

A review supported by the  
Better Regulation Executive  
and National Audit Office

# Medicines and Healthcare products Regulatory Agency:

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A Hampton Implementation Review Report



## Foreword

Philip Hampton's report: Reducing administrative burdens: effective inspection and enforcement, published in 2005, is one of the cornerstones of the government's better regulation agenda. The principles of effective inspection and enforcement set out in the report, putting risk assessment at the heart of regulatory activity, are designed to encourage a modern regulatory system which properly balances protection and prosperity. Since 2005, the Government has established an expectation that regulators will embed these principles in their approach to regulation.

In November 2006, the Chancellor of the Exchequer invited the National Audit Office and the Better Regulation Executive to develop a process of external review to assess how much progress regulators had made in implementing the principles of Hampton.

"Hampton Implementation Reports" covering the work of five major regulators were published in March 2008. The review process is continuing. At this point in the cycle we are publishing the results of reviews of three regulators, each of which has a significant impact on their specific economic sectors. Together, the Gambling Commission, the Medicines and Healthcare products Regulatory Agency, and the Animal Health agency cover a wide range of economic activity, and work to protect our interests. How they carry out their regulatory activities matters.

Full implementation of Philip Hampton's recommendations is a journey that could take several years. This review is a 'snapshot' in time of the progress of each regulator towards his vision.

Each of the reviews found examples of innovation and initiative by regulators who continue to move the regulatory agenda forward, as well as areas for further improvement.

The assessments were carried out by teams of reviewers with wide ranging experience and expertise in the field of regulation. Talking to a wide range of stakeholders, to staff at all levels within the regulator's organisation, through visits to business sites and analysis of data and papers, the review teams have reached the findings and conclusions set out in this report. The reports reflect the judgement of these review teams on the basis of the evidence put before them.

We would like to thank all of those who have continued to make these reviews a success. In particular, we are grateful to the regulators and their staff for providing support and making evidence available to the review teams, and to all the organisations that generously gave their time to offer evidence to the reviews. Finally, we are extremely grateful to all our reviewers, and their employers, for their involvement, enthusiasm and commitment to this project.



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## Summary and conclusions

This review is one of a series of reviews of regulatory bodies undertaken at the invitation of HM Treasury and focusing on the assessment of regulatory performance against the Hampton principles and Macrory characteristics of effective inspection and enforcement. It was carried out by a team drawn from the Better Regulation Executive (BRE), the National Audit Office (NAO), the Human Fertilisation and Embryology Authority (HFEA) and the National Consumer Council supported by staff from the BRE (see Appendix 1 for Review Team membership).

The Hampton report<sup>1</sup>, published in 2005, is one of the cornerstones of the government's better regulation agenda and regulators have been working since then to embed his principles in their approach to regulation. This review process is designed to identify where a regulator is on the road to full implementation and the issues each needs to address to become Hampton-compliant.

The Review Team is grateful to the Medicines and Healthcare products Regulatory Agency (MHRA) for its support during the Review period; staff working at every level in the MHRA were very open to the Review process and were generous with their time, experience and expertise. We are also grateful for the contribution of the Agency's stakeholders for their helpful insights into the nature of the industries and the wider contexts within which the MHRA operates.

## What we found

The Review Team concluded that in most of the areas under review, the behaviours and the instincts of the MHRA are highly Hampton compliant. Whilst the overall culture is 'Hampton-like', full Hampton compliance

remains a target for the organisation. We were impressed by the MHRA's achievements, direction of travel and its plans for improving its regulatory performance still further. We feel that the MHRA is a confident, transparent, and risk-aware organisation that has an outcome framework that is well understood across the organisation. Areas to develop include: its internal capacity for quantifying regulatory costs; formalising its risk-based approach; being more aware of the risk of 'gold plating' the implementation of EU regulation; the need to communicate reasons for its decisions; and fine-tuning its use of IT systems.

- **The MHRA has a cadre of highly professional staff who understand the sector and its risks well.** Better regulation appears to be an aim from the top-down as well as from the bottom-up of the organisation.
- **The MHRA is very effective at negotiating at the European level –** and is a thought leader in European negotiations.
- **The MHRA operates as a joined-up organisation.** The extent of interaction across the MHRA is impressive, and the large number of potential 'silos' that could exist are apparently avoided. A good example of this is the way in which European negotiations are conducted by the Agency. MHRA brings a strong grasp of implementation issues to its discussion of policy with European counterparts.
- **The MHRA generally understands its regulated sector and the economic impact of its regulation –** although its capacity for assessing and quantifying the costs of regulation could be improved.

<sup>1</sup> Reducing administrative burdens: effective inspection and enforcement, Philip Hampton, HM Treasury, March 2005

- **The MHRA is highly focused on its objective of protecting public health** – and this is understood throughout the organisation, as well as by stakeholders
- **The MHRA generally consults extensively with external stakeholders** – however on some occasions it could consult and communicate more fully. This would, if nothing else, clarify the Agency's position
- **The MHRA is developing a risk-based approach to inspection** – and this will build on the already strong understanding of risk within the organisation
- **The MHRA is self-aware and we saw good evidence of a learning organisation.** It has built on lessons learned from major projects such as Sentinel and sunset clauses. We would encourage this to continue.
- **The MHRA is developing strong approaches to simplifying medicines regulation in some areas.** The Better Regulation of Medicines Initiative (BROMI) has won an international award as a model of better regulation policy making, although the Review Team believes it could go further.

## Issues for follow-up

The following table sets out the key issues that the Review Team believes the MHRA needs to address to meet the Hampton criteria more

fully, measured against some of the symptoms<sup>2</sup> we were looking for to provide evidence of Hampton compliance.

Issue to be addressed	Hampton symptom
<p><b>Improving the MHRA's understanding of the economic implications of its activities.</b></p> <p>Whilst the MHRA has developed some good examples of impact assessments, it currently relies upon the Department of Health's economists to provide specific input into its cost-benefit analyses.</p> <p>We believe that the MHRA should strengthen the robustness of its impact assessments, and look to ensure that the importance of cost-benefit analysis is embedded throughout the organisation.</p> <p>More widely, we believe that there is scope for the MHRA to develop greater awareness of the economic implications of its decision making, and to streamline processes for business. We comment in this report on some relatively low risk cases where the MHRA could do more to take account of the sector's practical business needs.</p>	<ul style="list-style-type: none"> <li>The regulator undertakes robust cost-benefit analysis and impact assessments.</li> </ul>
<p><b>Gold plating</b></p> <p>The Review Team heard some stakeholders' views that there had been cases where there had been 'gold plating' going beyond the minimum legal requirements when implementing EU regulation.</p> <p>The Review Team found that these had some substance. This is particularly clear on the 'labelling and package leaflet regulations' where the MHRA chose to implement the requirement early and with additional retrospective application.</p> <p>While we do not question the rationale behind the Agency's decision in this case, we think it should be more aware of the impact that additional national legislative barriers can have over and above an agreed European approach. In these cases it should consider the need for an enhanced level of communication, particularly in order to make the reasons for its approach clear to industry.</p>	<ul style="list-style-type: none"> <li>Regulation has a clearly-defined purpose, is considered to be well designed, proportionate, effective at achieving outcomes and understood by business and enforcers.</li> </ul>

<sup>2</sup> From Hampton Implementation Reviews: Guidance for Review Teams, National Audit Office and Better Regulation Executive, July 2008

Issue to be addressed	Hampton symptom
<p><b>Improving the credibility and usage of the Sentinel IT system</b></p> <p>The MHRA's cross-Agency IT system (Sentinel) is now in place and working, but questions remain about the credibility of the system amongst industry - part of this relates to ensuring that the historical data stored on the system is accurate.</p> <p>The MHRA also needs to communicate and work with the industry to ensure that use of the system is increased. The Review Team sees this as a two-way process: listening to businesses about their needs as well as helping them improve their understanding of the system and its requirements.</p>	<ul style="list-style-type: none"> <li>• The regulator makes good use of IT solutions in data collection and provides alternatives to paper forms</li> </ul>
<p><b>Formulation and systematisation of the Agency's awareness and understanding of risk in relation to inspection.</b></p> <p>We recognise that the MHRA is constrained in developing a fully risk-based inspection approach.</p> <p>Some inspection cycles are prescribed by European legislation. Within these constraints we would strongly encourage and support the development of a more risk-based approach to inspection.</p>	<ul style="list-style-type: none"> <li>• The regulator focuses its greatest inspection effort on businesses where an explicit risk assessment shows that both:             <ul style="list-style-type: none"> <li>– There is a likelihood of non-compliance by business; and</li> <li>– The potential impact of non-compliance is high.</li> </ul> </li> </ul>

