
GHP

*Guild of
Healthcare
Pharmacists*



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Carol Brennan
MHRA
Market Towers
1, Nine Elms Lane
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Dear Ms Brennan

MHRA Concept Paper on the Review of the Regulation of Unlicensed Medicines: Informal Consultation

Response from the Guild of Healthcare Pharmacists

Thank you for the opportunity to comment on this draft document. The Guild of Healthcare Pharmacists represents UK wide around 4,000 pharmacists including the majority of hospital pharmacists, pharmacists employed by Primary Care Trusts (PCTs) and pharmacists employed by other public bodies such as the Commission for Social Care Inspection and the Healthcare Commission. The Guild is part of the health sector of the union Unite-Amicus section.

We agree with the aims of the review set out on page 1 of the consultation document.

In general we had some difficulty in interpreting the intention behind some of the questions.

Comments on various points are shown below in the order in which they appear in the consultation document.

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We query whether the information on unlicensed medicines in the BP is published anywhere else? It is not very accessible to its target audience for example prescribers, who are unlikely to go to such a document.

Questions and responses

What are reasonable expectations of Article 5.1 arrangements?

16. It would be helpful to clarify the expectations of various parties:

- What are the expectations of healthcare professionals and patients about the extent of regulatory or other safeguards that should apply in relation to the clinician's wish to use unlicensed medicines?

Patients will expect safeguards such that all products are safe. They would expect regulatory processes to achieve this. Some may wish to take risks on effectiveness: see below.

Pharmacists wish for a process that ensures that the preparation is safe to use and that some degree of effectiveness has been demonstrated. They consider that although the use of a licensed medicine at all times would be desirable, full licensing will never be achieved as a particular preparation may never be commercially viable due to relatively low use. There needs to be a workable way of using unlicensed medicines whilst putting in sufficient safeguards on safety and efficacy.

- To what extent, and how, will these expectations vary depending on the situation in which the unlicensed medicine is to be used?

How far should arrangements accommodate a situation in which the patient is willing to accept risk, for example a seriously ill patient where there are no effective alternative therapeutic alternatives; or a patient who has a strong preference to use, or to avoid using, a particular type of medicine?

Expectations of patients may vary according to their situation. A patient with a terminal illness might be prepared to accept a less safe or less effective product if there was some degree of hope that this might prolong their life. Arrangements should accommodate this type of situation.

How can clear accountability be achieved?

17. The essence of Art 5.1 is that an authorised healthcare professional makes a clinical judgement that a patient has a special need that can most appropriately be met by an unlicensed product. Against that background:

- To what extent and in what circumstances should regulatory arrangements seek to challenge or hinder the meeting of what the clinician judges to be the needs of their patient?

To meet all scenarios in 16 above the regulatory arrangements should address significant safety issues, but effectiveness to a lesser degree, recognizing that there may not be much information on the effectiveness of the preparation. However the arrangements should not be so stringent as to prevent use in cases of real need. Where there is no licensed product available a risk assessment should be carried out to ensure that the patient is not put at any more risk than absolutely necessary.

- Are there situations in which the accountability of the clinician might need to be modified? For example, there may be situations in which the NHS, on account of the lack of a UK licensed product or a shortfall in its supply, positively wishes clinicians to make use of a medicinal product that is not licensed in the UK. What should be the effect on professional indemnity of the prescriber?

In this situation the liability should perhaps rest with the NHS employer as it is unlikely that in a supply shortage situation of a licensed product that all the prescribers would be aware that the product being used in its place is unlicensed.

In what areas may specific safeguards for the public be desirable or necessary under any UK Article 5.1 arrangements?

18. The following are among issues that could be addressed:

- Safety issues inherent in the product (eg where a UK marketing authorisation has been refused, or has been granted and then subsequently withdrawn, on the basis that the risk of adverse reactions with the product outweighs likely benefits)

Regulatory arrangements should cover this type of product.

- Safety issues arising from quality of the product (eg risk of contamination if manufacturing were not required to meet set standards)

We query where such products might currently be made. NHS hospitals producing “specials” have either a manufacturing licence or are required to implement GMP through circulars EL(96)95 and EL(97)52 and are inspected by the regional Quality Controller. If private practice does not have equivalent safeguards where there is no manufacturing licence there would be scope for introducing comparable controls.

