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Analysis of NICE's consultation on the 'Value of Innovation'

This short report outlines the main conclusions derived from the analysis of NICE's consultation responses on 'the Value of Innovation'. The arguments expressed in the consultation can be divided into two broad groups:

- **Those that concern the framework of analysis within which technology appraisals are conducted, including such things as the use of QALYs, the ICER and the extent to which the appraisal can capture the distinctive features of innovative therapies.**

- **Those that concern the procedures that NICE adopts and the extent to which those procedures are transparent or procedurally fair.**

1. Background

In January 2009, the National Institute for Health and Clinical Excellence (NICE) commissioned Professor Sir Ian Kennedy to carry out a study into how NICE values innovation in health technologies. The background to the Kennedy study was in the politically charged debate about supplementary payments for expensive end of life therapies that took place in 2007.

The main tool NICE uses for assessing the value of new health technologies is the Quality Adjusted Life Year (QALY), which is an estimate of the incremental number of life years gained adjusted by an estimate of the quality of life of those years. In over words, the QALY is a measure of a person's length of life weighted by a valuation of their health-related quality of life (HRQL). The HRQL 'weighting' usually comprises two elements: the description of changes in HRQL itself and a valuation of that description of HRQL. To quantify the effects of technologies on health-related quality of life, the EQ-5D questionnaire is utilised. The EQ-5D comprises five dimensions of health: mobility, ability to self-care, ability to undertake usual activities, pain and discomfort, and anxiety and depression. This system has been designed so that people can describe their own HRQL using a standard descriptive system (NICE's guide to the methods of technology appraisal, June 2008).

The Kennedy study was asked to address the following questions: what approach should be adopted by NICE to ensure that innovation is properly taken into account when establishing the value of new health technologies? Should particular forms of value be considered more important than others? How should innovation in health be defined? What is the relationship between innovation and value?

Following a call for written evidence on the study's question, a public consultation involving representatives from the healthcare industries, the NHS as well as patients and the wider public was conducted in February 2009. Responses to the consultation came in the form of written submissions all of which were available electronically on the NICE web-site, with the name of the consultees, usually an organisation but sometimes an individual, attached.

This short report presents an overview of the consultation responses. It is divided into four sections; considering the above 'background' constituting the first section, the second section briefly introduces the method employed to analyse the consultation, the third section displays the detailed results produced by the software that we utilized for the analysis; the fourth section presents an analytical summary of the consultation responses.

2. Methodology

The Set of Respondents

A total of 37 written responses were received to the consultation. This total includes:

7 Patient Groups (i.e.: the National Rheumatoid Arthritis Society).
4 Academics (i.e.: the European Health Technology Institute for Socio-Economic Research).
2 NHS Professionals (i.e.: the Royal College of Nursing).
23 Pharmaceutical Industries (i.e: Roche).
1 Independent think-tank (Reform)

Method of Analysis

Respondents' answers were analysed using a computer-based method (the Alceste software package) which relies upon co-occurrence analysis (the statistical analysis of frequent word pairs in a text or *corpus*).

With Alceste, the text is conceptualised as *unités de contexte initiales* (UCI), which in terms of consultation responses are the submissions of each respondent. These UCIs can be tagged with 'passive' variables that provide information on the author, which in the case of this consultation pertains to a respondent's role as Parmaceutical Industry (coded as IND), Patient Group (PG), Academic (ACA) or NHS Professional (NHSP).

The statistical operations in Alceste are based upon the *unité de contexte elémentaire* (UCE), which are sentences or quasi-sentences. The basic data matrix on which statistical computations are built depends upon these UCE and the words making up the sentences of a speech or intervention. However, unlike many other textual analysis packages, Alceste does not require the analyst to compile a dictionary of key words. Instead, it runs its own analysis of the whole corpus, raw, and reduces various grammatical forms – for example tensed words – to a root form. It then divides the root forms of the vocabulary in the corpus into two classes: 'function' words, which enable sentences to operate as part of natural languages, and 'content' words, which contain the distinctive meanings of the text (Brugidou, 2003: 419). This is a purely syntactical operation conducted by the software, yielding an analysis that is internally coherent without manipulation of a text by the analyst.

3. Analysis of Results

The Alceste analysis of the consultation responses on 'the Value of Innovation' produced five classes.

Figure 1: Hierarchical Descending Classification: Classes

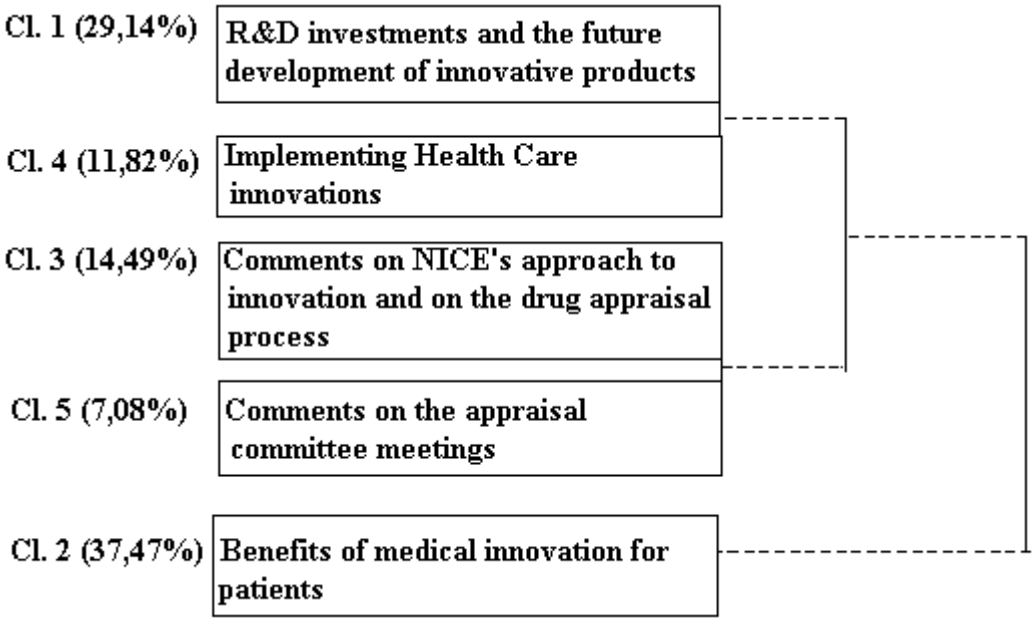
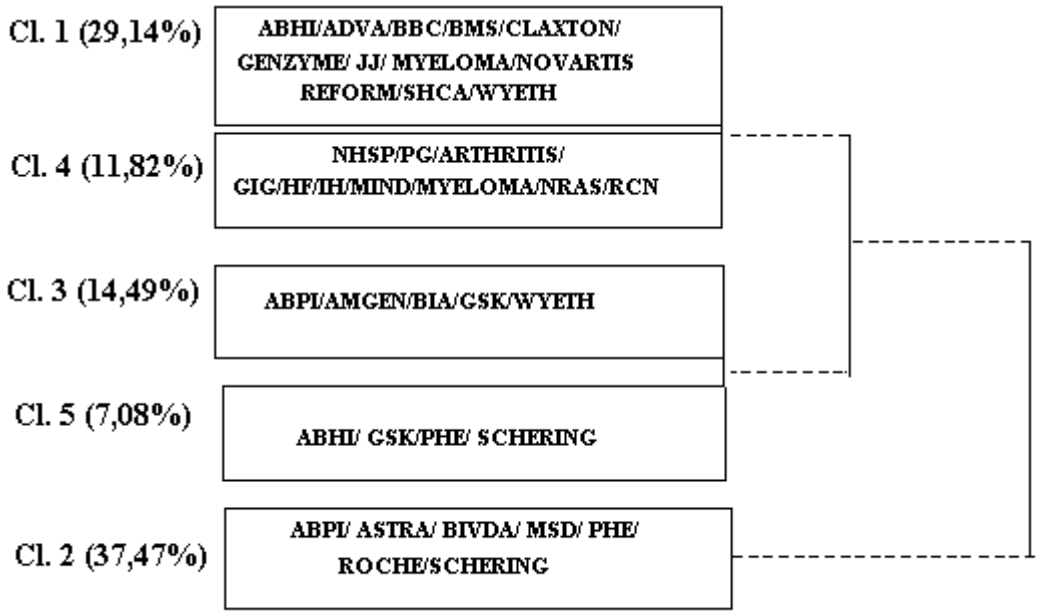