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## Introduction

- 1 This review of the Medicines and Healthcare products Regulatory Agency (MHRA) aims to provide a structured check on performance against the principles<sup>3</sup> and characteristics set out in the Hampton and Macrory reports (see Appendix 2).<sup>4</sup> The team reviewed the MHRA against a performance framework<sup>5</sup> developed by the BRE and the NAO which provided a guide for reviewers on the kind of evidence to look for and questions to consider. However, the process is not the same in scope or depth as a full value for money audit of economy, efficiency and effectiveness and the Review Team's conclusions are based on a combination of evidence and judgement. A brief description of the scope of the review and methods employed is at Appendix 3.
- 2 The MHRA was established on 01 April 2003, following the merger of the Medicines Control Agency and Medical Devices Agency. It is an Executive Agency of the Department of Health and the Secretary of State for Health has overall responsibility for the MHRA but is not involved in the day-to-day running of the Agency.
- 3 The MHRA's mission is to enhance and safeguard public health by ensuring that medicines and medical devices work and are acceptably safe. The MHRA also regulates tissue engineered products and blood products.
- 4 The MHRA is responsible solely for the quality and safety of medicines and medical devices. It does not make decisions on the cost effectiveness of products and consequently whether they are used by the NHS – the National Institute for Health and Clinical Excellence (NICE) has this responsibility. Equally, it is not responsible for regulating the markets for pharmaceuticals and medical devices. This rests with the Department of Health which governs the price that the NHS pays for the drugs that it uses through the Pharmaceutical Price Regulation Scheme (PPRS).
- 5 The MHRA was established as a trading fund. As such, it receives no central funding for its medicines-based activities. It must cover its costs through the fees that it charges for its services, such as assessing applications for licenses to market medicines or approvals for clinical trials. This means it operates along broadly commercial lines. Devices-based activities are funded centrally, through the Department of Health. In 2007-08, its total costs were £89.6 million and its income £93.5 million. The average number of staff employed by the MHRA in 2007-08 was 875 (full-time equivalent).
- 6 The pharmaceutical industry is of great economic significance in the UK. Expenditure on medicines accounted for 0.85% of UK GDP in 2007, with exports totalling £14.5 billion and a trade surplus of £4.3 billion. It is the biggest investor in research and development – £4.2 billion in 2007 – and 15 of the leading 75 medicines internationally were developed in the UK, more than any other country except the US. It employs 73,000 people, 28,000 of whom are in Research & Development and generates another 250,000 jobs in related industries<sup>6</sup>.
- 7 The medical devices sector is also highly important: in 2006 the UK devices sector included around 1,500 enterprises manufacturing medical and surgical

<sup>3</sup> Reducing administrative burdens: effective inspection and enforcement, Philip Hampton, HM Treasury, March 2005

<sup>4</sup> Regulatory Justice: making sanctions effective, Final report, Professor Richard B Macrory, November 2006

<sup>5</sup> Hampton Implementation Reviews: Guidance for Review Teams, National Audit Office and Better Regulation Executive, July 2008

<sup>6</sup> Source: Association of the British Pharmaceutical Industry and BERR websites

equipment and orthopaedic appliances, of which approximately 70% were small or medium sized enterprises. Manufacturers in the sector employed around 33,000 people in 2006 (excluding single operators)

and overall turnover was in the region of £4.3 billion. The overall size of the UK market for medical devices (excluding in vitro diagnostic devices) is valued in excess of £7.2 billion.

## The Hampton vision

- 8** Both the Hampton and Macrory reports are concerned with effective regulation – achieving regulatory outcomes in a way that minimises the burdens imposed on business. Key to this is the notion that regulators should be risk-based and proportionate in their decision-making, transparent and accountable for their actions and should recognise their role in encouraging economic progress.

### Risk-based

- 9** The Review Team found that the MHRA has a strong spontaneous understanding of risk amongst its staff and this has been built into relatively new areas of regulatory responsibility such as Pharmacovigilance and Clinical Trials, especially in relation to inspection planning. On the medical devices side, all EU medical devices Directives are inherently risk-based in terms of the required assessment process.
- 10** Corporately, the MHRA appears to be prepared to take managed risks that support its focus on public health outcomes. For example it has taken a risk in allowing self-certification of low-risk medicines licence variations (such as packaging changes) and also on its approach to new herbal medicines regulation. However the Review Team found that this could perhaps go further, and had been let down by failures of administration, which had been seen in some cases to have made the process more, rather than less, burdensome.
- 11** Stakeholders have on occasion accused the MHRA of being risk-averse in its decision making, for example in relation to restricting the supply of over-the-counter medicines containing pseudoephedrine. The MHRA can, at times, appear to be closer to a precautionary than a truly risk-based approach. A key point here is for the MHRA to articulate its thinking about risk more coherently and communicate this to industry more effectively.
- 12** We believe that more rigorous use of impact assessment would enable the MHRA to test its assumptions with stakeholders more fully and thereby ensure they achieve greater credibility for its proposals. Highlighting the costs and benefits of a proposed course of regulatory action in this way can provide robust justification to industry.
- 13** We believe that the MHRA is going in the right direction, for example graduating its approach in relation to risk in the area of medicines regulation with its Better Regulation of Medicines Initiative (BROMI). However, there are issues for the future where stakeholders will rightly expect a proportionate approach to implementation of new requirements such as Braille labelling on medicines.
- 14** The MHRA is currently developing a new risk-based system for inspection, and is conducting pilots with industry to inform this work. This is building on a strong understanding within the MHRA of the risk presented by specific businesses and their operations. This process is being taken forward thoughtfully and transparently. Inspections of devices manufacturers already follow a risk-based approach.
- 15** We welcome the systematisation of the MHRA's approach to risk in relation to inspection. However, we recognise that MHRA is constrained in some areas by inspection frequencies set by European legislation.
- 16** We also found that risk-based thinking was put to good use in areas other than inspections. For example, the MHRA used a

formal risk-assessment framework in prioritising and deciding the level of its formal enforcement action.

We found:

- **A strong, spontaneous understanding of risk amongst staff.**
- **A good direction of travel on developing a risk-based approach to inspection.**

## Transparency and Accountability

- 17 Generally, we consider the MHRA to be a transparent organisation in terms of the information it publishes.
- 18 The main issue for the MHRA in improving transparency is to be clearer and more open about its rationale for decisions made and the communication of these to industry and the public. A good example here would be regarding the communication of its work on user-testing, where there was a perception of 'gold plating'.
- 19 There is also a need for more transparency in some specific areas such as the enforcement strategy, and we welcome proposals to work up and publish this.
- 20 There are some industry concerns regarding the transparency of the Agency's Marketing Authorisation approvals system, with no redress for lengthy delays in processing applications and a perceived lack of awareness of the impact of this on business planning cycles. In addition, aspects of its website layout and functionality can hinder efficient access by stakeholders and the public to the information they seek.

