

Quality Decision-Making: Procedures and practices in drug development and the regulatory review

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Institute for Regulatory Science

CMR INTERNATIONAL INSTITUTE FOR REGULATORY SCIENCE

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Workshop on Quality Decision-Making Procedures and practices in drug development and the regulatory review

7-8 December 2006
The Woodlands Park Hotel
Cobham, Surrey, UK

Workshop Organisation

Workshop organised by: Professor Stuart Walker and Dr Neil McAuslane, CMR International, Institute for Regulatory Science

Report prepared by Margaret Cone, CMR International Institute for Regulatory Science

WORKSHOP ON QUALITY DECISION-MAKING: Procedures and practices in drug development and the regulatory review

Section 1: Overview

The concept of quality

Benefit and risk for patients, success or failure of companies' multi-million dollar research projects, credibility, for regulatory agencies, as the watchdogs of public health; all of these depend on the quality of the decisions made at critical stages as new medicines move from laboratory to clinic, through trials, regulatory review, approval and throughout their marketing life cycle.

The Workshop held by the CMR International Institute for Regulatory Science, in December 2006, examined the factors that contribute to quality decision-making in a week when two particularly pertinent items were in the news. The first was the publication, in the UK, of recommendations by an Expert Group¹ on the critical stage of first trials in humans and the second, at the other end of development, was a decision by a major international company to suspend advanced Phase III trials on a new cardiovascular agent².

Scope of discussions

Chaired by **Thomas Lönngren**, *Executive Director, European Medicines Agency (EMA)*, the first Session looked at best practices by companies and agencies. **Dr Peter Bonne-Eriksen**, *Novo Nordisk A/S, Denmark* set the scene with an analysis of the critical decision points in developing a new medicine and the importance of building a culture of quality management throughout pharmaceutical companies.

Caroline Vanneste, *TPD, Health Canada* described Canada's Good Review Practices project launched in 2004 and discussed the impact of increased transparency during the review process and in the post-approval stage.

A major study on *Building Quality into the regulatory review* is being undertaken by an Institute PhD research fellow, **Andrea Mallia-Milanes**, from the Maltese regulatory authority, who provided an interim report to the Workshop. **Dr Neil McAuslane** from the Institute also described the methodology and preliminary results for a 'scorecard' project being undertaken, as part of this study, to collect feedback to measure both industry and agency performance after the review of major applications for new medicines.

This project is in a feasibility stage and the early first-hand reactions that were provided by participants **Dr Paul Huckle**, *GlaxoSmithKline, USA* and **Omer Boudreau**, *Health Canada* were positive.

A structured approach to decision-making

The second session looked at models to improve quality and consistency in the decision-making process, with a particular focus on benefit and risk. The Session was chaired by **Dr David Jefferys**, *Eisai R&D Company Ltd, UK* and the topic was introduced with a comprehensive overview by **Dr Filip Mussen**, *Merck Research Laboratories, Belgium* who had studied a number of models available for benefit-risk decision-making as part of a PhD fellowship under the auspices of the Institute. In addition to the multi criteria decision analysis (MCDA) techniques that have been the subject of previous Institute Workshops³, Dr Mussen described a surprising number of different methods and models that have been investigated.

Two discussants gave an industry and an agency perspective. **Robert Reynolds**, *Pfizer Inc., USA*, looked, in particular, at the lessons to be learnt from epidemiology in assessing the benefit/risk equation. **Dr Eric Abadie**, *Vice Chairman, Committee for Human Medicinal Products (CHMP) EMA* gave an instructive insight into the way in which, following work initiated by CMR International to identify more appropriate qualitative approaches, the CHMP is addressing the question of procedures and criteria for benefit-risk decisions and, equally importantly, for documenting these with greater consistency.

