still awaiting a response to his letter of 7 February, or in reaction to his telephone conversation with Professor Littlejohns, all he needed to do was send a chaser enquiry to NICE. Whilst there may be all sorts of grounds for legitimate criticism in the editorial of NICE's model and assessments, it seems completely disproportionate to publish to the whole world

(the journal is Osteoporosis International) that "a response from NICE is still awaited" without, first, sending a single chaser. One is left with the impression that Professor Kanis wanted to underpin his immediately following reference to "the dysfunctional consultation process" of NICE.

135. At all events, when he did receive the email of 28 April and, with it, the letter of 5 March, Professor Kanis replied promptly on 1 May. Again, Mr Beloff is critical of that reply. I am not. The sentence in the first paragraph that "I had thought that my reply of 7th February was clear as was my later conversation with Peter Littlejohns" can only be a reference to the offer to meet with, or at any rate talk to, Mr Dillon, since that was the only content of the conversation with Peter Littlejohns. The letter goes on to make plain, in reply to the last paragraph of the letter of 5 March, that he was not seeking a private voice on the appraisals. The last sentence "If not, then my offer to NICE still stands" can only be the "in principle" offer, coupled with the offer to meet Mr Dillon to discuss the principles for disclosure.

136. Like Professor Kanis, I regard Mr Dillon's reply of 13 May as being inappropriate. Professor Kanis had patently not expressed in his letters of either 7 February or 1 May some blanket willingness that the data could now be disclosed. Mr Beloff argues that Mr Dillon wrote in the terms that he did in order to "flush out" Professor Kanis. What Professor Kanis clearly reasonably required was not to be flushed out, but to have a dialogue. I do not accept that he was, as Mr Beloff suggested, being evasive or playing cat and mouse.

137. Mr Dillon's final letter of 19 May was, with respect to him also inappropriate. It states "Your position is, finally, made clear." All Professor Kanis had actually done on 19 May was, effectively, to repeat exactly what he had said on 7 February by pasting and reincorporating the same letter. If it was not clear to Mr Dillon on 7 February, it could not "finally" be any more clear on 19 May.

138. Mr Beloff "tied the threads together" in a series of submissions, now at the transcript of proceedings Day 3, page 359, line 10 and following. He submitted that Professor Kanis volunteered nothing. He could have initiated dialogue with NICE. He was uncooperative. He did not take up the offer of Mr Dillon's telephone number. In my view all these points assume that the duty and onus was on Professor Kanis. It was the other way round.

139. In my very clear opinion, NICE in general, and Mr Dillon in particular, failed to take all reasonable steps to seek permission from Professor Kanis to release the data. They should have promoted a meeting with him and explored ways of making his in principle offer a practical reality; for example by proposing and seeking drafted terms and undertakings of confidentiality from named persons on behalf of each of the consultees. Whilst I afford a margin of appreciation to NICE, they fell outside it. My overall impression is that NICE moved rapidly from Dr George's option 2, to option 1, of merely going through the motions so they could claim they had done their duty.

**Outcome and relief on ground (a)**

140. So far, I have analysed the correspondence and events in January – May 2008 without regard to the contents of Professor Kanis' recent statements, save for his factual evidence as to the content of his telephone call with Professor Littlejohns and his admission to being upset by his removal from the GDG. His evidence does, however, become relevant in considering outcome and relief.

141. If there was evidence from Professor Kanis now that he will not release his confidentiality, then all the above would be of no practical effect. NICE could say that even if they had pressed him harder and had taken every reasonable step, it was all to no avail and, accordingly, that the undertaking as to confidentiality must prevail.

142. That is not, however, the stated position of Professor Kanis who has made his witness statements expressly "on behalf of Servier" (see bundle 8:1, page 1, paragraph 1). At paragraph 17 of his second statement, now at bundle 9:33, page 424, Professor Kanis says "I am …. more than happy to assist NICE in disclosing the fully executable version of this model to consultees, as long as I [can receive] undertakings about the ongoing confidential status of the data." At paragraph 23 he uses the past tense, but plainly implies that he still is open to discussion of disclosure to restricted groups of persons, namely designated individuals within the consultee groups, and also to nominated representatives of the NHS and patient groups; all subject to confidentiality undertakings by the named persons. He specifically states at paragraph 26 of his first statement (bundle 8:1, page 10) that he would be happy to disclose the coefficients themselves to a limited number of persons in confidence.

143. Although Mr Chamberlain represents Servier, not Professor Kanis, Professor Kanis is his witness and, as I saw, the two of them frequently communicated in the court room during the hearing. I must assume, therefore, that I can place reliance upon the assertion at paragraph 58 of the skeleton argument of Mr Chamberlain that had Professor Kanis been asked to consent to disclosure on the limited basis of disclosure to (all) consultees for the strictly limited purpose of making representations in relation to this appraisal, he would have done so. The plain inference is that he still would do so.

144. I proceed on the basis that Professor Kanis is a man of integrity who will not now resile or wriggle from what he has said. If, therefore, I were to quash the revised FADs dated 30 June 2008 I have every reason to suppose, first, that Professor Kanis would permit, on suitable terms, disclosure to all consultees of the fully executable model and the key data therein; second, that consistent with their avowed aim and their legal duty of transparency, NICE would give that disclosure on those terms to all consultees; third, that NICE would receive and evaluate any comments that any consultee may submit in response thereto; and fourth, that in the light thereof NICE would reconsider and, if they think fit, further revise the FADs.

145. I will decide the actual form of remedy in the light of submissions made after the parties have had an opportunity to consider this judgment.

