



House of Commons

Committee of Public Accounts

Safety, quality, efficacy: regulating medicines in the UK

**Twenty-sixth Report of
Session 2002–03**



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*Report, together with formal minutes, oral and
written evidence*

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The Committee of Public Accounts

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Committee staff

The current staff of the Committee is Nick Wright (Clerk), Leslie Young (Committee Assistant) and Ronnie Jefferson (Secretary).

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Summary

The Medicines Control Agency (the Agency) was responsible, from its creation in 1989 until merger with the Medical Devices Agency in April 2003, for protecting public health by ensuring the safety, quality and efficacy of medicines both prescribed and sold over the counter—some one billion products in the UK each year. It did this by licensing new medicines, by inspecting manufacturing and supply facilities, and by monitoring the risks and benefits of existing medicines. The Agency traced its history back to the response to the thalidomide tragedy of the 1960s.

The Government's policy since 1997 has been to increase the extent to which the public can self-medicate by making more medicines available over the counter and through initiatives such as NHS Direct. The range of health professionals who are allowed to prescribe medicines has also been widened, to help improve access and optimise treatment. The Agency had a central role to play in implementing these changes, not least because wider availability makes awareness of safety risks all the more important.¹

On 1 April 2003 the Agency merged with the Medical Devices Agency to form the Medicines and Healthcare products Regulatory Agency (MHRA),² with a new Chair and management structure. Ministers emphasised that public safety is to be at the heart of the new body and it retains the responsibilities of the Medicines Control Agency.

On the basis of the Report by the Comptroller and Auditor General,³ we looked at the Agency's performance against its key objectives of promoting and safeguarding public health through the regulation and provision of information on medicines, and its services to stakeholders.

Our main conclusions are:

- **There has been a lack of dynamism in the efforts of the Agency to drive further improvements in the protection of public health.** The Agency has been one of the leaders in its field internationally, but, at home, efforts to improve the reporting of adverse reactions by health professionals have had limited success. The quality of many information leaflets and labels, designed to alert patients and doctors to potential risks, is poor. There is also a widespread but unmonitored practice of prescribing to children drugs that, while licensed, are not specifically approved for paediatric use.
- **The Agency has tended to take a narrow view of its role as a provider of information and has no public profile to help it put across safety messages.** Although it has a mission to “provide information to contribute to the safe and effective use of medicines”, the Agency has not sought to develop a relationship with the public through awareness campaigns or advertising, unlike the United States Food and Drug Administration. Doctors too appear to have little awareness of the Agency and its role

1 C&AG's Report, paras 1.1, 2.17, 2.43

2 Department of Health press release, 1 April 2003

3 C&AG's Report, *Safety, quality, efficacy: regulating medicines in the UK* (HC 255, Session 2002–03)

because it has not reached out to them effectively. The Medicines and Healthcare products Regulatory Agency should take early steps to develop and implement a communications and awareness strategy.

- **The merger and creation of the Medicines and Healthcare products Regulatory Agency provides the opportunity to strengthen and clarify the regulatory function.** As well as its mission to protect public health, the Agency also had a remit to help develop a successful pharmaceutical industry, giving some potential for conflict of interest. It is also entirely funded by drug company fees, though activities such as safety monitoring, public information, and representing the UK in Europe serve wider interests than those of the industry. The new Agency needs to have a clear focus on improved public health, with performance measures that reflect its contribution to public health objectives.

1 Improving safety, quality and efficacy of medicines

1. The Agency has a good record in ensuring the safety of medicines coming on to the UK market. Its assessors examine the scientific evidence provided by companies about each new drug, and its inspectors and investigators check industry procedures to make sure that the final products reaching customers are safe and of good quality. Compared with the number in use—200 newly licensed in the five years to March 2002 and 4,000 already on the market—only 12 medicines have had to be withdrawn because of safety problems.⁴