**We concluded that, on the whole, the MHRA is transparent and accountable – however it could improve the transparency of its approvals system.**

## Economic progress

- 21 Regulators can have a significant impact on the economic conditions under which regulated businesses operate. This is recognised by the statutory Code of Practice for Regulators (the "Regulators' Compliance Code") which states that "Regulators should recognise that a key element of their activity will be to allow, or even encourage, economic progress and only to intervene where there is a case for protection"<sup>7</sup>. This requires regulations and their enforcement to be proportionate to the potential for harm and that regulators should be aware of their influence on economic progress.
- 22 The MHRA has a strong understanding of an industry with many different sectors and with different business models, particularly amongst front-line staff such as inspectors. We were impressed with the understanding of SMEs, for instance, in the devices sector; the MHRA was responsive to their needs for guidance on specific issues. In one case the industry identified the need for more guidance on the regulations applying to first aid kits, and the MHRA worked with them to fill this gap.
- 23 The MHRA has also clearly taken seriously its role in supporting the industry with regard to the new Herbal Medicines Directive. This is discussed more fully in the Design of Regulations section.
- 24 However, we found that the MHRA can on occasion:

<sup>7</sup> Regulators' Compliance Code: Statutory Code of Practice for Regulators, BERR, 2007, p11

- take insufficient account of costs where it believes there is an important public health issue at stake;
- neglect deadlines for processing licences that have an impact on companies' commercial interests.

- 25** The MHRA should try and communicate reasons for its actions, and show that it understands the particular sector or regulated bodies it is dealing with.

**We found that the MHRA recognises its role as a regulator in encouraging economic progress although this has been overridden from time to time on public health grounds. We recognise that this can be the right course of action; the MHRA should not be afraid to be explicit about its reasons on these occasions.**

## Design of regulations

### Hampton principles

*“All regulations should be written so that they are easily understood, easily implemented, and easily enforced, and all parties should be consulted when they are being drafted”*

*“When new policies are being developed, explicit consideration should be given to how they can be enforced using existing systems and data to minimise the administrative burden imposed”*

## Key findings

- The MHRA shows outstanding leadership in Europe and European negotiation.
- The MHRA’s capacity for modelling the economic impact of its regulatory actions should be improved.
- The MHRA should be aware that it has on occasion ‘gold-plated’ European regulation.
- The MHRA generally consults well with external stakeholders regarding legislation, however it should ensure that it consults equally well when developing guidance.
- The MHRA tries to take account of the impact of new regulation on business, however in the case of herbal medicines we would encourage the MHRA to undertake post-implementation review

## Background

- 26** The regulatory regime for pharmaceuticals is largely based on the Medicines Act 1968, which brought most previous legislation on medicines together and also introduced a number of other legal provisions for the control of medicines.
- 27** Medicines regulation today is largely based on European legislation and, subsequently, the Medicines Act has been amended to bring it into line with revisions to the EU regulatory regime. The current relevant legislation is given in Directive 2001/83/EC relating to medicinal products for human use, amended by Directives 2002/98/EC, 2003/63/EC, 2004/24/EC and 2004/27/EC.
- 28** Additionally, the MHRA has responsibility for implementing and ensuring compliance with other stand-alone pieces of EU

legislation. Recent examples have included legislation in clinical trials, advance therapy medicinal products and paediatric medicines.

### Medicines

- 29** EU rules set out the respective competences of national regulators and the European Medicines Agency (EMA) in relation to the regulatory framework for medicinal products. There are four possible methods of obtaining a marketing authorisation for a pharmaceutical product:

**1 Centralised authorisation procedure:** the European Medicines Agency (EMA) is responsible for this, and it is valid across the EU. It is mandatory for medicines that are:

- derived from biological processes, such as genetic engineering;
- intended for the treatment of HIV/AIDS,

- cancer, diabetes, neurodegenerative disorders or auto-immune diseases and other immune dysfunctions;
- officially designated “orphan medicines” (i.e. medicines used for rare diseases – there is specific EU regulation to encourage the development of more orphan medicines, which are expensive to develop, but for which the market is limited).

Medicines outside these categories may be submitted to the EMEA for approval, providing the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorisation would be in the interest of public health.

**2 National authorisation procedures:** That is, seeking authorisation for other products not covered by the centralised procedure through only one National Competent Authority (such as the MHRA or the equivalent bodies in other EU member states).

**3 Decentralised procedure:** Companies may apply for simultaneous authorisation in more than one EU country of medicinal products that have not yet been authorised anywhere in the EU and that do not fall within the centralised procedure by appointing one Member State as the Reference Member State.

**4 Mutual recognition procedure:** Gaining approval for a medicinal product in one Member State, then subsequently applying for marketing authorisations in other Member States, whereby the countries concerned agree to recognise the validity of the original national authorisation.

- 30** The respective roles of the EMEA and national regulators vary in other areas. National regulators are responsible for implementation and enforcement of clinical

trials<sup>8</sup> and medical devices regulation, while the EMEA is responsible for approving Paediatric Investigation Plans. The MHRA granted around 4,000 marketing authorisations in 2007-08.

## Medical Devices

- 31** Regulation of medical devices is similarly based on EU legislation. The original EU Medical Devices Directive dates from 1994 and has been revised on a number of occasions subsequently. Devices are also regulated by UK legislation implementing the General Product Safety Directive. The UK regulations implementing the EU Directives are made under the Consumer Protection Act.

- 32** The regulatory regime for the medical devices sector is more ‘light touch’ than is the case for medicines. Many low risk products – e.g. hospital beds – can be placed on the market once the manufacturer has self-certified compliance with the regulatory requirements and notified the MHRA.

## Review Findings

### The MHRA shows outstanding leadership in Europe and European negotiation

- 33** The MHRA is focused on the outcomes it wants to achieve and is a ‘thought leader’ in European negotiations. Its work is thought of highly and it ensures that it takes a lead and drives activity across the EU in relation to both medicines and devices regulation.
- 34** Stakeholder comments on the work of the MHRA in Europe were extremely positive. The MHRA was cited as one of the two best regulatory bodies in the pharmaceutical sector in the world, and one stakeholder group recognised that the MHRA ‘bats for UK plc’ when securing the right outcomes for business.

<sup>8</sup> Although the EMEA is responsible for maintaining a database of clinical trials conducted



### **The MHRA's capacity for modelling the economic impact of its regulatory actions should be improved**

- 35** The MHRA's work in assessing the costs and benefits of its activity on the regulated community, particularly around the Impact Assessment process, is an area we have identified for development. The Review Team saw some very good examples of Impact Assessments that had been conducted, such as the Traditional Herbal Medicines Directive Impact Assessment which received good feedback from the National Audit Office in its 2006-07 Evaluation of Regulatory Impact Assessments.
- 36** However, a robust approach to Impact Assessment did not always appear to be taken as a matter of course. The MHRA uses Department of Health economists for specific economic expertise and input, and the Review Team considers that a lack of in-house economic expertise may be a weakness for the MHRA, and we would encourage moves to recruit an economist to help with its assessments.

### **The MHRA should be aware that it has on occasion 'gold-plated' European regulation**

- 37** Industry stakeholders that we interviewed were concerned that the MHRA has interpreted new EU rules on "user testing" of patient information leaflets more strictly than other member states. Whilst the relevant Directive did not require it, the MHRA decided to make this requirement retrospective and industry has had to test all existing patient information leaflets, not just new ones. Additionally, the MHRA has asked companies to provide detailed information on how they have gone about user testing. Industry argued that this significantly increased the administrative burden of the regulations.

- 38** This example is a clear instance of 'gold plating', where implementation of EU rules nationally goes beyond the minimum requirements agreed in Europe. The UK rules were implemented early and made retrospective, two elements that went above and beyond minimum European requirements.
- 39** Whilst we understand the MHRA's rationale for this action – to improve public health outcomes – the Review Team believes that the MHRA could have better communicated its rationale for its action in this case to industry. The MHRA consulted on this issue, but we believe that it could have done more to communicate the impact of its decision: in particular, by working much more closely with industry to understand the cost and economic impact of the decision.

### **The MHRA generally consults well with external stakeholders regarding legislation, however it should ensure that it consults equally well when developing guidance**

- 40** The MHRA generally consults well with a wide range of stakeholders, for example through its Regulatory Forum (see box below). It also consulted on the implementation of the last review of EU medicines legislation (Directive 2001/83) through a network of industry representatives.
- 41** However, we found some examples of failing to consult on the substantive body of new guidance, for example the new pharmacovigilance 'purple guide' will be published by the MHRA with little or no stakeholder input to the substantive content. Whilst the MHRA argues that this is a best practice guide, they should be aware that from an industry perspective this can have the same impact as additional regulation.