In the final Session, chaired by **Professor Sir Alasdair Breckenridge**, *Chairman of the Medicines and Healthcare Products Regulatory Agency (MHRA), UK*, the theme of risk-benefit decisions was continued in a presentation by **Dr John Patterson**, *AstraZeneca Pharmaceuticals, UK*. This included a case study giving insight into the critical decisions that the company had to make when deciding to withdraw a new anticoagulant that had many benefits for patients over standard therapy with warfarin, but presented a major risk management dilemma.

Including patients' views

The workshop was rounded off by an inspiring presentation by **Mrs Mary Baker**, *MBE President, European Federation of Neurological Associations* who is one of two representatives of patients on the EMA Management Board. Mrs Baker stressed the importance of working in partnership and developing alliances between science and society. She underlined the importance of including patients' views in on-going discussions about re-shaping the way in which clinical trials are designed.

Syndicate discussions

The Syndicate groups were asked to discuss and make recommendations on best practices for quality decision-making by companies and by regulatory agencies and to look at the advantages and disadvantages of transparency in relation to decision-making during regulatory review.

A general formula for success

The workshop arrived at a general formula for making good decisions that consisted of taking clear well-defined processes and having them applied consistently by talented, well-trained people.

Company processes

The Syndicates identified six key for good practices by companies:

- 1. Establish a process** for an independent and objective review of each project at key milestones in the development process;
- 2. Ensure objectivity** through multi-disciplinary teams with decisions being made at the right management level;
- 3. Produce a target label** as the driver and use this as the marker that defines the parameters for decision points, identifying ideal, acceptable and unacceptable parameters;
- 4. Build Health Technology Assessment (HTA)** factors into the decision-making process as early as possible to ensure that potential reimbursement and access barriers are identified at an early stage
- 5. Involve other Stakeholders** to take account of the views of patients, physicians and other interested parties.
- 6. Encourage data sharing** between companies and agencies on problems arising during development in order to improve decision-making and avoid unnecessary duplication of effort.

Agency procedures

Good practices are often more formalised within regulatory agencies in terms of codes and guidelines, and five recommendations were made in relation to these:

- 1. Good Review Practices (GRP):** Information and experience should be shared between agencies with a view to harmonising best practices.

2. Lifecycle management: The same GRP principles should be applied to ensure quality decision-making throughout the life-cycle of products.

3. Review support: Peer reviews and external advisory reviews are valuable for confirming initial assessments or adding necessary expertise.

4. Quality Management: Methods for monitoring and assessing quality procedures should be encouraged and there was support for the Institute Scorecard initiative for obtaining feedback following review.

5. Benefit risk: Regulatory review procedures should utilise standardised templates for assessing benefit-risk criteria and reporting the outcome.

Transparency of decision-making

Transparency is important for good quality reviews and decision-making but enhanced transparency must not be seen as an end in itself. It should be applied at key decision points and under clear *rules of engagement*. The following additional observations were made:

Types of transparency: The information made publicly available on review processes and outcomes (*passive transparency*) is generally adequate but improvements could be made in *active transparency*, that is, encouraging specific involvement in decision-making by all stakeholders, but particularly patients

Hierarchy of evidence: There is a need to be mindful of the *hierarchy of evidence* (as applied in evaluating clinical trial data) when involving individual patients in the decision-making process.

Public expectations: A better understanding is needed of the general public's actual expectations for information on review and decision-making procedures or valuable resources will be wasted on creating transparency for its own sake.

Advantages and disadvantages: The pros and cons of transparency during different stages in a product's lifecycle were reviewed. Advantages included increasing public confidence and understanding in review processes and the major disadvantages were the resource-intensive nature of providing information and its potential for misuse.

¹Final report of the Expert Scientific Group (ESG) on Phase One Clinical Trials (Chairman: Professor Gordon W. Duff), following serious adverse in the first-in-man clinical trial of TGN412 in the UK, March 2006. 7 December 2006, Department of Health website www.dh.gov.uk

²FDA Statement, 3 December 2006, 'Pfizer Stops All Torcetrapib Clinical Trials in Interest of Patient Safety', via FDA website www.fda.gov

³CMR International Institute workshops on developing a model for Benefit-risk Assessment, March 2004, London, and June 2005, Washington



**WORKSHOP QUALITY DECISION-MAKING:
Procedures and practices in drug development and the regulatory review**

Section 2: Outcome

Syndicate Discussions

Session 3 of the Workshop, during which the Syndicate discussions took place, was chaired by **Professor Sir Alasdair Breckenridge**, *Chairman, Medicines and Health products Regulatory Agency (MHRA), UK*.

