

Government response to the UK Early Access to Medicines  
Scheme consultation – March 2014

## What is the Early Access to Medicines scheme?

### **Background**

On 5 December 2011 the Prime Minister announced a new *Strategy for UK Life Sciences*. The announcement was accompanied by a Department for Business, Innovation and Skills report which set out proposed activity to help ensure the continued success of life sciences in the UK. The publication detailed actions aimed at maintaining the UK's world-class reputation in life sciences, improving patient health and acting as a catalyst for economic growth.

One of these commitments was that ***the MHRA will bring forward for consultation proposals for a new 'Early Access Scheme'...***

The Strategy sets out the guiding principles for the Scheme as: ***“eligible products will be determined by a scientific opinion that the likely clinical benefits outweigh the risks identified to date where there is high unmet need; NHS funding for product must be cost effective; the UK economy should benefit from the scheme.”***<sup>1</sup>

The MHRA and DH joint public consultation ran from 13 July to 5 October 2012. There was broad support for the scheme in the consultation and we received 52 responses and advice from the Commission on Human Medicines. The Expert Group on innovation in the regulation of healthcare discussed the scheme at two of its meetings in 2013. **The Government Early Access Scheme proposal and response to questions asked in consultation are included in this document.**

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<sup>1</sup> <http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences>

## What is the Government's proposal?

### **Purpose of the scheme**

The purpose of the Early Access to Medicines Scheme (EAMS) is to support access in the UK to unlicensed or off-label medicines in areas of unmet medical need, thus enhancing the landscape for developing, licensing and procuring innovative medicines.

### **Aims of the scheme**

Early Access to Medicines is a scheme which:

- Addresses a public health need to improve access, on an unlicensed or off-label basis, to important innovative medicines for patients with life threatening or seriously debilitating conditions without adequate treatment options.
- Completes the landscape for early access to medicines which reflects the UK Life Sciences Strategy and NHS Innovation Health and Wealth reforms.
- Reflects the profound changes – driven by Genomics, Data, and the rise of Stratified and Personalised Medicines – transforming the drug discovery landscape away from the traditional 'blockbuster' model of the post-war years to the world of 'Translational' or 'Experimental' Medicine in which drugs are designed with and around patients, their data and tissues, in clinical research facilities and hospitals.
- Demonstrates a commitment from the UK to pharmaceutical innovation, through the Promising Innovative Medicine designation and earlier patient uptake of new innovative medicines in the health service.
- Encourages start-ups, patient groups and charities to collaborate within the extensive infrastructure via the National Institute for Health Research (NIHR) funded Clinical Research Facilities and Biomedical Research Centres and Units in leading NHS Trust/university partnerships.
- Is clearly distinguished from ideas being developed in relation to "adaptive licensing" which relates to the pro-active use of existing EU licensing flexibilities to gain an early marketing authorisation.

## How does the scheme work?

The Scheme will allow the UK to present a coherent landscape for a new model of fast-tracked medicines discovery and development based on an integrated pathway to facilitate and accelerate the development of innovative medicines, including stratified medicines, in three key stages.

## **STAGE 1: “PROMISING INNOVATIVE MEDICINE” DESIGNATION**

The most significant change following consultation will be the introduction of a new **“Promising Innovative Medicine” (PIM)** designation which provides an early indication that a product may be a possible candidate for the Early Access to Medicines Scheme (based on early clinical data for example from phase II studies). Designation could occur several years before licensing. The designation will be issued after a MHRA designation scientific meeting.

To support the PIM designation process the government is encouraging more interaction and collaborative working with the NHS through the National Institute for Health Research (NIHR) translational medicine infrastructure. This infrastructure supports industry access and collaboration with world-class expertise and facilities. Closer working with NIHR will support companies big and small understand the potential of their innovative medicines as they prepare for the PIM designation process.

Products that may apply for a designation include new biological or chemical entities but also re-purposing of established or recently approved drugs. The criteria are that the medicine is targeting life threatening, or seriously debilitating conditions which are either:

- Conditions for which there is no treatment, or
- Conditions for which the available treatment options are not satisfactory e.g. in the advanced cancer setting where the tumour is unresponsive to currently authorised medicinal products.

Alongside the PIM designation the Government recognises the need to provide developmental and scientific advice through earlier engagement with regulators. The MHRA’s scientific advice service and innovation office can be utilised to support the future later stages of development (e.g. advanced manufacturing issues, clinical trial design).