## GROUND (c)

**Ground (c) Non acceptance by NICE of the post hoc analysis**

146. This ground is highly case specific. TROPOS is an acronym for Treatment of Peripheral Osteoporosis. The TROPOS trial was a randomised control trial (RCT) conducted in 11 European countries and in Australia between 1996 and 2003. The trial is conveniently described in the Journal of Clinical Endocrinology and Metabolism (JCEM) in 2005 (now at bundle 8:12, pages 211-217). The TROPOS trial itself was a randomised, double-blind, placebo controlled trial, designed to assess the effectiveness of strontium ranelate in preventing non vertebral factures in post-menopausal women with osteoporosis, and also to assess its tolerability. Non vertebral fractures are fractures of hip, wrist, pelvis and sacrum, ribs-sternum, clavicle or humerus. The study was not designed or powered (i.e. sufficiently populated) to demonstrate an antifracture efficacy at each individual site.

147. The function of the European Medicines Evaluation Agency (EMEA) is to evaluate the quality, safety and efficacy of drugs and medicinal products and in the light thereof to grant a market authorisation. The EMEA evaluates efficacy, but not cost or cost effectiveness.

148. Servier applied to EMEA in 2003 for market authorisation for strontium ranelate, as Protelos. Servier submitted as part of its application the results of the TROPOS trial. However, as I have stated, that trial itself was not designed or powered to assess the effect of strontium ranelate specifically on hip fractures and did not do so. The relevant committee (the CHMP) of the EMEA requested that data be supplied specifically as to the reduction in the risk of hip fracture. To meet that request, Servier performed post hoc sub group analysis as now fully described by their head of the therapeutic research team for Protelos, Dr Patricia Iris Chatelain-Belissa, in her statement now at bundle 8:9, pages 190-198, paragraphs 12-13. The analysis analysed hip fractures in a subgroup of women aged 74 or older with a femoral neck BMD T minus score of -3 or less. A T-score is a measure of how far a particular patient's bone mineral density is below the expected mean. The study and the subsequent post hoc analysis is highly technical, but the narrative summary conclusion in the JCEM article is that:

> "This study shows that strontium ranelate significantly reduces the risk of all nonvertebral [fractures]" – that is, the conclusion of the RCT itself – "and in a high risk subgroup, hip fractures" – that is, the conclusion of the post hoc subgroup analysis – "over a 3 year period, and is well tolerated. It confirms that strontium ranelate reduces vertebral fractures. Strontium ranelate offers a safe and effective means of reducing the risk of fracture associated with osteoporosis."

149. In the light of the TROPOS data and the analysis, the CHMP reported that:

> "… from the efficacy viewpoint, the submitted documentation [which included the post hoc analysis] is considered sufficiently robust to support an indication for treatment of postmenopausal osteoporosis, to reduce the risk of vertebral and hip fractures …. For this indication, the demonstrated effect of strontium ranelate 2 g/d appears comparable with that of bisphosphanates, and the strategy to accept a therapeutic indication partly based on post hoc analysis of a revised target population of particular medical interest has regulatory precedent in the European licensing of bisphosphonates."

150. I emphasise the underlined words. In short, the CHMP, and through it the EMEA, accepted for their purposes the validity and outcome of the post hoc analysis. In due course EMEA granted a market authorisation for Protelos for the treatment of post-menopausal osteoporosis to reduce the risk of vertebral and hip fractures.

151. Unsurprisingly, when NICE commenced its appraisal, Servier submitted to NICE, and relied upon, the data from the TROPOS trial itself and also the post hoc subgroup analysis.

152. The ScHARR assessment group in their TAR were not impressed by the post hoc analysis and Servier made further detailed representations by their letter from Trefor Jones to Cathryn Fuller of NICE dated 27 September 2005, now at bundle 1:9, pages 266-277. Trefor Jones stressed that the analysis had been performed at the request of EMEA and was not a data-mining exercise, and that its validity had been endorsed by EMEA.

153. NICE's own appraisal committee patently gave consideration to the results of the TROPOS trial and the post hoc subgroup analysis for they referred to it in the initial FADs. The language (but not the paragraph numbering) of the references is the same in both the FAD for primary and the FAD for secondary prevention. I quote from that for primary prevention, now at bundle 2:27.

154. In section 4.1 the FAD addresses the clinical effectiveness of a range of drugs including, at 4.1.10, strontium ranelate.

155. At 4.1.10.2 the FAD records:

> "The Assessment Group reported the results of a published meta-analysis that resulted in an RR for vertebral fracture of 0.60 (95% CI 0.53 to 0.69, two RCTs, n = 6551) and an RR for all non-vertebral fractures (including wrist fracture) of 0.84 (95% CI 0.73 to 0.97, two RCTs, n = 6551). Hip fracture efficacy was established in one study; the RR for hip fracture in the whole study population was 0.85 (95% CI 0.61 to 1.19, one RCT, n = 4932). A post-hoc subgroup analysis in women over 74 years of age with a T- score of -2.4 SD resulted in an RR for hip fracture of 0.64 (95% CI 0.41 to 0.98, one RCT, n = 1977)."

156. It is accepted by Mr Chamberlain that that paragraph accurately summarises and records the results of both the TROPOS trial and the post hoc subgroup analysis.

157. In section 4.3 the FAD turns to "Consideration of the evidence" and at paragraph 4.3.3 states:

> "The Committee noted that strontium ranelate was effective in preventing vertebral and pooled non-vertebral fractures, and resulted in a non-significant 15% reduction in hip fracture risk. The Committee was also aware of the result of a post-hoc subgroup analysis showing a statistically significant reduction in the incidence of hip fractures in women over the age of 74 years who have a T- score of -2.4 SD or below."

158. At paragraph 4.3.23 the FAD concludes in relation to strontium ranelate as follows:

> "The Committee did not accept the estimate of efficacy for strontium ranelate in preventing hip facture from the post-hoc subgroup analysis, but accepted the statistically non-significant RR of 0.85 for hip fracture to acknowledge an effect on this important type of fracture. The Committee noted that strontium ranelate was dominated by alendronate (based on the price of £95.03 per year for alendronate); that is, strontium ranelate has a greater acquisition cost and is not more efficacious. Therefore, the Committee did not consider strontium ranelate to be cost-effective for the initiation of therapy for the primary prevention of osteoporotic fragility fractures in postmenopausal women."