Figure 2: Hierarchical Descending Classification: Respondents



Classes 1 and 4:
The first cluster comprises of Class 1 and Class 4. In Class 1, Industry and Academic respondents – such as GSK (GlaxoSmithKline) and Karl Claxton, respectively – express concerns regarding future research and the development of investments and innovative. For example, GSK responds:

'Pharmaceutical innovation is a continuing learning process, whereby new and unexpected findings are only discovered once health technologies enter the market. Providing a stable environment for R&D investment and the future development of innovative products comes from ensuring the integrity of the whole system. This should include: Encouraging and rewarding innovation. The recognition of value needs to occur in the early stages, allowing manufacturers to obtain an initial return on investment'.

Or, as Karl Claxton expresses:
'The question of how to value innovation and how to ensure that there are sufficient incentives for private investment in the development of socially valuable innovations requires a clear view of the social value of a health technology, its relationship to price, and the incentives this provides for private sector investment decisions'.

Generally-speaking, respondents in Class 1 raised economic and financial issues pertaining to the development of valuable innovations and the role played by NICE in that respect. For example:

'In making yes or no decisions about which medicines to make available on the NHS, NICE sends very strong signals to those investing in the research and development of the medicines of the future. It is important therefore, that NICE does not send signals to the market that disincentives the development of valuable innovations' (Bristol-Myers Squibb, BMS).

Or,
'The industry believes that NICE has an important role in identifying the value delivered by medicines – but it does expect that the regulatory and market environment for medicines should create incentives for sustained R&D investment that results in real benefits to patients and the health system' (Association of the British Pharmaceutical Industry, ABPI).

Class 4, closely associated with Class 1, collates responses focusing on the implementation of health care innovations. Responses here are typically from Academics, such as Ties Hoosman and Elisabeth Fenwick, and Industry, such as ABPI. For example:

'One way of ensuring "value for innovation" is by promoting the adherence to such innovations through active implementation. Nevertheless, implementation is not without costs. Decision making bodies like NICE should therefore carefully consider the potential worth of implementing health care innovations, using decision models and evidence synthesis. In a budget constrained health care system, decisions regarding investment in implementation must be made alongside those regarding investment in health care innovation and research' (Hoomans and Fenwick).

Or,
'The Kennedy Review will only be of value if the NHS adopts innovations sanctioned by NICE. Whilst outside the scope of the Review, it is important to remember that NICE depends on the NHS to implement its guidance. NICE provides a range of highly valuable support tools, but ultimately it is local decision-making that determines if innovation reaches patients. Whilst the NHS has a commitment to innovation, this has yet to be matched by responsiveness and speed of adoption at the local level. Local decision-making systems are often complex and bureaucratic. There are few sanctions on NHS organisations that do not fully implement NICE guidance and the Annual Health Check primarily checks that processes are in place to implement guidance rather than whether guidance is fully and effectively implemented (ABPI).

Classes 3 and 5
A second cluster comprises of Class 3 and Class 5. Class 3 displays comments from Industry on NICE's approaches to innovation and the process of drug/technology appraisal. For example:

'NICE is being called on deliver guidance as early as possible after the launch of a new medicine. An unintended consequence can be to prematurely terminate the innovation process and prevent the realisation of future benefits by making Short term decisions on new products very early in their lifecycle that prevent development and learning by companies, clinicians, and the health system as a whole, and deprive patients We would suggest that the scoping stage of the technology appraisal process should be used to clarify specific issues for consideration outside the ICER, e.g. degree of unmet need, attributes particularly valuable to patients, treatment of comparators, and areas of uncertainty in the evidence base (ABPI).

Or,
'We have taken the opportunity to outline a variety of approaches that NICE could consider to ensure innovation is properly taken into account when appraising the value of medicines. A revised framework for assessing value, which formalises how appraisals take differences between diseases and other relevant factors into account should be considered. This would need to incorporate a more holistic approach which balances the cost per QALY with other factors to ensure a broader definition of value is taken into account' (GSK).

Closely related to Class 3, Class 5 is made up of comments from Industry respondents and suggestions concerning appraisal committees' meetings. For example:

'It would be valuable if the industry sponsor of a technology, could have the opportunity to participate in the appraisal to a greater extent (for example at appraisal committee meetings) to provide greater clarity on the relevant information to be considered. This may have the additional benefit of enabling appraisals to be conducted more speedily as areas of uncertainty may be resolved at the time rather than requiring further consultation' (GSK).

Or,

'Meetings of NICE's independent Appraisal Committees are now held partly in public. Whilst this is a welcome move towards further transparency, it would in Schering-Plough's view be sensible to allow for dialogue between the Chair of the Appraisal Committee and representatives of consultee organisations, particularly where it is apparent that subsequently this could facilitate a more informed decision-making process. Better interaction with the HTA centres would also be helpful. At present there is little opportunity to have a discussion (at any stage accept appeal, where this is restricted) about the degree of innovation that a given product represents. No account is taken of this in the assessment reports produced by the HTA centres. Indeed innovation is rarely, if ever, referred to. Yet these are the reports that will provide the basis of most of the Appraisal Committee's decisions' (Schering-Plough's).