In addition, the MHRA and NICE will make available joint parallel scientific advice meetings in relation to clinical development programmes. These provide an important opportunity for early engagement with the quality, safety, and efficacy regulator and the health technology assessment body, in the latter case giving an understanding of how a company might best comply with subsequent appraisal requirements.

## **STAGE 2: AN “EARLY ACCESS TO MEDICINES” SCIENTIFIC OPINION**

The MHRA will issue a new benefit: risk scientific opinion that will support the prescriber to make a decision with the patient on using this medicine, when still unlicensed or used off-label.

The Government recognises that a clear route for earlier access is required following a PIM designation. This opinion could support access by patients to innovative medicines (outside of clinical trials) significantly earlier than the timeframes of the

normal drug development process – for instance, where compelling evidence exists, we envisage this opinion being potentially given on the basis of phase II studies instead of normally on the basis of phase III.

The MHRA will issue an opinion if the quality, safety and efficacy data provided in support of the application is sufficiently compelling for a positive benefit:risk balance and added clinical value. Information will be published on the MHRA website and, in addition, prescribers could be informed through stakeholder engagement with organisations such as the royal colleges and professional groups of specialists in the disease areas where opinions have been given. The MHRA is also considering the use of a number of alerting systems where healthcare professionals can sign up to receive an email alert for news items and the monthly bulletin Drug Safety Update for doctors and pharmacists.

The medicine will be made available free of charge by the company until the marketing authorisation is granted, after which it would be expected to be subject to standard NICE technology appraisal.

NHS England (or CCGs if relevant) would then act on the NICE guidance.

### **STAGE 3: LICENSING AND RAPID COMMISSIONING**

Complementing the designation and earlier access, a newly co-ordinated NICE technology appraisal and NHS England Commissioning process will be introduced by which:

- Once licensed, medicines which have been developed through the Early Access Scheme will be appraised by NICE for routine use on the basis of the evidence collected in the earlier stages of the Scheme.
- As part of the appraisal process, manufacturers would be able to make use of PPRS provisions for Flexible Pricing (or Patient Access Schemes) to adjust the value proposition for medicines, taking account of the value of:
  - The benefits of access and approval to the Sponsor.
  - The benefits of the innovative medicine to the patient and healthcare system.
- Medicines in the Early Access Scheme, once licensed, will typically be commissioned by NHS England through its specialised commissioning arrangements, delivering a single national approach to commissioning. NHSE has (like CCGs) a legal duty to fund technologies positively appraised by NICE within three months of publication.
- Academic Health Science Networks (AHSNs) will have significant potential to support this process.

## What are the key features of the Early Access to Medicines scheme?

- It will operate within the current regulatory structure and is voluntary and non-statutory.
- MHRA will provide a scientific opinion on promising new unlicensed or off-label medicines that will treat, diagnose or prevent life threatening or seriously debilitating conditions without adequate treatment options.
- The trigger for an Early Access to Medicines scientific opinion does not necessarily have to be the submission of a dossier for marketing authorisation application, but the availability of a sufficiently compelling case based on the total data and evidence collected to date as assessed by the MHRA.
- It is conditional on data from the development process of the product that indicates that the benefit:risk profile of the medicine is positive. The scheme will be limited to medicines representing a significant advance in treatment in an area of unmet need.
- The scientific opinion will describe the benefits and risks of the medicine, based on information submitted to the MHRA by the applicant.
- NICE will be involved at an earlier stage to advise on the health economics which inform commissioning and uptake decisions.
- The opinion will be made available on the MHRA's website to assist clinicians and patients in making treatment decisions, and to support informed consent by patients to the risks and benefits of the product as far as these have been identified in the development process for the product.
- NHS England's arrangements for clinical advice on medicines used in specialised commissioning will take into account the MHRA scientific opinion in guiding NHS prescribing practice for products given a positive assessment under the scheme. EAMS medicines will enter into clinical use in the same way as products under NHS England's Commissioning for Evaluation approach, and with the same objective of building the evidence base about the medicine.

## What does it mean for patients, clinicians, industry and the UK?

### **Clinicians and patients**

Patients will be able to access the next generation of breakthrough medicines before they are licensed and prescribers will have greater confidence in the safety and efficacy of prescribing designated products as the scientific evidence of their risk:benefit will be available to them earlier.