159. On Servier's appeal from the initial FADs, the appeal committee summarised their ground of appeal on this point as follows (now at bundle 4:3, page 12):

> "The appraisal committee has failed to take account of an important piece of scientific evidence; the appraisal committee has demonstrated internally inconsistent decision making with the generalisation of relative risk data generated in low risk patients and extrapolated to all patients under consideration; the appraisal committee has demonstrated inconsistent decision making in standards applied both within this appraisal and compared to other appraisals in their application of the hierarchy of evidence."

160. Dr Guy Yeoman and Dr Chatelain-Belissa made submissions for Servier. Professor Andrew Stevens, head of the Department of Public Health and Epidemiology at the University of Birmingham, and chairman of the appraisal committee which had produced the FADs, explained the position of that committee.

161. A complaint of Dr Yeoman was that the appraisal committee had given favourable regard to the drug etidronate on the basis of purely observational data, whereas it had disregarded evidence from a RCT (viz the TROPOS trial) of strontium ranelate that showed a statistically significant reduction in hip fractures.

162. Professor Stevens explained that that evidence was only found in a post hoc analysis of a sub group of high-risk patients [viz aged 74 or over with a BMD T - score of - 3] that had not been pre specified [i.e. built into the design of the RCT]. The appraisal committee had allowed for this weak evidence by setting the hip fracture rate with strontium ranelate to 0.85. He said that the observational studies had failed to show a significant beneficial effect on hip fracture rate with etidronate, and the value for etidronate had been set to 1.0 [An RR of 0.85 indicates greater effectiveness than an RR of 1.0. A value of 1.0 attributes no effect at all.]

163. Dr Chatelain-Belissa replied by explaining that the post hoc analysis had been requested by EMEA and that the request arose because EMEA had altered the rules for licensing medicines for osteoporosis after the TROPOS trial had been designed and conducted.

164. The conclusion of the appeal panel, now at bundle 4:3, page 12, was:

> "The appeal panel understood the difficulties facing Servier as a result of the change in the standards expected by EMEA. The panel also accepted that the appraisal committee had taken into account the evidence and evaluated it appropriately. It had not been unfair. The appeal panel therefore dismissed the appeal on this point."

165. The revised FADs accordingly repeated their references to, and treatment of, the TROPOS trial and post hoc analysis in the same terms as the original FADs which I have already quoted. As I have already said, the second appeal panel refused to entertain a further appeal on the point.

166. Mr Chamberlain accepts that the functions of EMEA and NICE differ. EMEA is concerned with the efficacy/benefit : risk ratio. NICE is concerned with the efficacy/benefit : cost ratio. But he submits that the measure of, and evidence as to, efficacy remains constant whether what is under consideration is its ratio to risk or ratio to cost. He stresses the acceptance by EMEA of the post hoc analysis data. The data has also been relied upon by the Scottish counterpart to NICE, the Scottish Medicines Consortium (SMC): see their published advice dated 8 July 2005, now at bundle 5:25, page 410, where they reproduce the post hoc analysis data and advise the use of Protelos for restricted use, but add the rider: "However equivalent cost-effectiveness to bisphosphonate therapy has not been demonstrated."

167. Mr Chamberlain submits that against this background there was a particular onus on NICE to justify why it came to a different view from EMEA and SMC, and why it did not accept evidence which those bodies had accepted.

168. In support of that submission he relied in particular on the observation of Carnwath J in R v Cardiff County Council ex parte Sears Group Properties Ltd. [1998] 3 PLR 55 at 64B – F where he said:

> " …. where a formal decision has been made on a particular subject matter or issue affecting private rights by a competent public authority, that decision will be regarded as binding on other authorities directly involved, unless and

> until circumstances change in a way which can be reasonably found to undermine the terms of the original decision …"

169. Carnwath J later said that underlying that approach "is the common sense view that, in the public sphere, once the matter has been formally decided, it should stay decided until circumstances change in some material respect."

170. Mr Chamberlain submitted that NICE is accordingly not entitled to depart from or reject a factual finding (viz as to efficacy) made by a competent and expert body (EMEA), and relied upon by a consultee, without providing substantial justification and reasons. He does not go so far as to submit that NICE could not depart from the view of EMEA.

171. Ex parte Sears itself concerned the extent to which a successor highway authority was bound by the view and decision of its predecessor. In my view there is a considerable difference between the role of highway, planning and similar authorities (including that of inspectors) and the role of NICE. NICE must act with fairness and transparency but is not a quasi judicial body. NICE has a duty to obtain and evaluate all relevant evidence, to apply its own expertise and that of the members of its committees, and to come to its own, non-delegable, view as to what recommendations and guidance it should give in discharge of its functions which I have earlier described.

172. It was plainly incumbent upon NICE to consider the results of the TROPOS trial and the post hoc analysis, since that had been submitted and relied upon by a consultee. It did do so. As part of the submission by Servier was the very fact that EMEA had accepted the validity, for its purpose, of the post hoc analysis, NICE cannot fail to have had that point in mind. But in my view it was in no way bound by it, and the decision how much weight to attach to the post hoc analysis was entirely a matter for NICE.

173. As to the requirement generally of reasons, Mr Chamberlain relied upon the approach described by Lord Brown of Eaton-under-Heywood in South Bucks District Council v Porter (No 2) [2004] 1 WLR 1953 at page 1964 paragraph 36, where he said:

> "The reasons for a decision must be intelligible and they must be adequate. They must enable the reader to understand why the matter was decided as it was and what conclusions were reached on the "principal and important issues", disclosing how any issue of ….. fact was resolved. Reasons can be briefly stated, the degree of particularity required depending entirely on the nature of the issues falling for decision …. A reasons challenge will only succeed if the party aggrieved can satisfy the court that he has genuinely been substantially prejudiced by the failure to provide an adequately reasoned decision."

174. When Lord Brown refers to "the reader" he plainly means, in a highly technical context such as the present case, the technically informed reader.