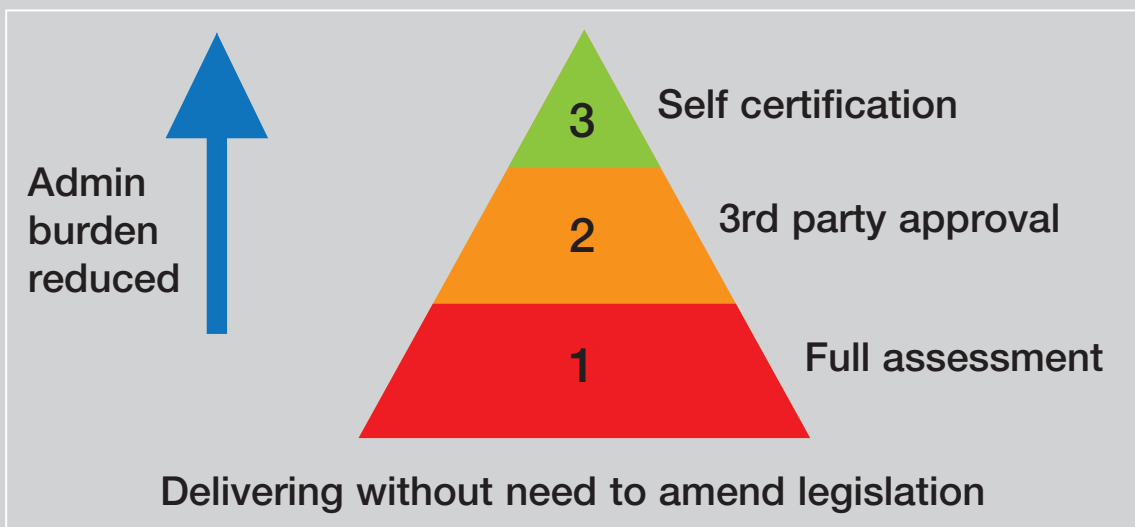
### Good Practice – BROMI

The Medicines and Healthcare products Regulatory Agency's Better Regulation of Medicines Initiative (BROMI) has won an international award as a model of better regulation policy making.

The Agency has introduced a system of self-certification by the pharmaceutical industry for simple changes to product

labelling and information. It is intended to allow a transition to self- and third party certification in low risk areas of medicines regulation. This saves unnecessary bureaucracy as companies no longer have to apply for formal approval from the Agency and can place products on the market more quickly.

This has been achieved without the need to amend legislation.



### The MHRA tries to take account of the impact of new regulation on business, however in the case of herbal medicines we would encourage the MHRA to undertake post-implementation review

- 42 The MHRA was responsible during 2002-05 for negotiating and implementing an EU Directive on Traditional Herbal Medicinal Products. Prior to this, although there had been some licensed herbal medicines, the UK market was dominated by the unlicensed sector. There was evidence that consumers were at risk from harmful products, reflecting the erratic and

sometimes low standards in parts of the unlicensed sector. The Directive required each EU Member State to introduce a simplified registration scheme in which over-the-counter traditional herbal medicines must meet standards of safety, quality and patient information and are permitted to make agreed minor claims on the basis of evidence of traditional use. The MHRA developed an approach aimed at ensuring a 'light-touch' regulatory regime for registered products which are demonstrably safe and have plausible efficacy, whilst enabling the MHRA to keep potentially unsafe products off the market.

- 43** The MHRA approach to applying the regulatory standards required by the Directive was tempered with pragmatism where this was possible. Additionally, given the inexperience of the sector with regulation, the MHRA instigated an extensive programme of help and advice, free of charge, including meetings at the Agency.
- 44** We understand that the MHRA is trying to regulate in a previously unregulated area and we commend the Agency's approach in many ways – in particular its concern to assist industry through this new legislative process. The MHRA has taken a decisive step forward in this area.
- 45** We had questioned whether the MHRA had gone slightly too far in regulatory support of the herbal industry in this specific instance. The MHRA provided us with further evidence on this point and we agree that they are investing support upfront for the herbal industry given that this is a major step-change for them moving into a systematic regulatory regime.
- 46** However, we believe that this level of support should not last and the industry has a responsibility to organise itself better. The MHRA needs to plan for a transition to a more formal regulatory relationship as the implementation date of 2011 approaches. MHRA recognises the need to keep the amount of help offered to industry under review, and in particular the extent to which regulatory meetings on the traditional herbal registration scheme are offered free of charge to companies.

### **Good Practice – Regulatory Forum**

The MHRA has established a Regulatory Forum, drawn from the pharmaceutical industry, healthcare professionals, patients' representatives and lay people. This body meets regularly to advise the Agency on the development of new policies and strategies in relation to medicines, particularly in terms of responding to new technologies. The MHRA has recently adopted the same approach in relation to medical devices.

- 47** We would welcome the MHRA analysing the impact of the herbal medicines legislation following implementation and ensuring it adequately meets its goal of public protection. As noted later in this report (paragraph 114), we recognise the difficulty in identifying and measuring outcomes for the Agency. The MHRA has successfully identified proxy measures for other workstreams however, and we would encourage a similar approach in this case.

## Advice and guidance

### Hampton principle

***“Regulators should provide authoritative, accessible advice easily and cheaply.”***

## Key findings

- The MHRA has a good range of contact channels, which it supplements with external engagement events.
- The MHRA is developing systems to facilitate better sharing of information across the Agency.
- The potential of the MHRA website is currently not being maximised as a communications tool in terms of layout and usability.
- MHRA guidance is, on the whole, extensive and issued in good time although it could be ‘road tested’ better in some cases.
- The perception and credibility of the MHRA’s approach towards better regulation can be hampered by occasional miscommunication.

## Background

- 48** The MHRA has a number of well-established mechanisms for cascading regulatory guidance and advice to its stakeholders. These include Guidance Notes and Directives Bulletins which advise industry on how to comply with regulation (e.g. changes to EU regulation, how to apply for a marketing authorisation or approval to conduct a clinical trial).
- 49** Likewise there are arrangements in place to ensure that healthcare professionals are made aware of safety issues which are reported to the Agency, such as drug alerts or “Dear Healthcare Professional” letters. These are sent electronically using an established distribution list and then cascaded by recipients. There is also a monthly electronic bulletin for healthcare professionals, “Drug Safety Update” which contains latest advice from the MHRA and the Committee on Human Medicines on safety issues.
- 50** The MHRA publishes new regulatory and safety guidance without charge on a fairly regular basis. Guidance can be either of a technical nature, or for use by patients, such as leaflets on how to report concerns on the safety of medicines or devices. Some of the MHRA’s communication material has been approved by the Plain English Campaign. The MHRA does not charge for such written guidance.
- 51** The MHRA publishes a large amount of information on its website and it also has telephone and email central enquiry points, which receive around 1,000 enquiries each week. The nature of enquiries varies widely, from healthcare professionals requiring scientific data, through to patients seeking reassurance about medicines they have been prescribed.
- 52** The MHRA organises regular conferences and other events around the country aimed at industry and healthcare professionals on various topics related to the regulation of medicines and medical devices.

## Review Findings

### **MHRA has a good range of contact channels, which it supplements with external engagement events**

- 53** The MHRA has a number of contact channels. It has a general enquiries helpline, and an extensive website. It supplements its general advice line with specific regulatory contact points by both phone and email. These regulatory contact points give specific and tailored advice and guidance to business on interpreting aspects of the regulatory regime.
- 54** In addition, we observed that MHRA inspectors provide valuable advice and guidance to industry. We were generally impressed with the consultative manner of the inspector visits we observed, and the way in which advice was used as a tool by the inspector to try to bring the regulated body into compliance. MHRA inspectors that we saw were both helpful and knowledgeable.
- 55** The Review Team found evidence of a good use of all modes of consultation by the MHRA and a move towards greater use of electronic means of communication with stakeholders. In addition to these more reactive channels of communication, the MHRA holds regular conferences and events on specific areas of regulation of medicines and devices to further supplement its normal consultation procedures.