2. Not all risks can be identified before a medicine is licensed. Some may only emerge when it reaches the wider population. The core of the Agency's safety work involved monitoring reports of adverse drug reactions using its Yellow Card Scheme, and the rates of reporting by the UK's health professionals are among the best in the world. But the Agency had not been able to increase reporting levels above the current estimate of 10–25%.⁵

3. While some of the reasons given by doctors for not participating in the Scheme (**Figure 1**) can be addressed through better systems, many are unacceptable. The Department told us that focusing the attention of doctors on safety was one of the Chief Medical Officer's priorities. The Agency was also aware of the need to do more to convince healthcare professionals of the importance of reporting these events.⁶

Figure 1: The most common reasons given by GPs and hospital doctors for not reporting adverse effects of medicines

recently tried to report online but found I couldn't so didn't bother	uncertain of the threshold for serious reactions
not my responsibility to report	not really sure what should be reported
too busy	it takes a long time to fill out the form
it is not easy to find yellow card when necessary	reporting generates too much extra work
too junior to fill in a card	the system is not convenient
it never comes to mind at the right time	

Source: National Audit Office survey of doctors

4. Whilst some other countries require doctors and others compulsorily to report adverse drug reactions, the Agency and Department did not intend to take this step, and in their view it would not bring about an increase in reporting. However, the Agency did propose to approach Royal Colleges and universities to incorporate medicines safety into undergraduate medical education. The

4 C&AG's Report, para 2.3 and Figure 7

5 Q 1

6 Qq 2, 41

Department agreed that it was clearly incumbent upon NHS Trusts to draw to the attention of doctors the importance of safety reporting.⁷ The introduction of patient reporting via NHS Direct could also help capture more information.⁸

5. An area of particular safety concern is the widespread prescribing to children of medicines that, are licensed, but not specifically approved for paediatric use and the potential for increased risks in the absence of any relevant data from clinical testing and regulatory assessment.⁹ Although the Agency had set up a study to look at fatal drug reactions in children it had had a disappointing response.¹⁰ In general there was a lack of urgency about proposals to tackle this problem. The main one appeared to be a European Directive likely in some three or four years' time. Even then, regulators would be able merely to offer incentives to encourage companies to get medicines approved for children, rather than use compulsion.¹¹

6. The internet is another route where access to medicines is being widened. In some cases where there has been a consultation and a written prescription this trade is legal, but there is also illegal supply (**Figure 2**). The Agency told us they were taking action to protect the public from this activity and had achieved five successful prosecutions out of 35 cases closed to date. A further 21 were under investigation, and over 150 more had been identified for enforcement action.¹²

Figure 2: Top ten prescription-only medicines marketed over the Internet in the UK

1	Xenical	Obesity
2	Proscar	Prostate disorders
3	Propecia	Hair loss
4	Viagra	Erectile dysfunction
5	Uprima	Erectile dysfunction
6	Reductil	Appetite suppressant
7	Zyban	Anti-smoking
8	Relenza	Influenza
9	Phentermine	Obesity
10	Meridia	Obesity

Source: Medicines Control Agency monitoring data

7. One of the Government's aims regarding increased self-medication by the public is to expand the role of pharmacists in increasing the benefits patients get out of medicines. The Office of Fair Trading has recently recommended much greater deregulation of medicines' dispensing. When considering these recommendations¹³ the Government would be taking account of the possible risks to patients if pharmacists were removed from the dispensing loop in favour of more dispensing doctors.¹⁴

7 Qq 72–77, 78–82

8 Q 3

9 Qq 4–18, 52

10 Qq 7–12

11 Qq 13–18

12 Qq 56–60; Ev 19 (ref to Q 58)

13 Qq 19–24, 108–118, 126–129

14 The control of entry regulations and retail pharmacy services in the UK

2 Improving the information available to clinicians and the public

8. An important aspect of drugs regulation is controlling patient information leaflets, but the number of people who read those provided with medicines is low.¹⁵ The Agency had recognised for some time the need to improve and clarify these leaflets but told us that the minimum requirements for their contents and layout are laid down in EU regulations and require the manufacturer to include the detailed information that appears on their marketing licence, but nothing more patient-orientated. Any changes to improve the flexibility and presentation of the information, for example requiring prioritisation of potential side effects or larger print, would have to go through the European route before they could be incorporated into UK law. There is scope to issue non-compulsory guidance and this the Agency had done, but there was no legal basis to enforce it and, given that there are 15,000 product leaflets on the market, compliance could take a long time.¹⁶