The Workshop participants formed three Syndicate groups and discussed quality decision-making from three separate, but related aspects:

- **Company** best practices for decision-making during drug development and throughout a product’s life-cycle, with particular reference to obtaining and maintaining product registration;
- **Authority** best practices for the review and decision-making processes of new medicines and the need to ensure consistency;
- **Transparency** of company and agency processes and the advantages and disadvantages in relation to ensuring the quality of decision-making, especially during the review process.

The Chairpersons and Rapporteurs for the three groups were:

Syndicate 1	<i>Chair:</i>	Graham Higson , <i>Vice President and Head of Global Regulatory Affairs, AstraZeneca, UK</i>
	<i>Rapporteur:</i>	Dr Phillip Chipman , <i>Head, Clinical Evaluation Unit 1, Therapeutic Goods Administration, Australia</i>
Syndicate 2	<i>Chair:</i>	Professor Bruno Flamion , <i>Chairman, EMEA Scientific Advice Working Party, EU</i>
	<i>Rapporteur:</i>	Dr Roy Baranello , <i>Assistant Vice President – Policy and Operations, Wyeth Pharmaceuticals, USA</i>
Syndicate 3	<i>Chair:</i>	Dr David Lyons , <i>Senior Medical Officer, Irish Medicines Board</i>
	<i>Rapporteur:</i>	Dr Susan Forda , <i>Executive Director, Regulatory Affairs (Europe), Eli Lilly and Company, UK</i>

The programme for the Workshop is set out in *Annex 1*

1. SUMMARY OF THE SYNDICATE OBSERVATIONS

The main observations and recommendations from the Syndicates are summarised below and these are discussed in more detail later.

General

The formula for quality decision-making that applies equally to industry and agencies is that:

$$\begin{array}{l}
 \text{Clear and well-defined processes} \\
 + \text{ Consistent application} \\
 + \text{ Talented, well-trained people} \\
 \hline
 = \text{ Good decision-making}
 \end{array}$$

COMPANY PROCESSES

The following elements were recommended for establishing good decision-making practices within the process of developing and registering new medicines and maintaining their regulatory status throughout the lifecycle:

- **Establish a process** for an independent and objective review of each project at key milestones in the development process;
- **Ensure objectivity** through multi-disciplinary teams with decisions being made at the right management level
 - The *culture* of the organisation and its management style might need to change to ensure that effective decision-making procedures can operate;
- **Produce a target label as the driver** and use this as the marker that defines the parameters for decision points
 - It may be appropriate, from the outset, to establish not only the ideal target label but also the limits of minimum acceptance and unacceptable factors that would lead to project being terminated
- **Build Health Technology Assessment (HTA) factors** into the decision-making process as early as possible to ensure that potential reimbursement and access barriers are identified at an early stage
- **Involve other Stakeholders** at relevant stages in the process to take account of the views of patients, physicians and other interested parties.
- **Encourage data sharing** between companies and agencies on problems arising during pre-clinical and clinical development in order to improve decision-making and avoid unnecessary duplication of effort when similar problems arise elsewhere.

AGENCY PROCESSES

Good practices are often more formalised within regulatory agencies in terms of codes and guidelines, which are often made publicly available. Templates and Standard Operating Procedures (SOPs) are also frequently employed to improve the consistency of reviews and procedures. Against this background the following recommendations were made in relation to agency activities:

- **Good Review Practices (GRP):** There should be coordinated efforts to share know-how and experience between agencies with, potentially, a view to harmonising best practices among different authorities.