### **MHRA is developing systems to facilitate better sharing of information across the Agency**

- 56** The Review Team was impressed with the moves the MHRA was taking to pool intelligence across the Agency, through its IT system Sentinel. The Review Team considers that having one common IT system across the MHRA to capture all regulatory data of interactions with

businesses will be invaluable in helping to ensure that the correct information is accessed by all levels of the MHRA to inform its regulatory interactions. However, we recognise that this is work in progress and the Sentinel system will be discussed in more detail under 'Data Requests'.

### **The potential of the MHRA website is currently not being maximised as a communications tool in terms of layout and usability**

- 57** The MHRA website was criticised by a number of stakeholders. It was seen as a potentially valuable tool with a large amount of excellent material available on it. However, there was a strong feeling that it was not currently being maximised as a communication tool in terms of its structure which is not always obvious to navigate from an external perspective.
- 58** This problem is compounded by the poor search facility which currently exists on the site. MHRA is aware of this issue and is currently planning to upgrade the search facility which will help stakeholders to find information more easily. However, we recommend that some more thought should be given by the MHRA to the structure and layout of its website to make it easier to navigate. MHRA is already planning to establish user communities, and to group information on this basis.

### **MHRA guidance is, on the whole, extensive and issued in good time although it could be 'road tested' better in some cases**

- 59** The Review Team saw some very good examples of advice and guidance from the MHRA. For example, guidance on medical devices was cited by stakeholders as a quality product that clarified an area of vague law without gold plating.
- 60** The MHRA publishes guidance to stakeholders sometimes well in advance of

the suggested 12 week limit prior to new regulations coming into force. For the recent user-testing requirements, the MHRA published guidance to industry some 18 months before the implementation date.

- 61** The MHRA also provides guidance to Notified Bodies, which conduct inspections and audit under the legislative regime for Medical Devices. Notified Body representatives that we spoke to stated that the guidance they received from MHRA was “as good as it gets”.
- 62** However, the MHRA can at times fail to adequately consult on aspects of its guidance – an example of this is the recent ‘purple guide’ on Pharmacovigilance which was published by the MHRA with limited consultation with stakeholders on the substantive content. Although the MHRA argues that this is a best practice tool, the MHRA should be aware that guidance it issues such as this can have the effect of acting like additional regulation – and it should ensure that all of its stakeholders are fully consulted when it is planning to introduce new guidance.

**The perception and credibility of the MHRA’s approach towards better regulation can be hampered by occasional miscommunication**

- 63** The Agency’s Better Regulation of Medicines Initiative (BROMI) has won an international award as a model of better regulation policy making. This model is intended to allow a transition to self- and third- party certification in low risk areas of medicines regulation. However,

stakeholders said that that there had been some issues in the way that BROMI had been put into practice. For example, there was a lack of clear communication within the MHRA regarding the validity of applications to a pilot scheme run as part of BROMI. This led to some applications being rejected erroneously by MHRA staff.

- 64** The MHRA has moved towards a less extensive system of scrutiny for low-risk cases. This means that, for instance, self-certification is approved by administrators who may have little expertise in the more complex regulatory problems posed by riskier applications. One of the prices of this more streamlined process for businesses is that they need to be more careful in the quality of their applications; IT-based systems that are not individually processed by more qualified staff do now allow room for error. Some stakeholders felt that the MHRA was being unnecessarily strict in turning down faulty applications; some indeed argued that they had stopped acting in a flexible and Hampton-compliant way in these cases. We thought that more could be done to educate the industry in their responsibilities here. Stakeholders also feel that BROMI could go further, and we would support MHRA expanding the approach into other regulatory areas that are appropriate.
- 65** However, in general the BROMI is an important initiative with a good direction of travel that we fully support and we would encourage the MHRA to do more in this area.

## Data requests

### Hampton principle

***“Businesses should not have to give unnecessary information or give the same piece of information twice.”***

## Key findings

- The MHRA has developed e-enabled systems to help improve efficiencies in the regulatory approvals system; however take-up of the full e-enabled system has been slow.
- The MHRA works well to join up with internationally equivalent bodies.
- The MHRA’s main cross-Agency IT system is now functioning as intended, but there remain issues of data cleansing and communication.

## Background

**66** The MHRA’s regulatory activities include making decisions on applications from companies for licences to undertake clinical trials, market new products, deal in wholesale, import or manufacture of medicines and devices. As such, the MHRA must request sufficient information to satisfy itself that at the end of the day, products used by patients are safe and will have therapeutic benefits.

**67** The MHRA has developed an information management system, Sentinel, which is designed to facilitate electronic submission through a portal for the various types of medicines marketing authorisations. Sentinel contains all historical scientific data submitted to the MHRA – some 30 million pages of documentation. The portal uses “smart” application forms which allow companies to check the data, at the point of entering it into the form, which removes the potential for errors which would otherwise require the form to be returned. There are

plans to extend this to other types of applications, as the system currently does not apply to clinical trials<sup>9</sup>.

**68** Training on how to use the MHRA portal is available free of charge, as is access to the database for up to 7 designated individuals at each company.

**69** The fees charged for assessing applications vary, depending on the amount of work the MHRA needs to undertake analysing the scientific data supplied by companies in support of their applications. This ranges from about £100,000 for an application for a marketing authorisation for a completely new substance, to £2,000 - £4,000 for a clinical trial application.

**70** The MHRA does not make formal data requests to either healthcare professionals or patients. However, it has arrangements in place for reporting adverse incidents. On the medicines side, the “Yellow Card Scheme” is a long established method of reporting suspected adverse drug

<sup>9</sup> Applications in relation to clinical trials are done through forms available on the EMA website

reactions. The Scheme has been progressively extended to a wide range of healthcare professionals and to patient and their carers. There is also an on-line form available for reporting adverse reactions to medicines.

- 71** Similar arrangements are in place for medical devices. Manufacturers are legally obliged under EU law to report adverse incidents to the MHRA and a voluntary process is in place for healthcare professionals and patients. The MHRA investigated 8,000 devices-related adverse incidents in 2007-08, leading to 100 devices alerts.

## Review Findings

**The MHRA has developed e-enabled systems to help improve efficiencies in the regulatory approvals system; however take-up of the full e-enabled system has been slow**

- 72** The MHRA has been moving towards e-enabled systems and self-certification over a number of years. However, currently only 2-3% of electronic applications submitted by industry through the portal are in the Electronic Common Technical Document (eCTD) format – which the MHRA argues gives the biggest regulatory efficiencies for industry. We find it puzzling that businesses are not utilising the full functionality of this system, especially as eCTD is a system that is already extensively used by the pharmaceutical industry.
- 73** We believe that messages about the benefits of fully engaging with the Sentinel system may have not been fully explained to industry. Again, industry perceptions may have been affected by frequent rejections of applications that are not compatible with

the demands of the system. More could be done to work with them to improve take-up.

**The MHRA works well to join up with internationally equivalent bodies**

- 74** The MHRA works closely with the equivalent bodies in other EU member states, the EMEA and other international counterparts, such as the Food and Drug Administration in the US to harmonise application forms and other data requests. In the past year it has also signed a bilateral agreement with the Chinese State Food and Drug Administration for co-operation on combating counterfeit medicines and exchange of information on herbal medicines.

**The MHRA's main cross-Agency IT system is now functioning as intended, but there remain issues of data cleansing and communication**

- 75** The MHRA has developed the Sentinel system to act as a cross-Agency IT system for regulatory matters. One of its intended benefits is to help streamline the medicines marketing authorisation process. This has been a number of years in development and has required considerable resource and effort on behalf of the MHRA to put in place a system that can not only deal with future workload, but also the historical authorisations data that has already been approved. This has involved the scanning of some 30 million pages of data onto the system.
- 76** However, as a result of the transition, issues have come to light regarding the accuracy of some of the historical data held by the MHRA. This has on occasion led to delays with the authorisation of new products. We believe that the 'cleansing' of historic Sentinel data is an important task for the MHRA in terms of establishing and



maintaining system credibility amongst stakeholders. The importance of maintaining accurate data going forward is equally crucial and in this respect ensuring the appropriate accountability for data quality within the MHRA is paramount. The MHRA is aware of these issues and has established a team to undertake the data cleansing process.