9. Clear and informative leaflets are likely to become increasingly important as the Government increases self-medication. There is also an increasing proliferation of quasi-medicinal products sold over the counter which could increase the risk of side effects and harmful drug interactions.¹⁷ The Agency told us it had recently issued guidance designed to encourage clearer labelling on the outside of drug packaging which it considered patients were more likely to read, but this too was voluntary and they could not give any timetable for completion of its implementation.¹⁸

10. While labelling and leaflets for over-the-counter medicines are important, clear packaging and labelling of drugs used in hospitals is critical, and it may be implicated in up to a quarter of medication errors, some fatal. The Committee on Safety of Medicines had on 3 March 2003 issued guidance to industry designed to reduce these errors and the Agency was prioritising changes on certain medicines where there were known risks.¹⁹

11. The Agency provided safety alerts, usually to prescribers of medicines, where there was evidence of a previously unidentified or increased safety risk. However, some safety messages have failed to get through to doctors, who carried on with potentially dangerous prescribing habits, as in the case of Cisapride, a drug introduced to treat acid regurgitation (heartburn) but later withdrawn.²⁰ Although it had access to information needed to establish which doctors were prescribing potentially interacting drugs, the Agency did not consider it part of its remit to share that information or pass it back to doctors to prevent potential harm to patients. The Agency had on occasion undertaken monitoring to see if prescribing habits changed as a result of its work, as in the case of Zyban (**Figure 3**), but not as a matter of course, and there was no mechanism for taking action against doctors who did not follow its advice. The Department agreed to consider urgently ways of sharing

15 C&AG's Report, paras 3.3–3.4

16 Qq 32, 105–106

17 Q 119

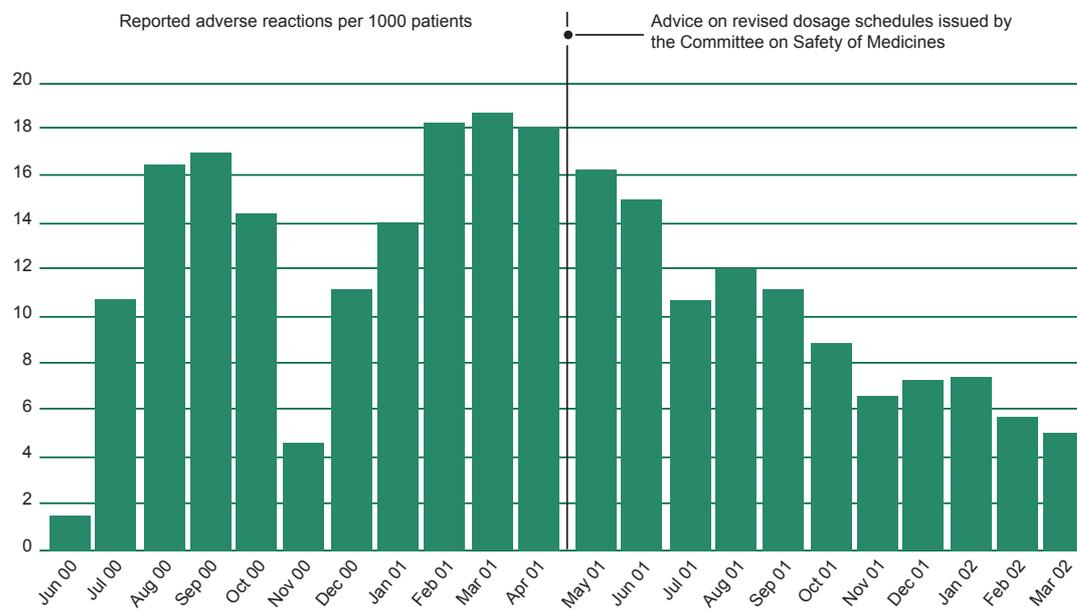
18 Qq 39, 132

19 C&AG's Report, para 3.7–3.8, figures 18–19; Ev 19

20 C&AG's Report, figure 21; Qq 34, 42

information between the Medicines and Healthcare products Regulatory Agency and the National Patient Safety Agency.²¹