175. Mr Chamberlain helpfully relied also on a very short passage in the judgment of Sedley J in R v Parliamentary Commissioner for Administration ex parte Balchin [1998] 1 PLR 1 at page 13 E – F:

> "What the not very apposite term "irrationality" generally means in this branch of the law is a decision which does not add up – in which, in other words, there is an error of reasoning which robs the decision of logic."

176. The only question for this court is whether the decision of NICE is intelligibly and adequately reasoned and whether there is an error of reasoning "which robs the decision of logic." Matters of weight are entirely the province of NICE and on a highly specialist topic such as this the court must be particularly careful not to stray into the substantive merits of the decision.

177. In assessing the intelligibility and adequacy of the reasons in the present case I bear in mind, first, that the reasons are addressed to a technically informed reader; and second, as Mr Beloff submitted, that the principal purpose and function of a FAD is to give guidance. A FAD needs sufficiently to explain to a technical reader the reasons for the guidance, but it does not need to make a detailed response to every point submitted by consultees. If it did do so it would risk becoming so overburdened by reasoning as not to give clear guidance.

178. A technically informed reader would know that subgroup analysis (particularly if conducted post hoc, after the trial itself without having been designed into the trial itself) may be less reliable and robust than a RCT itself, particularly as the subgroup is likely to lack statistical power. There is a risk of false positives and other spurious outcomes. (An account of these risks appears in an article, Subgroup analysis in clinical trials. MJA 2004: vol 180, March 2004, pages 289-291.) NICE itself expresses some caution about the use of subgroup analysis at paragraph 5.9.5 of its Methods Guide, now at bundle 5:18, page 214:

> "…. care should be taken to justify the clinical basis for the subgroup differences.
>
> …….
>
> There should be a clear clinical justification and, where appropriate, biological plausibility for the definition of the patient subgroup and the expectation of a differential effect.
>
> ….. The characteristics of the patients associated with the subgroups presented should be clearly specified to allow the appraisal committee to judge the appropriateness of the analysis with regard to the decision problem."

179. Professor Stevens adds to the reasons for this approach in paragraph 24 of his first statement, now at bundle 7:10, page 71:

> "…. results from the analysis of post hoc subgroups of randomised trials are not the same as randomised evidence. The point is a very elementary one. A randomised controlled trial may generate high quality data. It does not follow that any subsequent selective manipulation of the data must be of equivalent high quality."

180. Paragraphs 4.1.10.2, 4.3.3 and 4.3.23 of the FAD all indicate that the appraisal committee was well aware of the subgroup analysis results and did, accordingly, take them into consideration. In my view the very fact that it was the result of post hoc subgroup analysis expresses a reason why, ultimately, the committee did not accept it.

181. By way of very loose analogy, a judge may say that he does not take into account a piece of evidence because it is hearsay. He does not need to describe what is meant by hearsay, nor the limitations on the value of hearsay evidence. Simply to state that it is hearsay may sufficiently explain his reason.

182. At paragraph 4.3.3 of the FAD the appraisal committee referred to "a non-significant 15% reduction in hip fracture risk." That is a reference back to the following sentence in the summary at paragraph 4.1.10.2:

> "Hip fracture efficacy was established in one study; the RR for hip fracture in the whole study population was 0.85 (95% C1 0.61 to 1.19, one RCT, n = 4932)."

183. To the technically informed reader, that means that in the whole study population of 4932 people the risk reduction for hip fracture was 0.85, i.e. 15 per cent. However, that result has a confidence interval (about which one can be 95% certain) between a risk reduction as high as 0.61 (a 39% reduction in risk) and as low as 1.19 (which actually connotes a 19% <u>increase</u> in the risk of fracture if strontium ranelate is given). Since the range of outcomes with a 95% confidence interval is so wide, the committee were entitled to characterise the outcome as "non-significant."

184. At paragraph 4.3.3 the committee then referred to the post hoc subgroup analysis as showing "a statistically significant reduction in …. hip fractures in women over the age of 74 years who have a T - score of - 2.4 SD or below."

185. It described this result as "statistically significant" because, see paragraph 4.1.10.2, the subgroup analysis

> "…. resulted in an RR for hip fracture of 0.64 (95% C1 0.41 to 0.98, one RCT, n.= 1977)."

186. This means that, for the subgroup of women aged over 74 etc, the RR is 0.64 or 36% (cp. 15% for the whole study population). Further, the 95% confidence interval is between 0.41 or 59% and 0.98 or 2%. In the view of the committee such an outcome is "statistically significant." Nevertheless, the confidence interval is so wide that the committee were entitled to say at 4.3.23 that they "did

not accept the estimate of efficacy." They were, however, willing to "acknowledge an effect for this important type of fracture." (my emphasis)

187. Professor Stevens, the chairman of the appraisal committee, explains their reasoning in paragraphs 22 – 33 of his first statement, now at bundle 7:10, page 71. This is not, in my view, an exercise in reasoning after the event, but, rather, an interpretation and elaboration to a lay person, such as the court, of a process of reasoning which is actually contained in, and revealed to a technical reader by, the quoted passages in the FAD.

188. He says:

> "The committee had three options for setting the parameter for the relative risk of strontium on hip fracture rate. The first, the purist approach, would have been to set it at 1, as the overall trial results were not statistically significant (i.e., according to commonly accepted standards of scientific proof, we could not be sufficiently sure that the results attributed to the drug were not in fact arising by chance). The second, the claimant's preferred approach, as it favours their drug, was to use the post hoc subgroup data, setting the risk at 0.64. The third, the committee's approach, was to accept the overall relative risk from the trial as a whole, even though it was not statistically significant, and noting that it was not as impressive as the selective subgroup relative risk. In my view this was much the most reasonable approach, and it steered a middle course between the two extreme options."