## **Industry**

A PIM designation provides an early indication that a product may be a possible candidate for the Early Access to Medicines Scheme. The granting of the PIM designation could be used to secure investment and could confer a greater degree of credibility on the products and companies involved. This is likely to be particularly important in the case of smaller companies. The introduction of the PIM designation means the Scheme will also have additional value to companies earlier in drug development, in a similar way to “Breakthrough Therapy” designation in the USA.

At the next stage of scientific review, the MHRA will consider the evidence and can issue an Early Access to Medicines scientific opinion. This opinion will support the prescriber to make a decision with the patient on using this medicine, when still unlicensed or used off-label. Provision of the product at no cost to the NHS will remove any financial barrier which might have inhibited patient access. Medicines which have been developed through the Early Access Scheme will, following granting of a marketing authorisation, be appraised by NICE for routine use on the basis of the evidence collected in the earlier stages of the Scheme. Other benefits to life science companies could include greater exposure to prescribers in the UK and the opportunity to collect real world data on the profile of the medicine.

Companies seeking to engage with the nation's experimental medicine infrastructure will be supported to find collaborators with leading-edge research expertise, world-class facilities and technologies and appropriate patient cohorts by the NIHR Office for Clinical Research Infrastructure (NOCRI).

## **The UK**

The scheme will provide a mechanism by which UK patients will be able to access the next generation of breakthrough medicines earlier than would have been the case had the company producing it waited for the granting of a marketing authorisation. Any potential economic benefit of the scheme is likely to be in the area of creating a new, positive signal to companies developing medicines that their products are likely to gain traction in the NHS market. This may in turn help those companies in gaining investment. It is conceivable that an early access scheme would make the UK a more attractive location for carrying out clinical trials. This will, alongside the NHS's comprehensive R&D infrastructure, including the data resource provided by the Clinical Practice Research Datalink, put the UK in a leading position globally for health life sciences.

### What are the next steps?

The Government intends to launch the scheme in April 2014. The MHRA intends to publish guidance to coincide with the launch of the scheme. Further information will become available on the MHRA website in due course.

## **Annex – Government response to questions in the UK Early Access to Medicines Scheme consultation**

### **1. Should a scheme be established?**

*Question 1: Do you consider that a scheme that makes available in the UK certain new medicines before they are granted a marketing authorisation (licence) will be of value to patients?*

The responses received expressed overwhelming support for a scheme.

In discussion with trade associations and patient groups following the close of the consultation, it was considered that a ‘designation’ step for promising candidates could be included in the scheme.

#### *Government response*

The Government therefore intends to introduce the Early Access to Medicines Scheme. The scheme supplements existing mechanisms for patients who are on a clinical trial to continue treatment after completion of the trial. The Government intends to introduce an additional designation step called the “Promising Innovative Medicine” (PIM) designation. This designation would be an early indication that a product may be a possible candidate for the EAMS.

### **2. Scope**

*Question 2: Do you have views about the scope of the proposed scheme (for example the type of illnesses and conditions that will be included)?*

A number of respondents said that medicines developed under the Orphan Drug scheme (Regulation (EC) 141/2000) should be eligible.

Some respondents said that MHRA should clarify what is meant by definitions such as “life threatening.”

Off-label medicines as well as unlicensed medicines were thought to be eligible for the scheme as this would permit repurposing of old drugs for new indications.

#### *Government response*

The Government confirms that products with an orphan designation and off-label supply of existing medicines would be eligible for the scheme, but only if they meet the other EAMS criteria as well, and this will be clarified in guidance to be issued by MHRA. Guidance is expected to be published to coincide with the launch of the scheme. Applications will be assessed on a case-by-case basis. MHRA does not want to set criteria that are too prescriptive, but will ensure that the scheme operates within existing law and eligible products fulfil unmet medical need.

Responsibility for human medicines legislation is not a devolved matter, but the provision of health services in Scotland, Wales and Northern Ireland is, and it will be

for the relevant authorities in these countries to decide on whether to participate in this scheme.

### **3. Number of products**

*Question 3: Do you consider that our assessment of the likely number of medicines per annum to which the scheme will apply is accurate? If not, why not? What do you consider might be a more accurate assessment of the number of medicines to which the scheme might apply?*

In the consultation, MHRA envisaged that around two products per year would be granted an opinion under the scheme. This was based on preliminary data from industry. However, several respondents to the consultation thought that there could be more (figures between 5-12 were cited).