Class 2

Class 2, the last and largest of the classes, consists of comments from Industry respondents about medical innovations and their benefits for patients. These comments are often based on Industry experience(s) with medical innovations and frequently contain criticisms about NICE's evaluation system. For instance:

'Recent advances in oncology have provided medicines with similar efficacy to chemotherapy, but which are delivered orally rather than intravenously (for example, gefitinib (IRESSA) or erlotinib (Tarceva) for non-small-cell lung cancer compared to the use of i.v. docetaxel). This benefits not only the patients (in terms of increased comfort / avoidance of adverse effects associated with i.v. method of delivery) but also frees up valuable capacity and resources within the NHS (i.e. beds / nurse time / i.v. equipment etc.) […] within the current framework it is extremely difficult to capture the benefits that innovations such as these provide to patients. Generic quality of life instruments such as EQ-5D and SF36 do not appear to be sensitive to these types of changes, yet patients state that benefits such as these greatly impact their overall experience of drug treatment' (AstrsZeneca).

Or,

'A major concern with the current NICE evaluation system is that it is most difficult to prove cost-effectiveness for genuine breakthrough products where there has been little innovation in the past. In such areas "standard of care" can be non-existent or generic and very low cost. It is a mathematical quirk that it is easier to demonstrate the cost-effectiveness of minor improvements compared to other high cost medicines in well served conditions that it is to generate a QALY of £20-£30k in conditions where patients have limited alternatives. An example of this situation is the NICE appraisalof Velcade' (ABPI).

4. Analytical summary

The above responses show that a wide range of points are made in relation to the supposed shortcomings of the QALY approach. The benefits and value of innovation captured by QALYs are considered to be limited for Patients, for Society at large and for Science.

Shortcomings of the QALY for Patients

A number of respondees point that the QALY does not capture the full array of potential benefits for patients listed below:

- The need to take into account broader considerations, for example the extent of unmet need of a given condition.
- The significance of elements of a condition other than the QALY gain promised by a therapy, for example whether or not it delivers gain at the end of life.
- The broader consequences for well-being that a particular therapy might offer, for example treatment for fibroids that does not involve hysterectomy.
- The benefits that flow not purely from the health gain secured but also from the manner in which the treatment is administered, for example orally rather than intravenously.
- The benefits that occur in life-style improvement, for example in respect of incontinence.
- The value of experiential evidence is assessing the quality of life offered by a treatment.
- The benefits of *Non-Health Related* quality of life (improved sense of wellbeing, satisfaction, hope).

Shortcomings of the QALY for Society

The QALY approach is also frequently criticised for not being able to take into account productivity gains from the results of new treatments as well as the indirect effects of an individual's health on the wider economy and on society. The following potential benefits are thought to be overlooked by this approach:

- Potential reductions in health inequalities.
- Benefits to carers' and families mental and physical health.
- The broader benefits of employment and productivity, including the advantages of people being able to return to work.
- Improved community cohesion and sense of wellbeing and productivity.
- Productivity gains from deferred death, disability and debility (increased tax revenues from workforce participation, improved efficiency at work).
- Reduced social service and unemployment benefit.

Shortcomings of the QALY for Science

Finally, respondees point out that the QALY does not always sufficiently capture all the benefits likely to be important for Science and innovative technology. The following benefits are thought to be overlooked by this approach:

- Spillover effects of novel technologies yielding fresh avenues for scientific research and, consequently, further new treatments
- Spillover improvements in the service infrastructure to treat the disease (i.e. service redesign and reform around delivery of a treatment, increased learning for HCPs, forging better connections between aspects of healthcare system such as primary and secondary care, research and operational care).

The Use of EQ-5D

Even if one thought that conceptually the use of QALYs was correct, one could still hold that the way in which QALYs were operationalised via EQ-5D did not do justice to the full range of benefits that should be captured in the appraisal. As ABPI remarked:

> 'The primary instrument used to calculate the QALY, as preferred by NICE, is the generic (rather than disease-specific), preference-weighted health-related quality of life measure, EQ-5D. This instrument asks people to tick one of three options in each of five dimensions of heath benefit – it is not able to account for the full range of benefits that are important to patients, let alone encompass the value of innovation' (ABPI).

Some of the consultees, such as the Bio Industry Association (BIA), point to the general nature of EQ-5D with its basis in general population samples:

> 'There are limitations to the use of EQ-5D, particularly when patients are not able to articulate, have mental health problems or learning disabilities. This standard approach can be relatively insensitive to benefits gained or have a ceiling effect, and some dimensions are not well represented in EQ-5D e.g. mental health/cognitive functions' (BIA).

The ICER Framework

By definition an incremental cost-effectiveness ration compares an innovative therapy to an existing reference point. There are arguments that this poses a special problem for innovation, for the following reasons:

Some existing therapies are out of patent, and therefore have very favourable cost-effectiveness ratios. Novartis's, for instance, emphasized the following point:

> 'New breakthroughs after years of no new developments are at a considerable disadvantage, even if they offer significant additional benefits, if the comparator products are off patent and therefore significantly cheaper. In this instance the true value of the technology may not be fully appreciated if considered against the conventionally accepted thresholds for cost-effectiveness. This does not provide an incentive to innovate, as the cost-effectiveness gap would be so large that NICE would not recommend, and the R&D costs could not be recouped' (Novartis).

Also, some innovative therapies are developed for one limited condition, but then it becomes clear that the product has wider use, and so the benefits have been under-stated. This is a particular problem if the appraisal is done too early in the development of the product. According to BIA, for instance:

> 'One of the current problems in the innovation ecosystem is that while innovation is driven by the user/designer interaction, the users (doctors, clinicians) are no longer the decision makers, and the organizational adopters (managers, policy makers) do not appreciate the value of incremental innovation. Health Technology Assessments (HTA) are inherently innovation-stifling, are applied too early and lead to delays on uptake, diffusion and the realisation of benefits' (BIA).

ABPI claims that it is difficult to prove cost-effectiveness for genuine breakthroughs.

> ‘ The ICER is derived from a comparison of the costs and benefits against those used in routine clinical practice; where nothing has been available for years, this will by definition mean comparisons will be made against old (and therefore generic and very inexpensive medicines). Comparing an innovative medicine which includes substantial R&D costs against a benchmark that is virtually free makes it difficult, if not impossible, to demonstrate cost-effectiveness at a price that secures a return on investment. Thus an innovative medicine, with the potential to ultimately deliver significant patient benefit in some or all patient sub groups with a disease, can be blocked. This risks the use of a medicine and its full clinical potential being foregone. Even when the overall improvement is modest for the majority of patients, some patient subgroups who would yield substantial benefits from the new medicine would miss out. Incentives for further development are also severely compromised’ (ABPI).