Figure 3: Monitoring adverse reactions to the smoking cessation drug Zyban confirmed that safety messages had got through to the public following press publicity and a subsequent safety campaign



Source: Medicines Control Agency

3 Improving internal management and services to stakeholders

12. Since its creation, the Agency had fulfilled the initial aim of speeding up assessment of applications, and told us there was little room for further improvement on major new products.²² It had also responded to concerns from industry about its other services by surveying customers and focusing on reducing backlogs, although recently there had been delays in the progressing of applications for homoeopathic medicines licences.²³ The Agency was not able to provide figures for the likely number of applications under the forthcoming registration schemes for herbal and homoeopathic medicines, but it was likely that implementation of these schemes would require additional resources if backlogs were to be avoided.²⁴

13. The Agency had experienced dramatic fluctuations in its finances over recent years, in part because of a reduction in fees approved by Ministers, but there had also been problems with financial management.²⁵ The Agency had introduced a new finance team and strengthened financial controls. It was also confident that it had effective arrangements in place to manage the new ten-year IT improvement project. As regards protecting public health, fee reductions and fluctuating finances could again cause budgeting problems and threaten safety monitoring work, but the Agency had insufficient information about its own costs to clarify where the stress points could occur.²⁶

14. The NAO Report pointed out that the Agency's written objectives and performance targets failed to cover a number of key areas and focused mainly on outputs such as number of inspections, rather than outcomes.²⁷ This made it difficult for stakeholders to gauge its performance. The Agency explained that historically it had focused mainly on reducing assessment times for new drugs and that it was only two years ago that it had begun to recognise, for example, the need to provide better information to patients. It had yet to translate this shift into revised objectives and would be seeking to do so as part of setting up the new Medicines and Healthcare products Regulatory Agency.²⁸

15. Stakeholders were concerned, too, about the fact that the Agency was funded entirely by fees paid by the pharmaceutical industry, and saw this as a threat to its independence. The existence of an objective to “facilitate the development of a successful UK pharmaceutical industry” added to this concern.²⁹ The Agency, while maintaining that it had clear checks and balances in place to prevent any undue influence by industry,

22 C&AG's Report, paras 4.4–4.5; Qq 122–125, 135

23 C&AG's Report, paras 4.6–4.9; Ev 16–17

24 C&AG's Report, para 1.19; Qq 25–26, 28–30, 121

25 C&AG's Report, paras 1.27–1.28; Q 47

26 Qq 45–49

27 C&AG's Report, paras 1.8–1.14

28 Qq 135–136

29 C&AG's Report, para 4.16

acknowledged a perception that regulator and regulated might seem too close.³⁰ The Agency's funding sources differ from arrangements in some other countries (Figure 4).

Figure 4: Funding arrangements abroad differ from those of the Agency

Regulator	Percentage of funding derived from industry fees
Canadian Therapeutic Products Directorate	66%
US Center for Drug Evaluation and Research	52%
French Agence Française de Sécurité Sanitaire des Produits de Santé	50%
Swedish Medical Products Agency	95%
Netherlands Medicines Evaluation Board Agency	100%
UK Medicines Control Agency	100%

Source: National Audit Office

16. The Agency has had to compete for some of its work with European rivals. It expected the Medicines and Healthcare products Regulatory Agency to continue making a major contribution in Europe whatever the shape of the eventual system of medicines regulation, and did not consider that centralisation of licensing would bring increased risks to public health. The Agency acknowledged, however, that its successor could face management challenges in terms of retention of high-calibre staff, were more of the new drug licensing work to move to the central European Agency.³¹