#### *Government response*

The Government therefore confirms that there will not be a limit to the number of products that could be eligible for the scheme provided these meet the criteria set out.

### **4. Stage of development**

*Question 4: Do you have views on the proposed stage of development of a medicine that this scheme will be available?*

Most respondents considered that products will usually be eligible for the scientific opinion step of the scheme after Phase III clinical trials. This was because products will not usually have adequate clinical data on safety and efficacy before this point. Although this would often happen at the point of applying for an EMA licence under the centralised procedure, this could happen in advance on a case-by-case basis.

It was felt that certain medicines with exceptional data would be eligible for the scientific opinion step of the scheme after Phase II clinical trials on occasion on a case-by-case basis.

#### *Government response*

We propose no changes to this part. The MHRA will issue an opinion if the quality, safety and efficacy data provided in support of the application is sufficiently compelling for a positive benefit:risk balance and added clinical value. Where compelling evidence exists, we envisage this opinion being potentially given on the basis of phase II studies instead of normally on the basis of phase III.

### **5. Patient treatment if medicine fails to be granted a licence**

*Question 5: What do you think should happen to patients receiving treatment with a medicine under this scheme if the medicine subsequently fails to be granted a marketing authorisation?*

Predominantly responders thought decisions should be taken on a case-by- case basis by the clinician and patient (20 responses) and that where the patient was benefiting from the drug treatment should continue. There was discussion of exit strategies and several responses supported the continuing supply of the drug to those already receiving it. It was suggested that where possible prescribers should consider transfer to other treatments.

#### *Government response*

As for any medicine the clinician will be responsible for deciding when a patient starts and stops treatment. Even if a medicine does not gain a licence it can still be prescribed, provided that supplies are made available by the company. If safety issues about a drug in the scheme were to arise, MHRA would reconsider its opinion and if necessary publish updated information on the risk:benefit profile, amend or withdraw the scientific opinion and provide further guidance as appropriate through safety updates to health professionals.

## **6. Information requirements**

*Question 6: What information would patients, clinicians and other healthcare professionals want MHRA to publish on the website when a medicine is given an opinion under this scheme?*

*Question 7: What information about the medicine would be useful for MHRA to publish on the website for use by clinicians, other healthcare professionals and those making decisions about funding?*

*Question 18: What information (in addition to the scientific opinion - see question 6) would patients and clinicians find helpful in deciding about treatment with these medicines?*

*Question 19: How could such information best be presented?*

There was a clear focus in responses on providing the patient and healthcare professionals with as much information as possible presented in patient friendly terms, including on liability issues. Companies emphasised the importance of considering commercial confidentiality when making decisions about publication of data it had supplied to the regulator. There was support for MHRA and patient group websites/NHS Direct/other DH websites to signpost to increase patient awareness.

#### *Government response*

MHRA will publish the benefit/risk scientific opinion, stating how and why MHRA reached its decision. Further information will also be published in a 'treatment protocol' to assist prescribers and patients.

The patient education materials will be sufficient for physicians to use to obtain informed consent. They will make it clear that this product is not currently licensed (or is licensed for other indications), but has been made available under EAMS and that the MHRA has issued a favourable scientific opinion on its risk:benefit profile.

The materials should also provide an adequate summary of the current information available on the product, and the executive summary of the Risk Management Plan (RMP) may be used for this purpose.

Any other signposting could be done on a case-by-case basis so long as this was non-promotional.

## **7. Monitoring and surveillance**

*Question 8: How much will the impact of monitoring and surveillance arrangements influence your company's decision to use this scheme?*

*Question 9: Please estimate the cost per medicine of setting up a likely surveillance package and appropriate Risk Management Plan (RMP).*

*Question 10: We assume that as most of these medicines will go on to be licensed the need to develop a surveillance package and RMP will not be a critical factor in a decision to use this scheme. Is this correct? If not please explain why not.*

Respondents thought that disproportionate requirements could be a deterrent to applying. Many respondents pointed to the use of real-world and Clinical Practice Research Datalink (CPRD) data as an example of data that could mitigate this risk.

Costs of compliance varied from a ballpark estimate of £13,120 to £171K – £3 million over the lifecycle of a drug.

No voluntary or third sector organisations answered these questions.

### *Government response*

It will be important that there is a proportionate but robust surveillance package for the products eligible for and participating in the EAMS. We will put in place specific monitoring requirements including collection of some basic demographic information as well as safety information.