This could be assisted by making an inventory of current agency codes and templates, possibly as part of on-going studies on the quality of review being undertaken by the Institute¹

- **Lifecycle management:** The same GRP principles should be applied to ensure quality decision-making throughout the life-cycle of products.
- **Review support:** Peer reviews and external advisory reviews should be encouraged wherever feasible in order to confirm initial assessments or add necessary expertise.
- **Quality Management:** Methods for monitoring and assessing quality procedures should be sought with a view to continuous improvement. The Institute Scorecard initiative was supported as a way of obtaining and evaluating feedback following a major review.
- **Decision-making models for benefit risk:** Whilst models for decision-making can never replace the need for judgement there is scope for improving current procedures through the adoption of standardised procedures for benefit-risk assessment with templates for assessing criteria and reporting the outcome.

¹ Report on the project made to the Workshop by Andrea Mallia-Milanes, see Programme, Annex 1

- There is a need to develop harmonised guidance for the evaluation of specific risks, e.g., hepatic toxicity.

TRANSPARENCY OF DECISIONS-MAKING

There was consensus on the importance of transparency to good quality reviews and decision-making but enhanced transparency must not be seen as an end in itself but only in response to specific need, at key decision points and under clear *rules of engagement*.

- **Types of transparency:** The information made publicly available on review processes and outcomes (*passive transparency*) is generally adequate but improvements could be made in *active transparency*, that is, encouraging specific involvement in decision-making by all stakeholders, but particularly patients
- **Hierarchy of evidence:** There is a need to be mindful of the *hierarchy of evidence* (as applied in evaluating clinical trial data) when involving individual patients in the decision-making process.
- **Public expectations:** A better understanding should be sought of the general public's expectations for information on review and decision-making procedures or valuable resources will be wasted on transparency for its own sake.
- **Advantages and disadvantages:** The pros and cons of transparency at each stage of products' lifecycles were reviewed. Advantages related, in particular, to increasing public confidence and understanding in review processes and the major disadvantages were the resource-intensive nature of providing information and the potential for misuse.

2. DETAILS FROM THE SYNDICATE DISCUSSIONS

2.1 DECISION-MAKING BY COMPANIES

Best practices for decision-making by companies need to be applied throughout the life-cycle of a product from the decision to make the transfer from the laboratory to the clinic, through development and registration up to the decision that the product is no longer viable and should be removed from the market.

Process

Companies need establish a process for an *independent* and *objective* review of each project at key milestones in the product's development and life cycle:

- This may not be the same model for all companies and the practical application will differ according to the size and management structure of the company
- The decision-makers could be a panel of senior experts that are outside the project but resources will dictate, for example whether this is carried out internally or externally to the company.

Objectivity

This should be ensured through establishing *multidisciplinary* teams working at an appropriate level of responsibility. To achieve this it might be necessary to address flaws in the culture of the organisation or its management style, for example:

- Strong personalities that have undue influence on the decision-making process;
- The involvement of individuals who have invested so much 'of themselves' in a project that they are too involved to be truly objective;
- Decisions made at too low or too high a level in the management structure;

A multidisciplinary approach is important; Teams may focus on a specific therapeutic area, and they should not be left to struggle with issues outside their expertise, especially when these cross therapeutic boundaries, as in the case of QT prolongation.

Target product label

The *driver* for consistent decision-making, from the start of product development should be the target product label that is used as a marker whenever key decision points are reached. There may, in fact, be three versions of this notional label:

- An optimistic version that sets out the ideal target for a successful project;
- A more realistic version which is, in effect, sets out the minimum acceptable outcome;
- A set of unacceptable criteria and factors that would lead to the project being terminated.

In view of the length of time for drug development, the target label must be reviewed and revised to take account, not only of changes arising from study results but also of changes in medical practice and the availability of other competing therapies.