There is an assumption in a number of the responses that the use of RCTs induces a bias against innovation. The Association of British Healthcare Industries (ABHI), for instance, wrote as follows:

> ‘The reliance of the NICE Reference Case on Randomised Controlled Trials (RCTs) is too rigid for medical devices as blinding is difficult to ensure, clinical responses are particularly susceptible to inter-patient variation and the ‘learning curve’ and variation in technical proficiency affect outcome’ (ABHI).

Procedural Concerns

NICE makes it plain that this approach is a ‘tool not a rule’ and says that it supplements the formal analysis with judgement concerning such matters as the value of innovation or the quality of the patient experience, but this opens up the door to procedural arguments as to how this is done.

One line of argument says that the ICER framework is transparent and clear, but there is no equivalent clarity and transparency in respect of the additional considerations that NICE says it is committed to taking into account. One particular suggestion in this context is the development of multi-criteria analysis, advocated, amongst others by Bristol-Myers Squibb (BMS):

> ‘For the purposes of transparency, all criteria in addition to the cost per QALY should be clearly established and their scoring and weighting in the assessment process should be set out in the published guidance. Criteria should be developed for assessing both the clinical and innovative value of technologies and these should be related to clinical need. The ASMR rating system as utilised in France provides one model for this. We propose that NICE adopt a multi-criteria decision-making framework with explicit cost per QALY modifiers associated with each aspect of innovation and value’ (BMS).

Patients groups, such as the National Rheumatoid Arthritis Society (NRAS), advanced a similar point:

‘ The suggestion was made at an ABPI meeting on the Kennedy Review that the use of a multi-criteria decision analysis (MCDA) could be used whereby the weightings applied to the criteria were made very open and transparent. NRAS supports this view’ (NRAS).

One line of argument, developed by BMS, is that there is no democratic accountability with NICE’s decisions, and the decision on the threshold ought to be made by parliament:

‘Given that its decisions in effect determine how resources are allocated within the NHS, the work of NICE has obvious and extremely important implications in determining which patients receive treatment and which do not. It is inevitable therefore that NICE’s decisions have attracted huge controversy, where particular groups of patients have felt that NICE has denied them the opportunity of effective treatment. It is questionable whether such decisions should be made with so little democratic accountability. It is true that NICE operates within an overall framework established by the Secretary of State for Health. However, not only are its day-to-day appraisal decisions subject to no form of democratic review, nor are key elements of its methodology’ (BMS).

5. Appendix

Table 1: Typical sentences of each class

Class 1 R&D investments and the future of innovative products	Class 4 Implementing Health Care innovations	Class 3 Comments on NICE's approach to innovation and on the drug appraisal process	Class 5 Comments on the appraisal committee meetings	Class 2 Benefits of medical innovation for patients
u.c.i. : 11 *11 *cat_IND *name_EMIG *K_1 u.c.e. : 517 Classe : 1 Khi2 : 18 **pharmaceutical innovation comes** in many **forms; much** of the **development carried out by** EMIG members **is focused** on the incremental **innovation** of existing **products. however,** at **present, innovation is perceived to** be the **development and launch** of **new** chemical entities, NCes. u.c.i. : 9 *9 *cat_IND *name_BMS *K_1 u.c.e. : 420 Classe : 1 Khi2 : 17 **it is important therefore,** that NICE **does** not send signals **to** the **market** that **disincentivise** the **development** of **valuable innovations.** NICE s **role is** heavily biased towards assessing the cost **effectiveness** of **medicines and medical devices.** the vast **majority** of NHS expenditure, **however,** around ninety percent of the total, **is** not **subject to** any such assessments. u.c.i. : 30 *30 *cat_IND *name_WYETH *K_3 u.c.e. : 1149 Classe : 1 Khi2 : 17 in the **pharmaceutical industry this has** been **described** as the 3D **cycle,** or rather a spiral,	u.c.i. : 32 *32 *cat_PG *name_MIND *K_4 u.c.e. : 1253 Classe : 4 Khi2 : 45 **mental health service users** frustrations with NICE are **not about** access to **expensive** drugs **but** access to a range of **therapies** often **those** with the **least** developed **evidence base that** are experienced as **helpful.** u.c.e. : 1264 Classe : 4 Khi2 : 42 the **position** for less **established psychological therapies** is even more difficult. we **suggest that** a review of how **psychological therapies** are **evaluated** would be **helpful.** RCts **do** a **job that** other methodologies **cannot, but** we are **very concerned if** reliance on RCts **means that** recommendations are **made that** run counter to **mental health service users experiences** and **wishes.** u.c.e. : 1254 Classe : 4 Khi2 : 40 **service users** value highly approaches such as **self management** and hearing **voices groups,** particularly for the empowerment and peer **support** involved. **these** are **well established** approaches though they may be **regarded** as innovatory in the **sense that** user **led**	u.c.i. : 2 *2 *cat_IND *name_ABPI *K_2 u.c.e. : 45 Classe : 3 Khi2 : 42 the **scoping** stage **of** the technology appraisal process **should** be **used** to clarify **specific issues** for **consideration outside** the ICER, e. g. **definition of unmet** clinical **need** valuable to patients, treatment **of** comparators, areas **of uncertainty** in the evidence base NICE **should adopt** new **structured approaches** to **decision making** to **account** for these important **factors;** u.c.i. : 34 *34 *cat_IND *name_GSK *K_5 u.c.e. : 1340 Classe : 3 Khi2 : 33 revision **of framework** A revised **framework** for **assessing** value, which formalises **how** appraisals **take differences** between diseases and **other** relevant **factors into account should** be **considered.** u.c.i. : 2 *2 *cat_IND *name_ABPI *K_2 u.c.e. : 124 Classe : 3 Khi2 : 32 g. degree **of unmet need, attributes** particularly valuable to patients, treatment **of** comparators, and areas **of uncertainty** in the evidence base. NICE **needs** to **adopt** a **structured decision making framework** to	u.c.i. : 34 *34 *cat_IND *name_GSK *K_5 u.c.e. : 1380 Classe : 5 Khi2 : 75 it **would** be valuable if the industry sponsor of a **technology, could have** the **opportunity** to **participate** in the **appraisal** to a **greater extent,** for example at **appraisal committee meetings,** to **provide greater clarity** on the **relevant information** to be considered. u.c.e. : 1322 Classe : 5 Khi2 : 71 one possible **solution** may be to consider a **two stage process, where** the **appraisal committee would** focus on a **technical review** of the evidence, as happens **now** and then the **committee** or **another** group **would review** feedback from **stakeholders** and **deliberate** on the **broader impact** of the heath **technology.** u.c.e. : 1325 Classe : 5 Khi2 : 50 to **provide greater clarity** on the **relevant information** to be considered. this may **have** the additional benefit of **enabling appraisals** to be **conducted** more speedily as areas of uncertainty may be resolved at the time **rather** than **requiring further consultation.** u.c.i. : 24 *24 *cat_IND *name_PHE *K_2	u.c.i. : 2 *2 *cat_IND *name_ABPI *K_2 u.c.e. : 92 Classe : 2 Khi2 : 40 **velcade was** the **first** new **treatment for** relapsed **myeloma** in **over** a **decade.** the largest ever **randomised controlled trial** in **myeloma was** undertaken by the manufacturer, which **demonstrated** a **significant** clinical **advantage compared** to the **only** other **licensed therapy, dexamethasone.** u.c.i. : 17 *17 *cat_IND *name_JJ *K_1 u.c.e. : 701 Classe : 2 Khi2 : 39 **similarly, surgery** performed laparoscopically generally **offers significant** value to a **patient** as their **recovery time** and scarring **are reduced compared with** open **surgery.** A study **compared** inpatient **with** ambulatory **laparoscopic** cholecystectomy15 although mean operating and **total** anaesthesia **times were significantly shorter for** ambulatory **patients** and **post** operative **pain scores** at 24 h **were significantly lower/** u.c.i. : 6 *6 *cat_IND *name_ASTRA *K_2 u.c.e. : 262 Classe : 2 Khi2 : 35