189. At paragraph 25 Professor Stevens deals as follows with the complaint of Servier that NICE had irrationally and unfairly given favourable treatment to the observational data in support of the alternative drug, etidronate:

> "The claimant attempts to add to its argument by saying that etidronate was favoured despite its evidence being drawn from studies further down the "hierarchy of evidence". The committee could quite defensibly have taken the view that the non-statistically significant trial evidence for etidronate was well corroborated by observational studies. But, in fact, the committee did not do this for etidronate. In effect, this is what the committee did do for strontium ranelate, even without a helpful additional observational study. Relative to strontium ranelate it "discriminated" against etidronate, rightly or wrongly, by re-setting its relative risk at 1. I am bemused as to why this point appears in the claimant's documentation, when the point they make is so unequivocally the reverse of the truth." (his own emphasis)

190. When the FAD is read in this way I am quite satisfied that, first, the appraisal committee and NICE did take into account the results of the post hoc analysis; second, it must have had in mind the point strongly relied upon by Servier, that EMEA had accepted the validity of the analysis and placed weight upon it; third, it was entitled to come to a different view; fourth, its own decision is sufficiently and intelligibly explained; and fifth, its reasons and reasoning are permissible ones which were open to it. They are not irrational and there is no "error which robs them of logic."

191. I accordingly reject ground (c) of the claim for judicial review.

## GROUND (e)

**Ground (e) Disability discrimination**

**The factual background**

192. Section 21B(1) of the Disability Discrimination Act 1995, as amended (the DDA) provides that "It is unlawful for a public authority to discriminate against a disabled person in carrying out its functions." It is common ground that NICE is a public authority for the purposes of the relevant provisions of the Act.

193. Section 1 of the Act provides that:

> "1 (1) Subject to the provisions of Schedule 1, a person has a disability for the purposes of this Act if he has a physical impairment which has a substantial and long-term adverse effect on his ability to carry out day-to-day activities.
>
> (2) In this Act "disabled person" means a person who has a disability."

194. At paragraph 21 of its decision on the first appeal, now at bundle 4:3, page 6, the appeal panel stated:

> "Although not raised by the appellants there is a further matter on which the committee's actions in this appraisal must not be upheld. The appeal panel also decided that there were groups of patients with disabilities, as legally defined, such as those with Parkinson's disease, in whom alendronate would generally be contra-indicated. Failing to consider providing advice on the treatment of these disabled patients meant that they were disadvantaged. The appeal panel considers that this would amount to unlawful discrimination on the grounds of disability. To avoid this discrimination, the appraisal committee must consider providing advice on the value of other treatments in those patients who could not take alendronate. If it feels that it is unable to provide advice for those patients, it should give reasons."

195. In response to that direction the appraisal committee did make a recommendation in the revised FADs for strontium ranelate to be prescribed to certain categories of women who are unable to take alendronate or other alternative drugs or for whom alendronate and those drugs are contraindicated. See paragraphs 4.3.28 and 4.3.33 – 4.3.35 of the revised FAD for primary prevention, at bundle 3:39, pages 1102 – 1106. The recommendation in the revised FAD for secondary prevention is different but similar.

196. The appraisal committee stated:

> "4.3.33 The committee carefully considered the position of women who cannot take alendronate because of a condition which either makes

alendronate contraindicated or which prevents individuals from complying with the instructions for administration for alendronate. In doing so the committee noted that at least some women in this patient group were likely to be 'disabled' as defined by the Disability Discrimination Act 1995. The committee was aware of its duties under that Act to avoid unlawful discrimination, to have due regard to the need to promote equality of opportunity for disabled people, and the need to take steps to take account of disabled people's disabilities, as well as its broader legal duties to ensure that its guidance is fair and reasonable.

4.3.34 The committee noted that the drugs other than alendronate are cost effective only for patients at higher risk of fracture than the risk levels at which alendronate is cost effective. If these other drugs are recommended for use by patients who cannot take alendronate only when those patients meet the criteria at which these alternative drugs become cost effective, these patients will not receive preventative treatment unless they are at higher risk of fracture than the risk levels at which alendronate is recommended. The committee therefore considered whether, for women who cannot receive alendronate, the other drugs should be recommended at the same risk levels as alendronate (that is using the criteria established as being cost effective for alendronate) in order to provide access to preventative treatment for all patients with the same level of risk. The committee reviewed the ICERs [Incremental Cost Effectiveness Ratios] for risedronate and strontium ranelate within the criteria established to be cost effective for alendronate. The committee noted that the prices for risedronate and strontium ranelate are approximately five to six times higher than the price for non-proprietary weekly alendronate, and that the ICERs for these drugs compared with no treatment were very high. For example, the ICER for strontium ranelate for women aged 65–69 years with an independent clinical risk factor for fracture was approximately £90,000 per QALY gained (see section 4.2.21). The committee noted that strontium ranelate would be the most likely choice to be considered for women who are unable to comply with the instructions for administration of alendronate, because the instructions for administration of alendronate and risedronate are similar. The committee took the view that recommending drugs other than alendronate using the same criteria as alendronate for women who cannot take alendronate would not be justified in this case because of the very high ICERs for the alternative drugs. In reaching this decision the committee had regard to the fact that the impact of refusing the more favourable recommendation is that there is no generally recommended preventative treatment for a particular group of patients who are at the lower end of fracture risk for which treatment was considered, but that the alternative drugs are recommended when these patients are at higher risk of fracture.

4.3.35 The committee considered that it is important to maximise the number of patients who are able to take alendronate. Some women will be unable to take alendronate in any circumstances because of contraindication, intolerance or inability to comply with the instructions for administration. However, some women who have a disability that makes it difficult for them

to comply with the instructions for administration of alendronate would be able to receive the drug if they received assistance in taking it. The committee concluded that all reasonable steps should be taken to provide women who have a disability that makes it difficult for them to comply with the instructions for administration of alendronate, with such practical support and assistance with administration (for example through district nurse visits or other home support services), as will enable them to take the drug.