- 77** The Review Team believes that there is a key issue of communication with regards to Sentinel. For example, the MHRA generated a large number of stakeholder communications regarding user-testing based upon data that was drawn from the Sentinel system in June 2008. However

these letters were not sent until September 2008, by which time some of the data was out of date. This, compounded by the inaccuracy problems with some of the historical data, led to stakeholders receiving warning letters threatening suspension of marketing authorisation for issues that had already been dealt with.

- 78** This issue has been interpreted by industry as a consequence of systems failure in the Agency, which has had an impact on its credibility amongst stakeholders. The MHRA needs to be aware that Sentinel's credibility depends not only on the data it holds, but also on the uses to which that data is put.



## Inspections

### Hampton principle

*“No inspection should take place without a reason.”*

## Key findings

- **MHRA inspections are lengthy and rigorous, but stakeholders derive real value from the experience.**
- **We would encourage the MHRA to continue to develop a more outcome-focused approach to inspection within its current operational constraints.**
- **We would encourage the MHRA to work in the international arena to develop Memoranda of Understanding with non-EU countries so that international Good Manufacturing Practice inspections of business can be minimised.**
- **The MHRA’s inspector selection and training is rigorous and we would encourage moves to improve continuous professional development.**

## Background

### Medicines

**79** Inspection of research, development and quality control laboratories, clinical trials, manufacturers, wholesalers and pharmacovigilance systems is carried out by the Inspectorate Group of the Inspection, Enforcement and Standards Division in the MHRA. There are 5 main inspectorates within the MHRA:

**1 Good Clinical Practice (GCP)** – GCP inspectors assess compliance with the requirements of GCP guidelines and applicable regulation. GCP guidelines and regulations provide a standard for the conduct of clinical trial research;

**2 Good Manufacturing and (3) Distribution Practice (GMP/GDP)** – GMP inspectors assess manufacturers’ compliance with the provisions of their manufacturing authorisation and the principles and guidelines for GMP as detailed in the

appropriate European Directives. GDP inspectors assess Wholesale Dealers’ compliance with the provisions of their licence and the principles and guidelines for GDP;

**4 Good Laboratory Practice (GLP)** – GLP inspectors verify that test facilities which conduct non-clinical safety studies on pharmaceuticals, agrochemicals, industrial chemicals, food and cosmetics meet GLP requirements to the standards necessary for regulatory purposes;

**5 Good Pharmacovigilance Practice (GPvP)** – Pharmacovigilance inspectors assesses pharmaceutical companies’ compliance with UK and EU legislation relating to the monitoring of the safety of medicines given to patients.

**80** Inspections are undertaken by MHRA staff. There were over 1,400 inspections in 2007-08. Broadly there are three sorts of inspections:

- Routine national inspections: these are scheduled inspections that UK Market Authorisation Holders (MAHs) undergo on a periodic basis. MAHs are notified of these inspections in advance and are generally systems-based, meaning that inspectors examine the systems and procedures used by a MAH to comply with existing EU and national regulations and guidance;
- “For cause” national inspections: these are ad hoc inspections that are triggered as a result of, for example, safety issues, suspected violations of legislation relating to the monitoring of the safety of medicines, or referrals by other Member States. In rare circumstances MAHs may not be notified of these inspections in advance;
- The Committee on Human Medicinal Products (CHMP) requested inspections: the CHMP may request inspections of MAHs in association with specific centrally authorised products which can either be routine or triggered.
- Manufacturers will normally be informed 14 days before the date of the proposed visit. One of the aims of the visit is to confirm that the essential requirements – contained in the Medical Devices and General Product Safety Directives – are being complied with in practice.
- An authorised inspector supported, as necessary by MHRA's product specialist staff will undertake the inspection.
- Compliance inspectors have the right at any reasonable hour to:
  - Enter premises and inspect goods, other than premises occupied only as a person's residence.
  - Examine manufacturing procedures and testing arrangements.
  - Require the production of any records for examination and to take copies of, or copies of any entry in, the records.
  - Seize or detain suspect records or goods which may be required as evidence in proceedings for an offence in respect of a contravention.
- Visits will normally last for no more than a day.

**81** The MHRA produces a report of its findings within 30 days of the end of the inspection and the MAH then has a further 30 days to respond. Deficiencies are graded as “critical”, “major” or “other” depending on their seriousness. Critical findings are referred to an expert group within the MHRA to decide on what enforcement action may be necessary to safeguard public health.

### Medical devices

**82** The MHRA inspects manufacturers once their products have been placed on the market. Pre-market inspections are carried out by designated certification bodies known as Notified Bodies, such as Amtac Certification Services Ltd and BSI Product Certification, which have been designated as competent in the relevant fields by the MHRA. The broad process of the MHRA conducted inspections is as follows:

## Review Findings

### **MHRA inspections are lengthy and rigorous, but stakeholders derive real value from the experience**

**83** MHRA inspections (particularly those on the GMP side) can last between 2-5 days. The cumulative burden on the regulated in preparing for and hosting an inspection visit was estimated by the regulated body of a large site inspection we visited to be at least an additional 50 staff days per inspection.

**84** However, stakeholders we spoke to about the process were clear that they derived definite benefits from inspection. As an industry stakeholder stated, the MHRA inspection process provided a useful external validation of the company's internal quality control procedures and ensured that they remained "compliant not complacent". Indeed, industry representatives that we spoke to stated that the monetary costs of inspection were worthwhile given the breadth of knowledge and experience demonstrated by MHRA inspectors.

**85** One area that is at odds with the generally impressive feedback we had regarding MHRA inspection was from the Notified Bodies. MHRA audit these bodies to ensure that their work regulating the devices sector is sound. However, Notified Body representatives informed us that they feel that the approach of some MHRA inspectors, in one area, is not Hampton-like in that issues are raised in the final audit report that had not been raised by the inspector during the visit. We have been told by the MHRA that this is contrary to their standard practice of giving the Notified Body both an oral and written summary of its findings at the end of the audit and only to include in its final audit report those items so disclosed.

### **We would encourage the MHRA to continue to develop a more outcome-focused approach to inspection within the constraints that it currently operates**

**86** The Review Team recognises that in some areas, European legislation can limit the MHRA's options as it prescribes certain inspection cycles. However, within these constraints, we encourage the MHRA to explore the potential for a more outcome-focused approach, for example, in the use of other sources of assurance such as internal audit quality assessment. This might follow models used in the devices and BROMI regimes.

**87** We welcome the MHRA's approach to systematising its already good awareness of risk into a formal risk-based inspection model, and we would encourage it to continue to communicate clearly and work closely with industry regarding its development.

### **We would encourage the MHRA to work in the international arena to develop Memoranda of Understanding with non-EU countries so that international Good Manufacturing Practice inspections of business can be minimised**

**88** Industry in the pharmaceutical sector faces the cumulative burden of multiple national inspectorates from other nations looking at similar issues regarding the manufacture of medicines. One site we visited estimated that this in effect meant that they had, on average, an inspection from a pharmaceutical regulatory agency once a month. The MHRA is working with partners to try to minimise the need for multiple overlapping international inspections through a mutual recognition arrangement. We support this and encourage further work internationally, although we understand that

the MHRA can be constrained in this to a degree by a need to approve mutual recognition procedures through the EMEA.

- 89** We believe that the MHRA could use its 'international capital' to drive this agenda forward. Given the globalised nature of the pharmaceutical industry, and the rise of other international competent inspectorates, this will be an expanding area in future.

**The MHRA's inspector selection and training is rigorous, and we would encourage moves to improve continuous professional development**

- 90** The MHRA puts a great deal of effort into

ensuring that they recruit the right people to be an inspector. The selection process involves both psychometric testing and an assessment centre. There is thus a high personality-type 'hurdle' to pass, in addition to the technical knowledge required, to become an inspector.