as **follows:** the **output** of **an innovative** activity, **does** not **present itself** in countable easy **to measure** units of any sort.

u.c.i. : 9 *9 *cat_IND *name_BMS *K_1

u.c.e. : 454 Classe : 1 Khi2 : 16
it is important to remember that the **price** of a **new medicine is set** in a **global context.** the UK **is** a **price** reference point for **markets** accounting for 25%of **global pharmaceutical** sales.

u.c.i. : 2 *2 *cat_IND *name_ABPI *K_2

u.c.e. : 70 Classe : 1 Khi2 : 15
the **industry** believes that NICE **has an important role** in identifying the **value** delivered **by medicines** but **it does expect** that the regulatory **and market environment** for **medicines** should create **incentives** for sustained R&D **investment** that/

u.c.e. : 118 Classe : 1 Khi2 : 15
one **important implication is** that the **failure to recognise** or **reward innovation** in one area may compromise **an entire pathway** of **future, and** currently unidentified, **follow** on **developments** in **medical** technology of benefit in QALys **and** other **terms.**

u.c.i. : 21 *21 *cat_IND *name_MSD *K_2

u.c.e. : 799 Classe : 1 Khi2 : 15
innovative outputs must then go through **an increasingly rigorous and** complex framework of **regulation.** in **this** model of **innovation,** the **innovation cycle is** not complete until **market** diffusion.

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1383 Classe : 1 Khi2 : 15
GSK accepts that the **industry must play its** part **to** ensure **early access to innovative** approaches are constantly evolving and in **that** they may **still** be **regarded** as marginal or add ons in mainstream **mental health services,**

u.c.i. : 33 *33 *cat_ACA *name_HF *K_4

u.c.e. : 1277 Classe : 4 Khi2 : 40
in deciding **about reimbursement** and **research funding,** decision making **bodies like** NICE implicitly assume **that health care** innovations for which **guidance** is issued, automatically get **implemented** into **clinical practice** 1 3.

u.c.i. : 32 *32 *cat_PG *name_MIND *K_4

u.c.e. : 1244 Classe : 4 Khi2 : 38
what **mental health service users** often most value are **those** approaches which are **least likely** to have an **established strong evidence base** such as **self management,** peer **support,** talking **therapies** and **various** other **psychosocial** approaches.

u.c.i. : 33 *33 *cat_ACA *name_HF *K_4

u.c.e. : 1283 Classe : 4 Khi2 : 32
to **encourage health care professionals** and patients to use NICE **guidance** in daily **practice,** the development of **evidence** based **clinical guidance** must be complemented by **well** developed, **well** executed and **sustained implementation programmes** 3 5.

u.c.i. : 2 *2 *cat_IND *name_ABPI *K_2

u.c.e. : 140 Classe : 4 Khi2 : 29
local decision making **systems** are often complex and bureaucratic. there are **few** sanctions on NHS **organisations that do not fully implement** NICE **guidance** and the annual **health** check **primarily** checks **that** processes are in **place** to **implement guidance** rather than **whether guidance** is **fully** and effectively allow for **consideration of** the **above factors alongside** the ICER, **including** innovation,

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1341 Classe : 3 Khi2 : 32
this would **need** to **incorporate** a more **holistic approach** which balances the **cost per** QALY with **other factors** to **ensure** a broader **definition of** value is **taken into account.**

u.c.i. : 8 *8 *cat_IND *name_BIA *K_3

u.c.e. : 299 Classe : 3 Khi2 : 30
inclusion of specific measures **around** innovation in **relation** to patient, economic and **societal benefit.** in **particular,** measures that **take proper account of** disease severity and **unmet need,** incremental innovation, patient convenience and **benefits** to **carers** would be a **useful** staring point.

u.c.e. : 390 Classe : 3 Khi2 : 30
inclusion of specific measures **around** innovation in **relation** to patient, economic and **societal benefit.** in **particular,** measures that **take proper account of** disease severity and **unmet need,** incremental innovation, patient convenience and **benefits** to **carers** would be a **useful** staring point.

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1343 Classe : 3 Khi2 : 28
however, it appears to be **weighted** significantly **above other factors** in the **decision making** process. **we believe** it would be **useful** to have more visibility **of** a **structured approach** which highlights **how** NICE **considers** and incorporates **additional factors,** such as the level **of unmet need,** disease severity, patient convenience, government health priorities,

u.c.i. : 2 *2 *cat_IND

u.c.e. : 944 Classe : 5 Khi2 : 49
scoring criteria, and other design alternatives. the **two part** health **technology appraisal** we **propose** a health **technology** assessment **based** on the current ICER **evaluation, supplemented** with a **comprehensive** benefits and value, CBV, **review.**

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1378 Classe : 5 Khi2 : 49
following this, as a **second stage,** the **committee** or **another** group **would review** feedback from **stakeholders** and **deliberate** on the **broader impact** of the heath **technology.**

u.c.i. : 24 *24 *cat_IND *name_PHE *K_2

u.c.e. : 957 Classe : 5 Khi2 : 42
same product will be considered on **their** individual **merits** the **two part protocol** builds on the current the QALY **based** ICER approach to **technology** assessment. the **add** on nature of the CBV **review** promotes **feasibility, while** the transparency of the **criteria** upon which CBV **reviews** are **based provides** all **stakeholders** with **clear** guidelines for the **technology appraisal.**