- Safety issues concerning possible inappropriate use of the product (eg if arrangements do not require the patient to receive systematic information about safe usage)

Good practice and the EC Directive on information for patients dictates that the use of the preparation is explained to the patient and they are given written information in addition.

- Issues arising from prescribing an unlicensed product where the patient has no special need because a suitable licensed product, meeting comprehensive regulatory standards of safety, quality and efficacy, is available.

If the products are absolutely equivalent it would be logical that there might be a requirement to use the licensed product. However, where absolute equivalence does not exist, for example a different strength, size of ampoule or IV bag, or the presentation of the product itself for example in a syringe ready prepared rather than an ampoule, there may be reasons of safety in use which dictate that the licensed product is not use. For example, if the use of a licensed injectable product increases the in use risk score using the NPSA injectable medicines risk assessment score, the licensed product may not be acceptable. Another example might be really poor labelling of the licensed product. The MHRA needs to take a much stronger line on labelling for safety when approving market authorisations.

What types of safeguard are needed?

19. A range of forms of safeguards could be considered, possibly in combination:

- It will be helpful to identify how far desired safeguards and intended objectives could best be achieved by:

Updated and strengthened professional guidance and accountability

This might be one method which could be used provided that there is sufficient input from healthcare professionals working in the field and from patients/patient organizations.

Governance arrangements in the NHS and in private healthcare

In the NHS, and in larger private organizations this should be achievable, but smaller private organizations may not have the capacity.

Requirements in medicines legislation, eg operated by the MHRA

Requirements in medicines legislation should be the last resort, other than to create a level playing field for example between the NHS and private practice.

Any other means.

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20. It may be necessary to look well beyond the role of the individual clinician commissioning the unlicensed medicines, for example:

- Overall monitoring of UK Art 5.1 arrangements could be required to ensure that usage is consistent with the terms of Art 5.1 and with UK policy objectives as reflected in domestic legislation and/or guidance

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- Clinicians or those ordering unlicensed products at their request, might lack expertise or information on manufacturing standards; patients and clinicians may therefore benefit from arrangements which serve to identify which manufacturers of unlicensed medicinal products are operating to production standards deemed acceptable. (Under the current requirement “specials” manufacturers are required to have a licence demonstrating they meet Good Manufacturing Practice and are subject to MHRA inspection.)

This paragraph implies that unlicensed preparations are obtained from “unaccredited” sources. If this is the case it would be useful for the MHRA to publish a list of “specialist” manufacturers with a licence demonstrating that they meet GMP requirements and are subject to MHRA inspection. Guidance should indicate that unlicensed preparations should normally be obtained from such a source (apart from hospitals working under Medicines Act exemptions but which are meeting GMP standards and supplying only their own organization). This should be a minimum cost item for the MHRA as the information is already available. Where an organization such as a hospital manufacturing unit does not supply outside customers this could be indicated.

How can proportionality and targeting of safeguards be achieved?

21. The use of arrangements under Art 5.1 covers a wide variety of situations, from ones where public health risk may be low to others where there is considerable risk.

- How can any regulation or other safeguards best distinguish between areas of higher and lower public health risk and target the former?

Current systems for “vetting” the use of unlicensed medicines in the NHS and parts of the private sector in outline are as follows.

If a clinician request the pharmacy for an unlicensed product the request has to be supported by clinical and safety information on the product. The pharmacy carries out an evaluation of the use and presents it to the drugs and therapeutics committee or equivalent committee for approval. If there are safety issues these should be picked up and the request may be refused. However the process is extremely time

consuming and it is not always easy to access the information needed. Reasons for refusal have included safety issues for staff preparing the product, or products already deemed unsafe to use by other organizations.

- Possible ways of targeting could include positive or negative lists of products or types of products, or other criteria that distinguish between situations where a greater or lesser degree of control or scrutiny is required.

Published lists of high/low risk products/type of products and other criteria that distinguish between situations of high/low risk would be helpful.

Our reply may be made freely available.

Yours sincerely

Jean Curtis

Jean Curtis
Professional Secretary