As with all unlicensed or off-label medicines, the products will be used on the professional responsibility of the prescriber (it is expected that most of these products will be used within hospital settings). Patients must be informed about the status of these products. Transparency over the safety profile will be key.

MHRA considers that early access applicants should set up similar pharmacovigilance arrangements they would have in place for a licensed medicine to ensure proper patient protection. This would involve a monitoring programme akin to a Risk Management Plan, and could likely include a registry of patients.

MHRA understands that companies would only choose to apply if an application was commercially viable. That said, pharmacovigilance is a necessary part of ensuring patient protection and requirements would be similar to those a company would be legally obliged to put in place on achieving a subsequent licence. Post-licensing, it would be likely that these requirements would continue with minimal disruption or

additional costs to the company. In evaluation, MHRA would ask companies what the actual surveillance costs of the EAMS were.

In answer to points raised in consultation:

- The MHRA will intensively monitor these products in the same way as for licensed medicines, and encourage professionals to report side effects of these medicines. Yellow Card reports are welcomed by MHRA on any medicine, licensed and unlicensed.
- MHRA consider that side effect reports during the early access period should be included in a subsequent marketing authorisation application in the interests of transparency and the principles set out in paragraphs 7 & 11 of the introduction to Annex I of directive 2001/83/EC (as amended).
- MHRA consider that “risks of the product identified to date” that have to be submitted with an Early Access application are those identified at date of application.
- The viability of CPRD data to minimize the need for conventional pharmacovigilance activity will depend on the capacity of CPRD (as it develops from being a primary care dataset) to be able increasingly to link to secondary care data. CPRD is still in the process of linking to other datasets so this is unlikely to be of benefit in the first year of operation of the scheme but this will be reviewed in due course.

## 8. Questions on funding

*Question 11: Please provide an assessment of which of the 5 options (a-e) you consider would be best able to meet the requirement that NHS funding must be cost effective, most likely to most likely to ensure equity of access for patients and most acceptable to stakeholders (especially industry, patients, the NHS, NICE).*

*Question 12: Are there other approaches that we could have included here? Please describe*

Responses to these questions were divided. Each of the options identified received some support, and no single option emerged as the preferred option. Some responders argued that none of the options identified would meet the specified criteria.

### *Government response*

The scheme as designed envisages medicines being provided at no charge by the company until the point of licensing. Although some stakeholders have suggested that a dedicated fund should be created to support payment by the NHS for medicines used within the scheme, they did not explain how the criterion that products must be cost-effective could be met without some form of assessment of cost-effectiveness, which as set out below, responses did not support. A fund would also be unwelcome to NHS England (who have made clear that they would not be happy to be charged for medicines prescribed under the scheme). The Government does not, therefore, intend to establish a dedicated fund in support of the scheme.

*Question 13: Please comment on the assumption that whilst the options that include an element of NICE review will incur costs, these will simply advance those costs as the information required will also be required for a later full NICE review.*

*Question 14: Can you quantify likely costs of the limited NICE reviews described here?*

A number of pharmaceutical industry responses stated that they did not support any NICE review at this stage. Overall, of those that answered these questions, the majority of responses took the view that there would be additional costs, for both companies and NICE, associated with any NICE review (i.e. these costs would not simply be advanced from a later full NICE review).

#### *Government response*

As set out above, the scheme as designed envisages medicines being provided at no charge by the company until the point of licensing. In this context, the Government has concluded that a limited NICE review of EAMS products at the stage MHRA issues its risk:benefit opinion is unlikely to add sufficient value to justify the associated costs. However the MHRA and NICE will make available joint parallel scientific advice meetings in relation to clinical development programmes. These provide an important opportunity for early engagement with the quality, safety, and efficacy regulator and the health technology assessment body, in the latter case giving an understanding of how a company might best comply with subsequent appraisal requirements.

## **9. Macroeconomic gains to the UK**

*Question 15: Which of the options described is most likely to meet the requirement that this scheme must deliver economic benefit for the UK?*

*Question 16: Can you provide details of any other approaches that could be considered?*

*Question 17: Do you have any comments on the assumptions made in these options?*

There was no clear consensus in responses to these questions. Of the options identified, option b (scheme available as real world arm of phase III clinical trials) received the most support, though a number of responses expressed the view that none of the options would deliver economic benefits.