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1324 Classe : 5 Khi2 : 42
the **extent** and type of evidence to be submitted for demonstrating and measuring these benefits, and the **linkage between** assessment of value and funding decisions. in this respect, it **would** be valuable if the industry sponsor of a **technology, could have** the **opportunity** to **participate** in the **appraisal** to a **greater extent, particularly** at **appraisal committee meetings,**

u.c.e. : 1382 Classe : 5 Khi2 : 41
gefitinib, IRESSA, or erlotinib, tarceva, **for** non **small cell lung cancer compared** to the **use** of i. v. docetaxel. this benefits not **only** the **patients,** in terms of **increased** comfort/ **avoidance** of **adverse effects associated with** i.

u.c.i. : 24 *24 *cat_IND *name_PHE *K_2

u.c.e. : 935 Classe : 2 Khi2 : 34
technologies that **are associated with** more **convenient delivery** systems, more **convenient** location of **administration, reduction** in the **frequency** of **dosage,** or **reduction** in **regimen** complexity, have **been shown** to achieve **improved compliance** in pharmacological **treatments for cardiovascular diseases,** iskedjian et **al** 2002;

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1396 Classe : 2 Khi2 : 33
benefits that **are** important to **patients incremental** innovation in the form of **better** tolerability, **improved dosing schedules,** i. e. less frequent, **reduced side effects, better mode** of **administration, oral vs. intravenous, for example, can** deliver real benefit to **patients, improving** their **quality** of **life** and their **compliance with treatment.**

u.c.i. : 24 *24 *cat_IND *name_PHE *K_2

u.c.e. : 936 Classe : 2 Khi2 : 30
dickson and plauschinat 2008, psychiatric **illnesses,** pfeiffer et **al** 2008, HIV, boyle et **al** 2008, and **diabetes,** barnett 2006, among **many** others. further, **reductions** in **treatment** complexity and **frequency,** as well as more **convenient modes** and location of **administration are associated with reductions** in **patient** inconvenience and decreases in **financial** and **time** costs of **caregivers.**

technologies. **increasingly it is doing so by** offering patient **access** schemes **and flexible pricing** approaches **to** address **challenges** with data **and** reduce the cost/ QALY.

u.c.i. : 1 *1 *cat_IND *name_ABHI *K_5

u.c.e. : 17 Classe : 1 Khi2 : 14
too early an assessment of **value** in **an innovative** technology **might** ignore both the **learning curve** phenomenon **and** the fact that the process of **innovation** in **medical devices is** one of **continuous,**

u.c.i. : 17 *17 *cat_IND *name_JJ *K_1

u.c.e. : 669 Classe : 1 Khi2 : 13
in the NHS **next** stage review, the announcement that strategic health authorities **will** have a legal duty **to promote innovation is to** be **welcomed and is** a clear indication that **our policy makers recognise** the **importance** of **innovation and** the **value it brings.**

u.c.i. : 18 *18 *cat_ACA *name_CLAXTON *K_4

u.c.e. : 736 Classe : 1 Khi2 : 13
its relationship to price, and the **incentives this** provides for private **sector investment** decisions. these **important** issues were central **to** the recent **policy debate** about **value** based **pricing** in the UK **and** a **wider** international **debate.**

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1410 Classe : 1 Khi2 : 13
pharmaceutical innovation is a **continuing learning** process, whereby **new and** unexpected **findings** are only discovered once health technologies enter the **market. providing** a stable **environment** for R&D **investment and** the **future development** of **implemented.**

u.c.i. : 33 *33 *cat_ACA *name_HF *K_4

u.c.e. : 1275 Classe : 4 Khi2 : 28
nevertheless, implementation is **not** without costs. decision making **bodies like** NICE should therefore **carefully** consider the **potential** worth of **implementing health care** innovations, **using** decision **models** and **evidence** synthesis.

u.c.i. : 32 *32 *cat_PG *name_MIND *K_4

u.c.e. : 1262 Classe : 4 Khi2 : 28
if this genuinely protected **individuals** from ineffective **therapies,** it would be one **thing but these** are **established therapies** which many **people find very helpful.** the draft of the full **guideline** explicitly states **that** a therapy **that** is **not** recommended may **still** be **effective** and **that services** should **maintain** a wide range of **expertise** and **therapies.**

u.c.i. : 33 *33 *cat_ACA *name_HF *K_4

u.c.e. : 1299 Classe : 4 Khi2 : 28
in a **budget** constrained **health care system,** decisions **about implementation, research** and **health care provision** are ideally **made** on an integral **basis.** as a **means** of supporting a **system objective** of maximizing population **health gain** subject to **budget** constraints,

u.c.i. : 32 *32 *cat_PG *name_MIND *K_4

u.c.e. : 1261 Classe : 4 Khi2 : 27
in the case of **psychological therapies** the **potential** impact is devaluing the skills of **individual** practitioners, and **loss** of **jobs** or retraining in a therapy **that** may **not** align with the **professional** s beliefs, **experience** or skills.

u.c.e. : 1260 Classe : 4 Khi2 : 26
*name_ABPI *K_2

u.c.e. : 42 Classe : 3 Khi2 : 24
how NICE **assesses factors other** than the ICER in its **decision making** and **how** the **benefits of** innovation are **weighed** against QALys **gained** is **unclear.** more **transparency** is needed.

u.c.i. : 8 *8 *cat_IND *name_BIA *K_3

u.c.e. : 374 Classe : 3 Khi2 : 24
this would **factor** in more **effectively** the **societal costs. other approaches should** also be **considered.** option 1: **some of** the **above factors** could be expanded **into** the **pre** existing **cost per** QALY **approach.**

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1385 Classe : 3 Khi2 : 24
alongside the QALY, **we believe** there **should** be greater visibility **of how additional factors** are **considered** by NICE and **how some factors** could be better **represented.**

u.c.i. : 9 *9 *cat_IND *name_BMS *K_1

u.c.e. : 441 Classe : 3 Khi2 : 23
NICE **claims** to use the **cost per** QALY as a **tool** not a **rule** in its **decision making** process and **claims** to also **take into account factors** such as the innovative **nature of** the treatment being **considered** and the severity **of** the disease being treated.

u.c.i. : 2 *2 *cat_IND *name_ABPI *K_2

u.c.e. : 44 Classe : 3 Khi2 : 22
in **particular,** the **following factors should** be given **additional weight** in **decision making: unmet need,** lack **of** alternative treatment; disease severity; disease rarity, **attributes of** high importance to patients, **carers, families** and society **generally** impact on future innovation this may require a change in the
as **part** of this, we **would** also reiterate our **recommendation** that NICE s **appeal process** should be **independent, rather** than referring **cases back** to the **appraisal committee** for **further review** if an **appeal** is upheld.