- 91** This selection process is then followed and supplemented by an approach to ensure quality and continuous professional development, with a minimum of ten days being assigned each year to the continued professional development of inspectors. The MHRA is considering improving its ongoing professional development for inspectors and we would support this move.

## Sanctions

### Hampton & Macrory principles

*“The few businesses that persistently break regulations should be identified quickly, and face proportionate and meaningful sanctions.”*

*“Regulators should be transparent in the way in which they apply and determine administrative penalties.”*

*“Regulators should avoid perverse incentives that might influence the choice of sanctioning response.”*

*“Regulators should follow-up enforcement actions where appropriate.”*

## Key findings

- The MHRA takes a strong outcome-focused approach to the use of sanctions. The emphasis is on compliance, and there is a strong recognition that the use of advice and guidance is often more effective than formal enforcement action.
- The MHRA has a clear and effective system for prioritising investigation and enforcement cases.
- There are however gaps in the sanctions available to the MHRA which limit its flexibility in practice to deal with serious cases.
- Feedback from enforcement action, or failures of enforcement action, is put to good use throughout the Agency.

## Background

- 92** The MHRA is, essentially, a licensing, and – on the devices side – an accreditation body. This has implications for its enforcement activity: where it is dealing with non-compliance by a licence holder, it has a number of sanctions available to it, including review, variation to and, potentially, withdrawal of a licence. This gives the MHRA considerable flexibility in bringing licence-holders into compliance.
- 93** Where no licence is held, the Agency’s main sanctioning tool is prosecution; the MHRA takes forward approximately 20 prosecutions per year and has quite wide-ranging powers to deal with non-

compliance. The MHRA publicly states that it tries to work with industry to ensure compliance. In the event of serious breaches, or wilful failure to comply, a range of possible sanctions exists, such as:

- Withdrawal of a product from the market;
- Suspension of a clinical trial;
- Referral of individuals to the appropriate professional body (e.g. the General Medical Council);
- Forfeiture orders for unsafe products;
- Criminal prosecutions.

- 94** Most criminal prosecutions that the MHRA takes are in relation to medicines and relate to supply of counterfeit or illegal

supply of medicines (e.g. clinics supplying Viagra without either a medical examination or a legal prescription).

- 95 The MHRA may prosecute under the Medicines Act and the Trade Marks Act. The Proceeds of Crime Act is also used as part of its enforcement strategy. Prosecutions for medical devices can take place under either the Medical Devices Regulations or the General Product Safety Regulations.
- 96 In 2007-08, the MHRA opened 302 new investigations, of which 22 were referred to Government lawyers. Thirteen further prosecutions were completed, 38 formal cautions for breaches were handed out and in 200 cases, compliance was achieved through the MHRA issuing warnings and advice.
- 97 In the use of sanctions as elsewhere, the MHRA works in a highly globalised context: one of the most serious enforcement challenges facing the MHRA is the need to deal with counterfeit medicines and medical devices, many of which are the product of crime operating on an international level.

## Review Findings

**The MHRA takes a strong outcome-focused approach to the use of sanctions. The emphasis is on compliance, and there is a strong recognition that the use of advice and guidance is often more effective than formal enforcement action**

- 98 The MHRA staff that we spoke to had a clear understanding of the sanctioning options available to them, and a commitment to only using serious sanctions that warrant formal action: the critical factors here are the extent of harm that may have been caused to a patient, and the level of criminality involved.
- 99 In other cases, the MHRA believes that advice and guidance are the most appropriate initial responses to cases of non-compliance.
- 100 The MHRA routinely follows up on all allegations of non-compliance in the devices sector. Many of these will involve questions about devices which are produced by micro-businesses that are doing their best to comply with the law within the limited resources available to them. In these cases the MHRA works with the business to put things right, and to minimise the anxiety and disruption that an interaction with the regulator can mean for the business. We found that the MHRA combined this approach with a determination to take swift and decisive formal action where it is necessary. The MHRA also publishes the results of such action where this would send out a useful message to the sector.

**101** The MHRA basic approach is thoroughly compatible with the Hampton and Macrory principles in practice. The Review Team notes however that it has not published an enforcement policy that would set these principles and processes out for the benefit of stakeholders. We have seen a draft of this policy and we would encourage the MHRA to publish it as soon as possible.

**102** Stakeholders that we spoke to who operated within the licensing regime were strongly supportive of the action MHRA takes to prosecute counterfeit operators.

**The MHRA has a clear and effective system for prioritising investigation and enforcement cases**

**103** The MHRA deals with a large number of referrals relating to cases of possible non-compliance in any given year, both reactive and proactive. The MHRA prioritises its work according to a system of scoring which takes into account risk factors (like the number of people on whom the case would potentially impact), and factors like the compliance record of the individuals and businesses involved.

**There are however gaps in the sanctions available to the MHRA which limit its flexibility in practice to deal with serious cases**

**104** The costs and administrative burdens associated with criminal prosecution for a regulator can be prohibitive, and careful consideration is given before a case progresses to court.

**105** The MHRA has recognised that some of the sanctions available under the Regulatory Enforcement and Sanctions Act 2008 – notably Variable Monetary Penalties – would allow for more flexible and effective sanctioning for low level regulatory breaches in practice. They would allow, for instance, for the imposition of a level of fines under a civil procedure which would reflect the seriousness of the case, or, where appropriate, ‘naming and shaming’ of offenders.

**106** The MHRA is currently exploring how this expanded range of sanctions might be applied, particularly in respect of advertising of medicinal products, EU imposed deadlines for submitting data, variations to existing marketing authorisations and the implementation of the Paediatric Medicines Regulation.

**Feedback from enforcement action, or failures of enforcement action, is put to good use throughout the Agency**

**107** Elsewhere in this Report we have commented on the extent to which work between parts of the MHRA are co-ordinated: the same is true with its enforcement staff.

**108** Where in a serious recent case it became clear that prosecution would not be possible on grounds relating to the existing law on disclosure requirements, the MHRA developed both proposals for changes to UK law (which are now in place) and to strengthen EU law.



## Focus on Outcomes

### Hampton principle

***“Regulators should measure outcomes and not just outputs.”***

## Key findings

- The MHRA has a strong sense of its ultimate outcome – to secure public health.
- However, measuring the Agency’s input and contribution towards public health outcomes is difficult.
- The MHRA should ensure that the quality of the regulatory service that it provides to industry is consistent.
- The MHRA has made good efforts to avoid ‘silo’ working across its regulatory regime.

## Background

**109** The MHRA’s performance and delivery against its 2007-08 Key Targets, and its 2008-09 Key Targets, together with the associated performance measures, are set out in its 2007-08 annual report. There are 12 targets for 2008-09 under 4 headings:

- Safeguarding public health
- Communicating effectively
- Shaping a balanced regulatory framework
- Running a successful organisation

These represent a good attempt to set out how the MHRA will take forward its statutory objectives and to focus on tangible outcomes.

**110** The Agency’s 2008-09 Business Plan and 2008-13 Corporate Plan set out how the MHRA will deliver on its key targets at the working level. Additionally, the MHRA has a Communications Plan to the end of 2010 setting out in detail how it will

communicate with stakeholders (industry, healthcare professionals and the public).

**111** The MHRA has specific targets to turn around some applications, for example for completing assessments for clinical trials authorisations within 30 days. Information on its performance against these targets is published annually and available to stakeholders.



## Review Findings

### **The MHRA has a strong sense of its ultimate outcome – to secure public health**

**112** Public health is emphasised and appears to be widely understood as the overarching outcome of the MHRA, and there is a consistent view on this ultimate outcome within and outside of the Agency.

**113** We were impressed with the strong sense of outcome-focus from staff at all levels of the MHRA. This cascades well from corporate targets to individual work plans. For example, staff working both on enforcement and on giving advice demonstrated a clear understanding that compliance is key to achieving regulatory outcomes and is the best means of achieving this.