30 Qq 153–156

31 Qq 18, 66–69

Conclusions and recommendations

1. There is a low level of participation by health professionals in the Agency's Yellow Card Scheme for reporting adverse drug reactions. The Scheme underpins the Agency's work on monitoring medicines' safety but a large proportion of doctors do not contribute reports, some because they do not think it is their responsibility or are too busy. The Medicines and Healthcare products Regulatory Agency should increase awareness of the arrangements by working with Royal Colleges and universities to develop training on medicines' safety monitoring and integrating it into doctors' professional education.
2. The Medicines and Healthcare products Regulatory Agency should expand the work it does to measure the effectiveness of the safety alerts and warnings it issues in changing prescribing habits. The impact should be monitored in all cases where there is a significant risk to public health.
3. The Agency does not make use of the information it has on prescribing practice to give feedback to doctors. The Medicines and Healthcare products Regulatory Agency should develop and implement a method for providing direct feedback to doctors where there is evidence of risky prescribing practice.
4. To highlight and respond to cases where prescribing habits may be putting patients at risk of adverse drug reactions, the Department should facilitate the transfer of information between the Medicines and Healthcare products Regulatory Agency and the National Patient Safety Agency.
5. To promote better medicines safety, the Medicines and Healthcare products Regulatory Agency should obtain better information on the extent of adverse reactions resulting from the prescription to children of medicines which are licensed but not specifically approved for paediatric use. It should use this information to devise guidance for prescribers in the UK and to exert more influence on industry and the European Union to bring in changes that will increase the number of medicines specifically approved for use with children.
6. EU legislation on improving patient information leaflets and labelling is still some way off. In the meantime the Medicines and Healthcare products Regulatory Agency needs to set targets for compliance with the voluntary good practice guidance and work with manufacturers to meet them.
7. The Agency has been working to introduce both a national rules scheme for registration of homoeopathic medicines and, in due course, EU legislation on compulsory registration of herbal medicines. The Medicines and Healthcare products Regulatory Agency should identify the resources needed to cope with applications when these schemes come in to force, and build these into planning assumptions.

Formal minutes

Wednesday 4 June 2003

Members present:

Mr Edward Leigh, in the Chair

Mr Brian Jenkins

Mr George Osborne

Mr David Rendel

Mr Gerry Steinberg

Jon Trickett

Mr Alan Williams

The Committee deliberated.

Draft Report (Safety, quality, efficacy: regulating medicines in the UK), proposed by the Chairman, brought up and read.

Ordered, That the Chairman's draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 16 read and agreed to.

Conclusions and recommendations read and agreed to.

Summary read and agreed to.

Resolved, That the Report be the Twenty-sixth Report of the Committee to the House.

Ordered, That the Chairman do make the Report to the House.

Ordered, That the provisions of Standing Order No 134 (Select Committees (Reports)) be applied to the Report.

[Adjourned till Monday 9 June at 4.30 pm]

Witnesses

Wednesday 5 March 2003

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Dr Gordon Munro, Medicines Control Agency, and **Mr Andy McKeon**,
Department of Health

Ev 1

List of written evidence

1 Department of Health

Ev 16

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Third Report	Tobacco Smuggling	HC 143 (<i>Cm 5770</i>)
Fourth Report	Private Finance Initiative: redevelopment of MOD Main Building	HC 298 (<i>Cm 5789</i>)
Fifth Report	The 2001 outbreak of Foot and Mouth Disease	HC 487 (<i>Cm 5801</i>)
Sixth Report	Ministry of Defence: Exercise Saif Sareea II	HC 502 (<i>Cm 5801</i>)
Seventh Report	Excess Votes 2001–02	HC 503 (<i>N/A</i>)
Eighth Report	Excess Votes (Northern Ireland) 2001–02	HC 504 (<i>N/A</i>)
Ninth Report	The Office for National Statistics: outsourcing the 2001 Census	HC 543 (<i>Cm 5801</i>)
Tenth Report	Individual Learning Accounts	HC 544 (<i>Cm 5802</i>)
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