Using outside advice to shape Phase III trials

Companies are accustomed to adapting their Phase III programmes according to the outcome of the Phase II studies and the toxicity or adverse event profiles that emerge. Procedures also exist for obtaining scientific advice from regulatory agencies that may shape the Phase III programme. There is, however, an increasing trend towards building other considerations into the design of late-Phase studies, namely:

- *Health Technology Assessment* (HTA) factors and the need to generate data to demonstrate cost-effectiveness and justify reimbursement;
- The views of patients, physicians and other stakeholders on acceptable risk in relation to the perceived benefits of the product within its therapeutic area.

Mechanisms need to be found for obtaining such outside advice and building it into the decision-making process for clinical development.

(It was noted that the CMR International Institute would be holding a Workshop on *Regulation and Reimbursement* in 2007 that would address some of these issues²)

Willingness to share data

The quality and efficiency of decision-making within development programmes could be greatly improved if companies were willing to make information available on products that have run into toxicity problems and on projects that have been terminated before registration. Such data sharing should take place not only between companies but also between companies and agencies and would help identify whether certain problems are molecule-specific or a class effect.

It is acknowledged that, when projects are terminated at a pre-registration stage there is little interest in following this up at a scientific level or in publishing results. With a willingness to share data, however, and the resources to carry out independent research on the reasons why some products fail, valuable research could be carried out on the underlying aetiology of unexpected toxicity. This would be an important contribution to improving companies' decision-making on similar products and would reduce the waste of resources on fruitless duplicative research.

2.2 PARALLELS BETWEEN COMPANIES AND AGENCIES

Many parallels can be drawn between good practices by companies and agencies, namely the need for clear, well defined processes, consistently applied and operated by appropriately trained people. In many ways, however, agency processes have become more formalised, particularly with an increased emphasis on transparency, and it was suggested that companies could learn from the agencies, particularly with respect to:

² Workshop on 'Regulation and Reimbursement: two sides of the same coin', 4-5 October 2007, Cobham, Surrey, UK. Further information from institute@cmr.org

- Independent expert review procedures;
- Processes for internal peer review of decisions;
- The adoption of cross-functional review teams to bring together expertise in CMC, pre-clinical and clinical assessment.

A recommendation that is clearly common to all parties is the importance of recruiting and retaining *talented* trained staff. 'Talent' in this context, involves:

- Defining the competencies that are needed;
- Provided training, in particular, in decision-making.

2.3 DECISION-MAKING BY AGENCIES

Good Review Practices (GRP)

The CMR International Institute survey³ showed that many agencies have either adopted GRP or have some aspects in place, for example SOPs, assessment templates. A greater adoption of such practices should be encouraged and this should be handled in a transparent manner with publication of standards and procedures to take the 'mystery' out of decision-making by agencies.

It was **recommended** that there should be coordinated efforts to share know-how and experience between agencies with, potentially, a view to harmonising best practices among different authorities.

- For this, it would be important to establish a focus of responsibility within each agency and give the individual or team responsibility for driving efforts to define good practice and move it forward.

It was further **recommended** that an inventory of GRP codes and review templates should be made with a view to facilitating harmonisation initiatives. This could be undertaken, under the auspices of the Institute, possibly as part of the current study on *Building quality into the regulatory review*³

Lifecycle management

There is a focus on quality decision-making when agencies are reviewing applications for new molecular entities, especially where these may represent a therapeutic breakthrough and be in the public eye. There is a perception, however, that 'Life-cycle' applications to extend the use and scope of existing medicines do not benefit from the same level GRP.

It was **recommended** that that the same GRP principles should be applied to ensure quality decision-making throughout the life-cycle of products and not only at the initial approval stage.

- It was noted that risk management plans, especially when there is greater experience of these, will have a role to play in life-cycle management.

Review support

The review procedures of most agencies involve procedures for *confirmatory* or *external* reviews. This may be through internal peer review or through the use of outside expert advisors. In some cases, agencies may participate in joint or shared reviews.

It was **recommended** that peer reviews and external advisory reviews should be strongly encouraged where feasible, to confirm the initial assessment and/or add specialist expertise.