u.c.i. : 24 *24 *cat_IND *name_PHE *K_2

u.c.e. : 945 Classe : 5 Khi2 : 33
the **two part protocol** is as follows: NICE **applies** the current QALY **based** approach to **evaluate** cost effectiveness **manufacturers** may elect to **have their technology** undergo a CBV **review** in addition to the conventional cost effectiveness **analyses,**

u.c.i. : 31 *31 *cat_IND *name_SCHERING *K_2

u.c.e. : 1208 Classe : 5 Khi2 : 33
at present **there** is **little opportunity** to **have** a **discussion,** at **any stage accept appeal, where** this is **restricted** see **below,** about the **degree** of innovation that a **given** product represents.

u.c.i. : 34 *34 *cat_IND *name_GSK *K_5

u.c.e. : 1377 Classe : 5 Khi2 : 32
one possible **solution** may be to consider a **two stage process.** in the first **stage,** the **appraisal committee would** focus on a **technical review** of the evidence as happens **now.**

u.c.i. : 24 *24 *cat_IND *name_PHE *K_2

u.c.e. : 941 Classe : 5 Khi2 : 31
indeed, considerable residual variability surrounds NICE **recommendation** decisions, even controlling for the **estimated** ICER, jena and philipson 2009. **consistent** and **systematic** assessment **requires clear** articulation of the **criteria** for **evaluation.**

u.c.e. : 943 Classe : 5 Khi2 : 31
u.c.i. : 35 *35 *cat_IND *name_NOVARTIS *K_1

u.c.e. : 1430 Classe : 2 Khi2 : 30
novartis products **such** as lucentis, ranibizumab injection, **for** wet **age related** macular degeneration, AMD, marked a **significant** step forward in the **treatment** of this **condition.** this could include second **line treatments** where none **are available** or where a **treatment offers** a **significantly improved adverse event profile.**

u.c.i. : 2 *2 *cat_IND *name_ABPI *K_2

u.c.e. : 64 Classe : 2 Khi2 : 29
similarly, verapamil, still in **use for treatment** of arrhythmias, angina pectoris and **hypertension, was launched** in the 60s as the **first** calcium antagonist. seven further products **were developed** in the 70s and 80s **with** greater tissue specificity, targeting **illness** more specifically and **with fewer adverse effects.**

u.c.i. : 17 *17 *cat_IND *name_JJ *K_1

u.c.e. : 719 Classe : 2 Khi2 : 27
velcade was specifically designed to **treat multiple myeloma** and is the **first** in a new **class** of **agents known** as proteasome **inhibitors.** to **demonstrate** the effectiveness of **velcade,** the largest ever **randomised controlled trial** in **myeloma was** undertaken which **demonstrated** a **significant** clinical **advantage compared** to the **only** other **licensed therapy dexamethasone.**

u.c.i. : 31 *31 *cat_IND *name_SCHERING *K_2

u.c.e. : 1215 Classe : 2 Khi2 : 26
potential clinical benefits **for** the **use** of **sugammadex** include **increased patient safety** and **reduced**

innovative products comes from ensuring the integrity of the whole system. u.c.i. : 1 *1 *cat_IND *name_ABHI *K_5 u.c.e. : 2 Classe : 1 Khi2 : 12 para 51, **this** research into **value and innovation is** particularly **critical** for **medical devices** as the **current** evaluation landscape **is** more favourable **and** more adapted **to pharmaceutical innovations.** u.c.i. : 8 *8 *cat_IND *name_BIA *K_3 u.c.e. : 295 Classe : 1 Khi2 : 12 **it is** aimed at **providing** a **methodology** that **focuses** on **short term** cost **containment** at the expense of recognizing the **longer term and wider** benefits of **innovation.** u.c.i. : 9 *9 *cat_IND *name_BMS *K_1 u.c.e. : 462 Classe : 1 Khi2 : 12 we would **question** whether **this** would be the intention of the **government** or **supported by** the **public.** in the **short term** the **threshold** should rise **to reflect** the affect of **inflation.**	the **research** and development **consequences** of non **approval** are **very** different as between drug and **psychological therapies.** in the case of a drug there is **commercial** ownership and it is the company **that** bears the **losses; health professionals carry** on **prescribing** other drugs. u.c.e. : 1258 Classe : 4 Khi2 : 26 the **reason** is the **potential** squeezing out of non CBT approaches. the draft **guideline** concludes **that** the **evidence** for counselling is weak in comparison to CBT and **various** low intensity **psychosocial interventions** and therefore does **not positively** recommend counselling for **depression.** u.c.i. : 5 *5 *cat_PG *name_ARTHRITIS *K_4 u.c.e. : 221 Classe : 4 Khi2 : 25 arthritis **care** is **concerned that** NICE **places** excessive emphasis on **clinical evidence at** the **expense** of **that** which could **help** form a better **understanding** of the **potential** impact of **health** conditions and technologies on the life of the **service** user,	secretary **of state** s directions to NICE. u.c.e. : 132 Classe : 3 Khi2 : 22 there is a **need** for **transparency** and ABPI **believes** that NICE **should adopt** a **structured framework** to **decision making** that is summarised **clearly** in final guidance. u.c.i. : 30 *30 *cat_IND *name_WYETH *K_3 u.c.e. : 1193 Classe : 3 Khi2 : 22 **conclusion** wyeth **believes** that innovation **should** be **assessed** separately from **cost** effectiveness, and both, **together** with **other considerations, should** be **factored into** a multiple criteria **decision making framework.**	**note** that **while** the specificity of the **proposal** is intended to illustrate the mechanics and **feasibility** of a fully **designed protocol,** we **recognize** the illustrative nature of this **proposal** with **regards** to **choice** of **protocol parameters,** value **categories,** u.c.i. : 34 *34 *cat_IND *name_GSK *K_5 u.c.e. : 1318 Classe : 5 Khi2 : 31 in certain **circumstances, there** may be a **case** for some new health **technologies** to be **exempt** from **appraisal,** if they fulfil specific **criteria,** for example if they **have** a relatively **low** budget **impact.** u.c.e. : 1369 Classe : 5 Khi2 : 31 we **would** like to see the **appraisal committees have** the **opportunity** to **apply** more **pragmatism** and flexibility in the decision making **process,** in addition to the **discussions** on the **technical requirements** and evidence base.	incidence of residual **blockade** on **recovery.** there **are also** possible benefits **associated with** the **ability** to **reverse** neuromuscular **blockade** more **quickly** and predictably **from** any level of **blockade with sugammadex compared** to **existing agents,** u.c.e. : 1220 Classe : 2 Khi2 : 26 the benefits that **sugammadex offers,** particularly in terms of potential efficiency **improvements, are difficult** to incorporate **within conventional** health technology assessment. **patient reported** outcomes **such** as health **related quality** of **life** or health **status are unlikely** to be **significantly** impacted by **sugammadex** in a routine **surgical setting.** u.c.i. : 27 *27 *cat_IND *name_ROCHE *K_2 u.c.e. : 1049 Classe : 2 Khi2 : 25 **for example,** it has **been shown** that when **comparing intravenous** chemotherapies and **oral** chemotherapies, **patients often** have a strong preference **for oral over intravenous treatments. similarly,** extended **dosing schedules for** medicines, **for example,** monthly **versus daily** or weekly **treatments can also** be **highly valued** by **patients.**