197. To reflect these considerations the revised FADs provided for strontium ranelate to be used in specified circumstances where another drug (in particular alendronate or one of the other bisphosphonates) could not be used. Paragraph 1.3 of the revised FAD for primary prevention, now at bundle 3:39, page 1058, provides:

"1.3 Strontium ranelate is recommended as an alternative treatment option for the primary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to comply with the special instructions for the administration of alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate … **and**

- who also have a combination of T-score, age and number of independent clinical risk factors for fracture (see section 1.5) as indicated in the following table.

| **Age** | **0 ind. risk factors** | **1 ind. risk factor** | **2 ind. risk factors** |
|---|---|---|---|
| 65-69 | Not recommended | - 4.5 | - 4.0 |
| 70-74 | - 4.5 | -4.0 | -3.5 |
| 75 or older | - 4.0 | - 4.0 | - 3.0 |

…….

1.5 For the purposes of this guidance, independent clinical risk factors for fracture are parental history of hip fracture, alcohol intake of 4 or more units per day, and rheumatoid arthritis."

198. Professor Stevens, the chairman of the appraisal committee, gives a narrative account at paragraphs 3 – 16 of his second statement, at bundle 7:23, pages 153 – 157, in which he begins by stating "The treatment of patients with disabilities occupied a great deal of the time and attention of the appraisal committee including the greater part of its meeting to finalise the guidance in this case."

199. He continues at paragraph 4:

> "The committee's approach to these issues can be seen in the guidance itself. In essence, the committee considered that every effort should be made to assist patients who need help to take the most cost-effective drug (as I noted in my first statement, alendronate is both less costly and more effective than strontium ranelate). We also made some favourable assumptions about the costs of identifying patients who might still be contraindicated to alendronate …. But thirdly, we had to approach the criteria for access to the more expensive (and less effective) drugs with some caution, bearing in mind the need not to harm other NHS patients who could be treated more cost-effectively than those referred onto, for example, strontium ranelate treatment. That is the essence of NICE's role."

200. The bottom line is, however, that the effect of the revised FADs is that there are categories of patient who (because of disability) cannot take drugs other than strontium ranelate but for whom strontium ranelate is only recommended at a greater age and/or lower T – score than is alendronate. At paragraph 8.1 of his skeleton argument Mr Chamberlain put it as follows:

> "Patients who are disabled in this way are, under the guidance contained in the new FADs, left without any publicly funded treatment for osteoporosis (at least until bones become much thinner and/or they suffer a fracture or attain the age where such treatment may be provided) in circumstances where a patient without the relevant disability would have it."

201. In their revised written submission NOS express and explain the case as follows:

> "The current FADs for both primary and secondary prevention recommend bisphosphonates for patients at an earlier stage of their disease, to the exclusion of other products [viz strontium ranelate]. This means that patients who are unable to take bisphosphonates due to a physical disability are deprived of treatment of their osteoporosis until their disease is at a more advanced stage.
>
> In order to take bisphosphonates effectively in accordance with the directions for use, a patient must fast prior to taking the medication and continue to fast whilst in an upright position for a period of 30 minutes to 1 hour (depending on the specific bisphosphonate) after taking the medication.
>
> Some patients may be prohibited from sitting up due to immobility, possibly resulting from a fracture of the hip or spine, or other infirmity, making the use of bishosphonates inappropriate. Furthermore, for patients who are on multiple medications, the matter of having to fast can mean they are unable to take other prescribed medications for the stipulated period. This can be

particularly difficult for those requiring pain relief. Other patients are simply unable to swallow generic alendronate or are unable to tolerate bisphosphonate treatments.

Far from being resolved in the most recent FAD, the problem has been entrenched. Now patients face being told that they are at sufficient risk to warrant treatment, attempting to use generic alendronate, many then finding that they cannot tolerate the treatment, only to be told that although there are a range of other cost effective treatments available, they will have to wait for their condition to deteriorate before access to those treatments is granted. This places clinicians in an impossible position and will have a damaging affect on professional-patient relationships. The proposal does leave some patients without any treatment at all because they cannot take or cannot tolerate the first line treatment. Again, this situation is discriminatory against persons with physical disability and, we believe, contrary to the ECHR."

202. Professor Spector in his statements gives some illustrative examples of categories of patient who cannot take or tolerate bisphosphonates, or for whom they are contraindicated, but to whom, under the revised FADs, strontium ranelate should not be prescribed.

203. The second appeal panel did entertain Servier's appeals from the revised FADs on this ground, but in paragraphs 47 – 49 of their reasons, now at bundle 3:41, pages 1197 – 1198, concluded as follows:

"47. As regards disability discrimination contrary to the DDA, the panel accepted that, consistent with its previous decision, [viz on the first appeals] there will be some patients who are unable to receive alendronate due to a disability, and that some of those patients would not be recommended for treatment with an alternative drug. However in the light of the House of Lords decision in *LB Lewisham v Malcolm* the panel was not persuaded that this amounts to discrimination. The conduct in question is the patient not being recommended for treatment with an alternative to alendronate. The panel regards the reason for these patients not being recommended for treatment as being the decision that the treatments are not sufficiently cost-effective. That is not a reason relating to the patient's disability. Further, in the light of *Malcolm*, these patients fall to be compared with a patient who also cannot take alendronate but for a reason unrelated to a disability. Those patients would be treated in exactly the same way as patients for whom the reason for not taking alendronate was a disability. Therefore there is no difference in treatment and no discrimination.

48. Furthermore, the panel would have held that any difference in treatment was justified, being proportionate, and in pursuit of a legitimate objective.

49. Finally under the DDA the panel considered the general duty under s.49A, but concluded that the committee had clearly been very mindful of the position of patients with disabilities, and indeed had made specific recommendations with such patients in mind. The appeal panel itself carefully considered the position of the relatively lower risk women who were unable to tolerate alendronate but were not recommended for treatment, and

was satisfied that the recommendations were an appropriate balance between their needs and the need to secure cost effective use of NHS resources."