- Decision-making within an agency should not rest on the opinion of a single individual;
- Individuals serving as external advisors or on advisory committees should receive appropriate training or orientation in the regulatory process in order to better understand their role.

³ Report presented to the Workshop by Andrea Mallia-Milanes – see programme in *Annex 1*

Quality Management

There was discussion of the need to implement management procedures not only to ensure that GRP is being consistently applied but also to monitor the impact. This would involve looking at the objectives of GRP and deciding if there are metrics that would be meaningful, either through auditing or retrospective analysis.

It was noted that the Institute is investigating the feasibility of a 'Scorecard' system⁴ to collect data from both companies and agencies, following a major review. It was felt that this would provide useful support for greater dialogue and sharing of experience, in future.

It was **recommended** that methods for monitoring and assessing quality procedures should be sought with a view to continuous improvement and there was support for the Institute Scorecard initiative as a way of obtaining and evaluating additional feedback.

Structured decision-making Models

The workshop had received reports on the development of a range of models for risk-benefit analysis and their practical application⁵. Such models attempt to standardise qualitative and quantitative aspect but cannot replace the need for judgement to be built into the decision-making process.

It was, however felt that there was a need for a more standardised approach to the overall assessment of benefit and risk for a new product with criteria and templates that define the elements and give guidance on the type of risk to be taken into consideration by the assessor.

It was noted that valuable harmonised guidance relating to QT prolongation had been agreed by ICH⁶ and that similar advice would be useful when assessing, for example, hepatic risk. There were, however, concerns about the length of time to prepare and agree guidance through the ICH process and the hope was expressed that mechanisms could be found to accelerate the process.

It was **recommended** that regulatory review processes should include standardised procedures for benefit-risk assessment with templates for assessing criteria and reporting the outcome.

- Mechanisms should be sought to develop guidance on specific, common risks such as hepatotoxicity, with a view to adoption under the ICH process, with minimum delay.

2.3 TRANSPARENCY: THE ADVANTAGES AND DISADVANTAGES

The stages in the development and review process at which subject transparency might have a particular relevance or impact was considered in relation to the diagram given in *Figure 1*.

Transparency in context

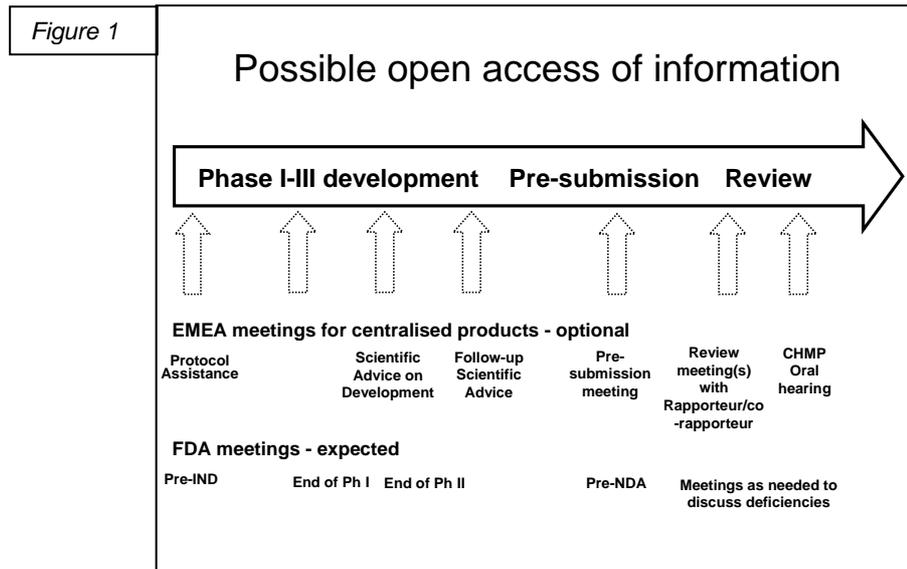
There was consensus on the importance of transparency as one of the building blocks of a good quality review and enhanced transparency is therefore to be encouraged and supported but with the following caveats:

- Transparency is not an end in itself and resource-consuming measures should only be adopted if there is a specific need;
- Enhanced transparency measures should be restricted to key decision points in the life-cycle of a product
- The 'Rules of Engagement' for implementing transparency measures must be clear to all stakeholders.