#### *Government response*

The scheme will provide a mechanism by which UK patients will be able to access the next generation of breakthrough medicines earlier than would have been the case had the company producing it waited for the granting of a marketing authorisation. Any potential economic benefit of the scheme is likely to be in the area of creating a new, positive signal to companies developing medicines that their products are likely to gain traction in the NHS market. This may in turn help those companies in gaining investment. It is conceivable that an early access scheme

would make the UK a more attractive location for carrying out clinical trials. This will, alongside the NHS's comprehensive R&D infrastructure, including the data resource provided by the Clinical Practice Research Datalink, put the UK in a leading position globally for health life sciences.

## 10. Fees

*Question 20: Do you have any comments on the proposed charges under this scheme?*

8 respondents thought the fee level acceptable, although 3 commented that it should more closely match the Clinical Trials Application fee. One suggested the fee should be deducted from the subsequent MA application fee. 5 respondents thought the initial fee was too high. 5 also thought the renewal fee should be lower.

### *Government response*

The fee has been set at a cost recovery level and we propose no changes to this part of the proposal.

## 11. Other questions

*Question 21: What do you think will be the most likely constraints in uptake of this scheme (eg bureaucracy, uncertain NHS uptake, cost of the medicines)?*

Several respondents cited multiple reasons which may act as constraints on uptake of the proposed scheme. Uncertain funding & uncertainty about whether the NHS would purchase the drugs were the most common comments. Administrative burden was cited by 8 respondents, but other comments included: publication of a negative opinion would deter investors, fears that MHRA may publish commercially confidential material, liability issues & patient safety issues.

### *Government response*

Complementing the designation and earlier access, a newly-coordinated NICE technology appraisal and NHS England Commissioning process by which:

- Once licensed, medicines which have been developed through the Early Access Scheme will be appraised by NICE for routine use on the basis of the evidence collected in the earlier stages of the Scheme.
- As part of the appraisal process, manufacturers would be able to make use of PPRS provisions for Flexible Pricing (or Patient Access Schemes) to adjust the value proposition for medicines, taking account of the value of:
  - o The benefits of access and approval to the Sponsor.
  - o The benefits of the innovative medicine to the patient and healthcare system.
- Medicines in the Early Access Scheme, once licensed, will typically be commissioned by NHS England through its specialised commissioning arrangements, delivering a single national approach to commissioning. NHSE

has (like CCGs) a legal duty to fund technologies positively appraised by NICE within three months of publication.

- Academic Health Science Networks (AHSNs) will have significant potential to support this process.

*Question 22: Is this scheme likely to be more or less attractive than other schemes that currently offer early access to medicines*

Responses were mixed. 7 respondents thought the scheme would be more attractive than others available.

#### *Government response*

No modification to the scheme is proposed as we believe this scheme can be accommodated and would benefit public health. We will monitor its attractiveness in evaluation of uptake of the scheme.

*Question 23: We understand that schemes in the US that offer early access to medicines are used more extensively than those available in the EU. Is this correct and if so why?*

Those who commented mostly referred to the US system for pricing and reimbursement of medicines as the likely reason for the positive uptake.

#### *Government response*

The comments are noted but did not offer sufficient insight to suggest practical modifications to the scheme.

*Question 24: Do you have any further comments to the content of the scheme that have not been addressed by your previous answers?*

#### *Government response*

Comments made have been considered in answers to previous questions in this document.

*Question 25: Can you identify any costs to your business that might arise as a result of these proposals, particularly administrative and policy or compliance burdens? We would particularly like to hear from you if you can identify an impact upon small businesses.*

Comments included shipment costs for the drug, and maintaining a delivery platform, project management costs, costs to Medical Information Departments. Packaging requirements, costs of adapting HTA requirements, costs of establishing and maintaining patient registries, developing Risk Management Plans for the UK scheme, dealing with ADRs that occur.

#### *Government response*

The comments are noted but no modification to the scheme is proposed as we believe some transitional costs and those arising from mandatory requirements are inevitable. We will discuss further with trade associations to see if any administration burdens can be reduced.

*Question 26: We believe that no small pharmaceutical companies will be attracted to participate in the Early Access Scheme because, as a minimum, these companies would have to have financed Phase II clinical trials, and this suggests that their annual turnover would be higher than the £6.5 million threshold below which companies are classified as “small”. Please comment on our assumption here.*

Most did not comment but those that did said the scheme should be designed to be attractive to all companies.

*Government response*

Discussions with trade associations have indicated that the scheme as designed will be attractive to some, and the new designation step might assist SMEs secure investment.