Table 2: Key Terms

Classes	Key terms
Class 1 **R&D investments and the future of innovative products**	innov+ (163), valu+(159), pharmac<(44), continu+(13), futur+(27), role+(21), import+ant(48), medica<(41), access(29), incentiv+(21), innova+(47), narrow(10), policy(17), recognise+(28), uptake(10), vita+l(7), an+(80), cycle+(11), lord+(6), short+(15), industri<(6), methodolog<(18), pres+ent(12), addressing(6), carrie+(8), countries(8), darzi(5), delivering(12), deliver+(20), determining(10), drive+(7), efficiencies(5), embrace+(5), environment+(6), european(8), focuse+(9), government+(13), has+(53), healthcare(24), however(29), increasingly(12), industry(22), is(191), it(101), itself(8), market+(22), medicine+(55), must(22), nor(5), out(21), pathway+(7), play+(10), products+(29), rewarded(6), to(278), determine+(10), globa+l(3), indirect+(6), inflation<(4), question+(12), chang+er(14), flexi+ble(5), adopted(7), aim+(5), behind(5), best(8), characteristic+(7), continuing(3), counterparts(4), define+(15), describe+(8), develop+(43), emphasis+(6), encouraging(6);
Class 4 **Implementing Health Care innovations**	implement+(19), about(19), care+(31), practic+(17), adherence(6), bodies(7), funding(9), guidance(13), professional+(8), resource+(16), valuing(10), commercia+l(6), budget+(9), intervention+(14), loca+l(4), service+(15), encourag+er(7), base+(8), economists(4), established(8), group+(10), guideline+(7), helpful(5), implementing(5), knowledge(8), least(5), natural(3), paper+(5), poor(4), therapies(17), voice+(4), whom(5), depressi+f(3), menta+l(8), nationa+l(6), job+(4), programme+(3), respect+(4), evid+ent(26), across(7), added(4), agenda(4), at(26), carefully(3), clinic+(25), commitment+(4), concerned(6), creating(3), ensuring(4), establishing(5), fact(6), fair(6), funded(4), health(45), level+(11), like(6), looking(5), made(13), promoting(4), published(3), receive+(6), reimburse+(5), right+(5), that(79), undermine+(3), users(7), sense+(4), experience+(7), support+(9), remettre.(3), objectiv<(7), organisat+ion(3), possi+ble(7), almost(2), body(3);
Class 3 **Comments on NICE's approach to innovation and on the drug appraisal process**	consideration+(29), dimension+(18), transpar+ent(17), account+(44), considered(29), factor+(40), into(45), making(35), should(67), taken(23), transparency(18), issue+(20), attribut+ion(13), decis+ion(44), consider+(20), how(26), incorporate+(12), tool+(11), weight+(14), aspect+(10), guide+(4), alongside(7), believ+(20), captured(12), factored(4), following(11), gained(9), particular(14), societal(13), specific(15), structured(5), take+(22), useful(7), weighed(5), weighted(6), document+(3), nature+(11), resoudre.(5), additional(15),

	adequately(9), adopt+(6), all(20), analysis(9), appraising(6), approach+(22), carer+(12), clearly(7), ensure+(11), ethic+(3), explicit(3), framework+(13), holistic(4), incurred(3), introducing(4), need+(35), other+(32), proper(5), regarding(6), relating(4), represented(5), rule+(4), scoping(6), separate+(4), modification+(3), relation+(6), calculat<(4), stat+16(10), around(10), assess+(22), explicitly(4), flexibility(5), include+(16);
Class 5 **Comments on the appraisal committee meetings**	select+f(8), discussion+(6), pragmati<(5), appeal(5), apprais+(33), committe+(19), criteri+(15), exempt+(5), review+(20), stakeholder+(12), technical(6), timely(5), topic+(8), would(26), clarity(4), meeting+(6), consultati+f(5), dialogue+(3), feasibility(4), scoring(5), multipli+er(2), deliberat+ion(3), technolog<(36), variat+ion(3), allowing(4), had(5), independ+(6), particularly(8), second+(4), case+(10), categori<(3), engagement+(2), manufactur+er(3), propos+er(2), relev+er(6), comprehensi<(4), protocol<(4), appropriate(8), below(3), between(8), conducted(3), could(14), extent(4), followed(2), informed(3), insight+(3), open+(3), opportunity(6), process+(22), proposal+(2), proposed(2), provide+(12), response+(4), two+(7), weighting+(4), have+(18), centre+(2), option+(5), consist+er(3), evaluat+ion(7), refer+ent(2), agreed(2), another(3), category(2), choice+(3), circumstances(3), clinically(2), comparison+(3), given(8), impact+(12), input+(3), little(3);
Class 2 **Benefits of medical innovation for patients**	disease+(94), treat+(131), example+(71), phase+(22), associat<(27), pati+ent(164), reduct<(20), compliance(21), reduce+(35), with+(145), cancer+(24), pain+(17), inhibit<(12), molecul<(17), biologic+(13), can(84), chronic(12), day+(14), first(29), for+(208), target+(14), treated(14), was(43), initia+l(12), large+(17), ora+l(9), agent+(10), condition+(35), mode+(7), point+(17), test+(18), combin+er(11), gre+er(7), act+ion(12), administrat<(10), cause+(11), symptom<(8), al(9), alzheimer+(9), awarded(8), block+(10), burden(10), children(8), class(16), compared(17), compound+(7), control+(7), conveni+(18), delivery(17), demonstrate+(21), diabetes(7), disability(11), disorder+(8), drug+(54), effect+(33), enhance+(14), fewer(8), financial(17), frequency(8), illness+(14), improve+(61), increase+(22), likelihood(7), living(9), lower(8), marketing(9), once(16), productivity(19), related(20), rheumatoid(7), schedule+(7), shown(10), sick+(7), side(11), studie+(15), sugammadex(9);