⁴ Presentation to the Workshop by Dr Neil McAuslane – see Workshop Programme Annex 1

⁵ Presentations to the workshop by Dr Filip Mussen, Dr Robert Reynolds and Dr Eric Abadie

⁶ ICH Guideline S7B on *The Nonclinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals*. www.ich.org



Types of transparency

In terms of decision-making, transparency can be considered from two aspects:

- **Passive transparency** where information is made available outside the agency in specialised publications or in the public domain (predominantly via the web) and interested parties are informed of the decision-making process, the criteria applied and the outcomes;
- **Active transparency** is a more inclusive way of bringing stakeholders, sponsors, healthcare professionals and patients, for example, into the decision-making process and seeking their views and input.

It was agreed that existing levels of 'passive' transparency are acceptable for most agencies but that there are aspects of 'active' participation, for certain products or issues, that could be improved:

- participation in hearings
- consultation with patients

Open discussion meetings

Stakeholder participation: There was general agreement on the advantages of opening up the decision-making process at hearings and scientific advisory committees to other stakeholder, including patient representatives and sponsors. This would apply, in particular, to CHMP processes that are currently closed.

There was less agreement on a proposal that industry could be represented at such discussions but through a company not directly concerned with the particular application.

Hierarchy of evidence

Involving patients: Procedures for obtaining the views of patients will normally involve consulting individual patients or individuals representing patient groups. In all cases it is necessary to be mindful of the *hierarchy of evidence* (as, for example, applied to the evaluation of clinical data).

Understanding public expectations

Transparency policies: Steps should be taken to ascertain the general public's expectations of an agency's responsibilities and transparency policies should be tailored to meet those expectations. Otherwise it may be a case of transparency for transparency's sake, using large amounts of scarce and valuable resources and failing society.

Transparency at different stages in the development and review

Referring to *Figure 1* the advantages and disadvantages of transparency at different stages in the lifecycle of a new product were reviewed.

The pre-submission stage

Advantages

Patient interest: Transparency at this stage is important in terms of keeping patients informed of new developments and access to clinical trials but this has, to some extent, been taken up by the global clinical trial registry set up by IFPMA.

Competitor/industry interest: If information on the outcome of scientific advice consultations were published, this would be of value to other companies working in a similar field.

Educational opportunity: Information on this relatively unknown area of drug development would provide the educated public with insight into the product development process.

New guidelines: The development of regulatory guidance, particularly therapeutic guidelines, could benefit from greater transparency at this stage.

Disadvantages

Little real benefit: Much information would be redundant in that the majority of candidates that enter development do not make it to the market;

Confidentiality: Much of the information from this stage of development is considered 'privileged and confidential' by companies and there would be time/resource-consuming difficulties in agreeing the data that could be published

During the review process

This refers to information provided after the initial submission, including the question of open hearings and publication of summaries of assessments.

Advantages

Stakeholders: Greater openness at this stage was regarded as being in the interests of patients and the public as well as the sponsor.

Controversial decisions: These can be more easily defended if information on the decision-making process is in the public domain.

Increased trust: It provides an educational opportunity with the public to increase ; increase in trust and confidence in the regulatory process

Risk management: There are opportunities to include patients and patient groups in the development of Risk Management Plans for new medicines.

Disadvantages

Resource intensive: providing information and allowing greater access during the review process involves an intense use of resources.

Political activists: Active participation by patients and patient groups carries the risk that such parties might be 'hijacked' by unreasonable advocates seeking media attention that can distort impressions of the decision-making.

Challenges: Greater transparency during the decision-making process can lead to more challenges from the public or special interest groups which, again, can be very resource-intensive.