### **However, measuring the MHRA's input and contribution towards public health outcomes is difficult**

**114** The Review Team recognises the difficulty and complexity of measuring the MHRA input to such a broad outcome as 'securing public health'. But we were reassured that the MHRA has developed a process of monitoring the impact of its programmes through discrete pieces of research work. A good example of this would be its work to establish the impact of its decision to withdraw the painkiller co-proxamol from the market.

**115** A key issue for the MHRA has been to find and define proxy measures for it to assess its impact, and on a project level there has been some success here: for example, on the judgements to be made in licensing new products and developing a balance between the risk of harm and the immediate therapeutic impact. This allows new drugs to come onto the market, but with a specific risk-management plan. In this way the drug is released as early as possible (therapeutic benefit), whilst still recognising that there

may be risks associated with this action that need to be specifically managed (reducing the risk and impact of harm).

**116** We would encourage the MHRA to continue to develop its thinking on this area, and we would encourage it to ensure that its proxy measures cover all aspects of the MHRA's activities, and so provide a full measure of the success of the organisation.

### **The MHRA should ensure that the quality of the regulatory service that it provides to industry is consistent**

**117** Whilst the MHRA generally understands the impact of its work on the industry, there is one sector of the industry which perceives itself as a 'Cinderella sector'. Representatives of the over-the-counter medicines sector put it to us that its needs are being trumped by the prioritisation it deems the MHRA gives to European decentralised Marketing Authorisation work. These decentralised processes have mandatory timescales for approval and industry feel the Agency's prioritisation of this work has negatively affected the quality and timeliness of the regulatory service it provides to other sectors.

**118** The MHRA accepts that the assessments it performs on behalf of the EMEA, or applications processed within the Mutual Recognition or Decentralised Procedures, often have priority over national applications which are being delayed as a result.

**119** In practice, this means there is little discipline placed on the MHRA to give low-risk applications the priority that businesses need to get their products on the market quickly. It also means that there is no clarity for industry on the length of time approval could take – which can have (sometimes serious) commercial implications. We understand that the MHRA recognises this issue, and is recruiting

additional staff and making process improvements. Transparency is also an issue. While the MHRA states that it has time metrics that are agreed with trade associations and are published on a monthly basis, these targets, and performance against them, need to be more prominent amongst their own priorities and in communications to the industry.

**The MHRA has made good efforts to avoid ‘silo’ working across its regulatory regime**

- 120** The MHRA was formed from the merger of two regulatory bodies in highly different ways due to major differences in legislative

approach. Despite having been merged for some 5 years, it has largely maintained an organisational distinction between its work on medical devices and on medicines regulation. The Review Team found this approach was justified given the fundamental differences in legislative basis. However, this did not appear to have led to ‘silo’ working within the MHRA as it is good at forming collegiate groups when cross-cutting work is discussed.

- 121** We consider the MHRA to be joined up and outcome-focused. We consider it a strength of the MHRA that it has policy, enforcement and inspection all in one place.

## Appendix 1: Review Team membership

**Trish Davies** is the Deputy Chief Executive and Director of Regulation of the Human Fertilisation and Embryology Authority (HFEA), having joined the organisation in March 2004. Before then, Trish was the Director of Corporate Policy and Communications for the National Care Standards Commission, which she joined at its inception in 2001, from the Department of Health, where she was the project manager for National Minimum Standards during the development of the Care Standards Act 2000. Her previous career includes two years as an inspector in the Social Services Inspectorate, five years as Head of Inspection in Hertfordshire, setting up and managing a joint unit between the County Council and the Health Authorities and five years as Assistant Regional Director with NCH. Trish is a qualified social worker and has also worked in social work education, staff development and family placement.

**Paul Holland** is an Audit Manager at the National Audit Office, responsible for the Financial Audits of a number of bodies within the Department of Health, including the MHRA. He has previously worked on the audits of a number of central government organisations, including the Electoral Commission; House of Commons and House of Lords and the Ministry of Defence.

**Dawn Muspratt** was, until recently, Acting Deputy Chief Executive of the National Consumer Council (NCC) working as part of the leadership on the merger with energywatch and Postwatch. Before then Dawn was Head of Organisational Development at NCC working at Board level and across the National, Scottish and Welsh Consumer Councils implementing improved structures and systems and staff development. Dawn is a qualified youth and community worker and has a strong background in the voluntary sector. She spent a number of years working for voluntary organisations in inner London in community development and youth work where she fundraised and delivered multi-million pound building redevelopment projects.

**Elizabeth Surkovic** was, at the time of the review, a Director at the Better Regulation Executive within the Department for Business, Enterprise and Regulatory Reform (BERR). Her background is in chemicals, having spent 20 years in that industry. She more recently moved to the Civil Service where she has worked in Defra and the Cabinet Office.

## Appendix 2: Key findings and conclusions of the Hampton and Macrory reports

### Hampton principles of inspection and enforcement

- Regulators, and the regulatory system as a whole, should use comprehensive risk assessment to concentrate resources on the areas that need them most
- No inspection should take place without a reason
- Regulators should provide authoritative, accessible advice easily and cheaply
- All regulations should be written so that they are easily understood, easily implemented, and easily enforced, and all interested parties should be consulted when they are being drafted
- Businesses should not have to give unnecessary information, nor give the same piece of information twice
- The few businesses that persistently break regulations should be identified quickly, and face proportionate and meaningful sanctions
- Regulators should recognise that a key element of their activity will be to allow, or even encourage, economic progress and only to intervene when there is a clear case for protection
- Regulators should be accountable for the efficiency and effectiveness of their activities, while remaining independent in the decisions they take
- Regulators should be of the right size and scope, and no new regulator should be created where an existing one can do the work
- When new policies are being developed, explicit consideration should be given to how they can be enforced using existing systems and data to minimise the administrative burden imposed

Source: Hampton Report, Box E2 page 7

## Macrory's principles and characteristics of an appropriate sanctioning regime

### A sanction should:

1. Aim to change the behaviour of the offender;
2. Aim to eliminate any financial gain or benefit from non-compliance;
3. Be responsive and consider what is appropriate for the particular offender and regulatory issue, which can include punishment and the public stigma that should be associated with a criminal conviction;
4. Be proportionate to the nature of the offence and the harm caused;
5. Aim to restore the harm caused by regulatory non-compliance, where appropriate; and
6. Aim to deter future non-compliance.

### Regulators should:

1. Publish an enforcement policy;
2. Measure outcomes not just outputs;
3. Justify their choice of enforcement actions year on year to stakeholders, Ministers and Parliament;
4. Follow up enforcement actions where appropriate;
5. Enforce in a transparent manner;
6. Be transparent in the way in which they apply and determine administrative penalties; and
7. Avoid perverse incentives that might influence the choice of sanctioning response.

Source: Macrory Report, Box E1 page 10

## Appendix 3: Review scope and methodology

The review focused on those aspects of the MHRA's activities where we considered that its actions have the most impact on business. These areas included the majority of its work on medicines, devices and clinical trials regulation.

The following areas were excluded from the scope of the review

- MHRA activity facing towards non-industry groups such as enforcement and sanctions action against criminals
- Advice and guidance to patients (except where this leads to disproportionate impacts on industry)
- Some of Agency's 'niche' areas, such as blood products, tissue engineering and nanotechnology

Our methods included:

- interviews with a wide range of MHRA staff including senior managers;
- interviews with other stakeholders including the trade bodies in the pharmaceutical sector and medical devices sector and business representative groups;
- focus groups of MHRA inspectors, policy staff and enquiry staff
- observational visits including Good Manufacturing Practice inspection and Good Clinical Practice inspection; and
- document review, including the MHRA's high level strategies and plans.

The review process is described in *Hampton Implementation Reviews: Guidance for Review Teams*. It is not the same as a full value-for-money audit of economy, efficiency and effectiveness and the Review Team's conclusions are both evidence- and judgement-based. These judgements, however, have been made drawing on a range of evidence from different sources, including those described above. Judgements have not been based on evidence from a single source – the Review Team has sought to bring together evidence from a number of different businesses or organisations, and from MHRA front-line staff, policy officials and senior managers.



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