204. The appeal panel accordingly rejected the appeal on this ground.

**The general duty under DDA section 49A**

205. Section 49A of the DDA places public authorities under a general duty as follows:

> "49A **General duty**
>
> (1) Every authority shall in carrying out its functions have due regard to -
>
> (a) the need eliminate discrimination that is unlawful under this Act;
>
> (b) ……..
>
> (c) ……..
>
> (d) the need to take steps to take account of disabled persons' disabilities, even where that involves treating disabled persons more favourably than other persons;
>
> (e) the need to promote positive attitudes towards disabled persons; and
>
> (f) ……."

206. In relation to a similar general duty under section 71(1) of the Race Relations Act 1976, Dyson LJ said in R (on the application of Baker and others) v Secretary of State for Communities and Local Government [2008] EWCA Civ 141, [2008] LGR 239, at paragraph 31:

> "….. the duty is not a duty to achieve a result …. It is a duty to have due regard to the need to achieve these goals. The distinction is vital …. What is due regard ? In my view, it is the regard that is appropriate in all the circumstances. These include on the one hand …. [the target need] ….; and on the other hand, such countervailing factors as are relevant to the function which the decision-maker is performing."

207. The appraisal committee in its FADs, and the appeal panel in its reasons, clearly gave consideration and due regard to the position of disabled persons, and balanced that against other countervailing factors relevant to the decision - making

function of NICE. In my view there was no breach by NICE of its "general duty" under section 49A.

**Section 21D and 21E**

208. The issue is, accordingly, whether NICE has, is in breach of section 21B of the Act, unlawfully discriminated against disabled persons.

209. So far as is material, section 21D of the Act provides:

> "**21D Meaning of "discrimination" in section 21B**
>
> (1) For the purposes of section 21B(1), a public authority discriminates against a disabled person if-
>
> (a) for a reason which relates to the disabled person's disability, it treats him less favourably than its treats or would treat others to whom that reason does not or would not apply; and
>
> (b) it cannot show that the treatment in question is justified under subsection (3), (5) or (7)(c).
>
> (2) For the purposes of section 21B(1), a public authority also discriminates against a disabled person if -
>
> (a) it fails to comply with a duty imposed on it by section 21E in circumstances in which the effect of that failure is to make it-
>
> (i) impossible or unreasonably difficult for the disabled person to receive any benefit that is or may be conferred, or
>
> (ii) unreasonably adverse for the disabled person to experience being subjected to any detriment to which a person is or may be subjected,
>
> by the carrying-out of a function by the authority; and
>
> (b) it cannot show that its failure to comply with that duty is justified under subsection (3), (5) or (7)(c).
>
> (3) Treatment, or a failure to comply with a duty, is justified under this subsection if -

(a) in the opinion of the public authority, one or more of the conditions specified in subsection (4) are satisfied; and

(b) it is reasonable, in all the circumstances of the case, for it to hold that opinion.

(4) The conditions are

(a)……

(b)……

(c) that, in the case of treatment mentioned in subsection (1), treating the disabled person equally favourably would in the particular case involve substantial extra costs and, having regard to resources, the extra costs in that particular case would be too great;

(d) that the treatment, or non-compliance with the duty, is necessary for the protection of rights and freedoms of other persons.

(5) Treatment, or a failure to comply with a duty, is justified under this subsection if the acts of the public authority which give rise to the treatment or failure are a proportionate means of achieving a legitimate aim.

(6) …."

210. So far as is material, section 21E of the Act provides:

"**21E Duties for purposes of section 21D(2) to make adjustments**

(1) Subsection (2) applies where a public authority has a practice, policy or procedure which makes it-

(a) impossible or unreasonably difficult for disabled persons to receive any benefit that is or may be conferred, or

(b) unreasonably adverse for disabled persons to experience being subjected to any detriment to which a person is or may be subjected,

by the carrying-out of a function by the authority.

(2) It is the duty of the authority to take such steps as it is reasonable, in all the circumstances of the case, for the authority to have to take in order to change that practice, policy or procedure so that it no longer has that effect.

……..”

**Section 21D(1)(a)**

211. The first question under section 21D(1)(a) is whether “for a reason which relates to the disabled person’s disability” NICE treats him “less favourably than it treats or would treat others to whom that reason does not or would not apply.”

212. In my view there are two complete answers to the claim under section 21D(1). First, the sole reason why NICE has limited, and ordinarily not recommended, treatment with strontium ranelate is that in the opinion of NICE it is less effective and much more expensive than treatment with alendronate, and is not cost effective. There is no “reason” within the reasoning of NICE for not recommending it which relates to a disabled person’s disability. Second, NICE does not treat a person who cannot take alendronate because of a disability (e.g. a patient who, because of disability, cannot sit upright for the 30 or more minutes required after swallowing the drug) any differently from, or less favourably than, a patient who cannot take alendronate for some other reason (e.g. an allergy or intolerance). In either case, the much more expensive drug, strontium ranelate, is only recommended if the same higher threshold combination of age, T – score and independent clinical risk factors for fracture are present (see the table in paragraph 1.3 of the revised FAD, as reproduced in paragraph 197 above).

213. Mr Chamberlain argued at paragraph 91 on page 31 of his skeleton argument (under “Thirdly”) that “the appropriate comparator for a patient unable (because of disability) to remain upright for 30 minutes is a patient who (not suffering from that disability) can remain upright for the required length of time and therefore can take alendronate. Such a patient would not be denied treatment for osteoporosis.” In my view that is fallacious. The appropriate comparator (or, as Lord Scott of Foscote and Lord Brown of Eaton-under-Heywood put it in Lewisham LBC v Malcolm [2008] UKHC 43, [2008] 3 WLR 194 at paragraphs 32 and 113 respectively, the “meaningful comparison”) is another patient who (for a reason other than disability, such as intolerance or allergy) cannot take alendronate. NICE treats both categories of patient the same. Indeed in certain respects it has discriminated in favour of a patient with a disability as Professor Stevens explains.

214. Even if I am wrong in the above view, I consider that NICE can show justification under section 21D(1)(b) for the reasons given in paragraphs 218 to 227 below.