Post approval

It was felt that the routine publication of information following the review and authorisation of a new medicine is currently comprehensive and satisfactory

Advantages

Value: The information can be well understood by the educated public and by patient groups and provides a valuable resource.

Labeling: In certain instances it may be useful to obtain the views of patients on labelling issues, at this stage, as part of post-authorisation maintenance and management.

Openness: Complete, routine disclosure at the end of a review makes the decision-making process less secretive and increases public confidence.

Disadvantages

Legal challenges: The availability of information to lawyers can fuel law suits

Resources: complying with requests for information under FOI laws, in response to 'crank' requests or to company competitors can be very time and resource consuming.

Responding to major safety Issues after marketing

There is obviously a greater obligation for transparency and making information available if a problem arises after a product has been approved and launched. In such circumstances a summary of the data on which the conclusions were based be made available as soon as possible.

Advantages

Risk tolerance: 'Active' transparency at this stage would provide an opportunity to consult with patient groups to ascertain their reaction to the potential and understand their tolerance to risk in the light of the benefits of the medicine.

Practical advice: Open communications on safety issues provides an opportunity to provide practical advice to physicians and patients on how they should react.

Disadvantages

Timing: The disadvantage of involving patient groups in the decision-making process is that this adds a time factor. There is no mechanism to put an urgent matter on 'hold' and agencies need to take action and to be seen to be responding rapidly.

WORKSHOP PROGRAMME

SESSION 1: IDENTIFYING BEST PRACTICES FROM DEVELOPMENT TO REVIEW	
Chairman's Introduction	Thomas Lönngren , <i>Executive Director, European Medicines Agency (EMA)</i>
Process or data? A company perspective on the keys to quality regulatory decisions	Dr Peter Bonne-Eriksen , <i>Senior Vice President, Regulatory Affairs, Novo Nordisk A/S, Denmark</i>
Building quality into the regulatory review	Andrea Mallia-Milanes , <i>Research Fellow, CMR International Institute for Regulatory Science</i>
The impact of transparency in improving quality and consistency of regulatory reviews	Caroline Vanneste , <i>Project Manager, Good Review Practices, Therapeutic Products Directorate, Health Canada</i>
Measuring industry and agency performance	Dr Neil McAuslane , <i>Director, CMR International Institute for Regulatory Science</i>
Discussant – Industry Perspective	Dr Paul Huckle , <i>Senior Vice President, US Regulatory Affairs, GlaxoSmithKline, US</i>
Discussant – Regulatory Perspective	Omer Boudreau , <i>Director General, Therapeutic Products Directorate, Health Canada</i>
SESSION 2: BENEFIT-RISK ASSESSMENT: A STRUCTURED APPROACH TO DECISION-MAKING	
Chairman's Introduction	Dr David Jefferys , <i>Vice President, Global Regulatory Affairs, Eisai R&D Company Ltd, UK</i>
Are there appropriate models available for a structured approach to benefit-risk decision-making?	Dr Filip Mussen , <i>Senior Director, Regulatory Affairs Europe, Merck Research Laboratories, Belgium</i>
What are the benefits of having a structured approach to benefit-risk decision-making in the registration process?	
Industry view	Robert Reynolds , <i>Executive Director/Global Head, Epidemiology, Pfizer Inc., USA</i>
Regulatory View	Dr Eric Abadie , <i>Vice Chairman, Committee for Human Medicinal Products (CHMP) EMA</i>
SESSION 3: SYNDICATE DISCUSSIONS -	
Chairman	Prof Sir Alasdair Breckenridge , <i>Chairman, Medicines and Healthcare Products Regulatory Agency (MHRA), UK</i>
How do companies make benefit-risk decisions during drug development?	Dr John Patterson , <i>Executive Director, Development, AstraZeneca Pharmaceuticals, UK</i>
Syndicate discussions and reports	<i>See report Part 2</i>
Does the patient have a role in healthcare decisions?	Mary Baker , <i>President, European Federation of Neurological Associations and Vice President of the European Brain Council</i>