**Sections 21 D(2) and 21 E**

215. NICE expressly accepts that if the relevant “benefit” is taken to be preventative treatment for osteoporotic fracture, the recommendations in the revised FADs amount to a practice, policy or procedure which makes it either “impossible or

unreasonably difficult" for some disabled patients to receive that benefit – namely those disabled patients who cannot take alendronate but who do not fall within the higher threshold criteria in the table in paragraph 1.3 of the FAD. Accordingly NICE accepts that section 21 E(1) applies and that NICE is under the duty under section 21 E(2), namely "to take such steps as it is reasonable, in all the circumstances of the case, for the authority to have to take in order to change that practice, policy or procedure so that it no longer has that effect."

216. Mr Chamberlain submits that "there was an obvious, and reasonable, step which the appraisal committee or appeal panel could have taken …..: recommend strontium ranelate for these patients whose disability made them intolerant to alondronate."

217. This, however, is too simplistic. The circumstances of the case include the duty of NICE to have regard to the broad balance of clinical benefits and costs. The question whether or not it was reasonable to recommend strontium ranelate for all "disabled patients" raises, on the facts of the case, the same issues that arise when considering justification for the purposes of sections 21 D(1)(b) or 21 D(2)(b), and to this I now turn.

**Justification**

218. The justification under subsections (3) – (4) and under subsection (5) of section 21D is clearly separate and distinct. The justification under subsection (5) is by reference to an objective test of the proportionality of the means of achieving a legitimate aim. The justification under subsections (3) and (4) is by reference to the opinion of the public authority and the objective reasonableness for it to hold that opinion.

219. On the facts of the present case, it does not seem to me that justification under subsection (5) could succeed if justification under subsections (3) and (4) fails. Put another way, any defence under subsection (5) is, in this case, subsumed in a defence of justification under subsections (3) and (4).

220. In considering subsection (3) it is important to note that (3)(a) refers specifically to the opinion of the public authority itself. The task of the court at the stage of considering subsection (3)(a) is not to form its own opinion, but to identify what opinion the public authority holds. The question for the court at the stage of considering subsection (3)(b) is not whether that opinion is right, or the only possible opinion. Rather, the question is whether it is reasonable, in all the circumstances of the case, for the public authority to hold the opinion that it does hold.

221. As to the "conditions" in subsection (4), those plainly in point in the present case are the conditions in paragraphs (c) and (d).

222. Quite clearly it is the opinion of NICE, expressed first by its revised FADs, second by its appeal panel, and third by the narrative explanation given by Professor Stevens in his statements, that the conditions in both paragraph (c) (which applies in the case of treatment mentioned in subsection (1)) and (d) (which applies both to such treatment and also to non-compliance with the section 21 E (2) duty) are satisfied.

223. It is reasonable for NICE to hold that opinion? NICE has given very careful and specific consideration in its revised FADs to the position of disabled patients. The core of its reasoning is in paragraph 4.3.34, quoted above. The ICERs for strontium ranelate compared with no treatment are very high, and the example is given for women aged 65 – 69 years with an independent clinical risk factor for fracture of appropriately £90,000 per QALY gained. This is three times higher than the normal upper limit set by NICE of £30,000 per QALY gained.

224. The very reason for the existence of NICE is to make hard choices, and in my view it is reasonable for it to hold the opinion that substantial extra costs would be involved which are too great (condition (c)); and, further, that it is necessary for NICE not to make a more generous recommendation for the protection of the rights of other persons, namely other patients who also require a fair share of the resource of the NHS (condition (d)).

225. Mr Chamberlain placed much emphasis on the suggestion or recommendation in paragraph 4.3.35 of the revised FAD that "all reasonable steps should be taken to provide … such practical support and assistance with administration …. as will enable [disabled patients] to take the drug." He submitted that the cost of such nursing support must inevitably greatly exceed the amount by which the cost of strontium ranelate exceeds that of alendronate – i.e. that it would be much cheaper to prescribe the more expensive drug than to provide the required extra nursing support.

226. This, in my view, is beside the point. The essential decision of NICE, by its FAD, is to draw the lines or criteria for prescribing strontium ranelate as it has done in paragraph 1.3 and it was reasonable of it to do so.

227. In my judgment NICE has not unlawfully discriminated against disabled persons and I reject ground (e) of the claim for judicial review.

## The European Convention on Human Rights

228. Servier argue in their detailed grounds and in Mr Chamberlain's skeleton argument that, independently of the DDA, NICE has unlawfully discriminated against disabled patients contrary to Article 14 (read with Article 8) of the European Convention on Human Rights. Mr Chamberlain did not press this strongly as a discrete ground at the hearing and in my view he was right not to do so. When Parliament has legislated in detail on the topic, as it has in the DDA, it seems to me that the lawfulness of the acts and decisions of NICE stand or fall by

reference to that Act. In any event, if, as I consider, the decisions of NICE are justified under the Act, they are also, as Mr Chamberlain conceded (see transcript, Day 2, pages 196 – 197), justified for the purpose of the Convention.

**Outcome**

229. In the result I reject grounds (c) and (e) but allow this claim for judicial review on ground (a).

230. I am aware of the interest in this case of many doctors, patients and patient organisations, and of the media interest. I conclude, therefore, by summarising very briefly the effect of this decision so that there is, I hope, no future misunderstanding. NICE must now negotiate with Professor Kanis and the consultees so that the full economic model and its risk equations, coefficients and other data are disclosed and supplied, on suitable terms as to confidentiality, to all consultees (not just Servier) or identified representatives of them. NICE must permit all consultees (who include NOS) to make further submissions or representations in response to that disclosure. I have no idea what may emerge or be submitted, but NICE must give due consideration to it and, if it thinks fit, further revise the FADs in the light of it. It must be understood, however, that the final decision of NICE may be not further to revise the FADs. Provided they have meantime appropriately disclosed the model and the data, and have duly and fairly reconsidered in the light of further submissions and representations made, it would not necessarily follow that fresh FADs in the same terms as the current revised FADs are unlawful. No one should gain false hope from this judgment.