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Establishing good authentication practice (GAP) in secondary care to protect against falsified medicines and improve patient safety

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Sustained growth of falsified and counterfeit medicines in the legal supply chain is a critical threat to patients, (bio)pharmaceutical companies, caregivers, payers and pharmacists.^{1–2} The European Union (EU) Falsified Medicines Directive (FMD) is a tractable opportunity to mitigate this threat and optimise healthcare delivery, including through the optimisation of pharmacy workflows and support of patient adherence. In order to deliver these benefits, and ensure FMD compliance, the production and regular review of Good Authentication Practice (GAP) guidelines is an essential step.

FALSIFIED MEDICINES

'Falsified medicines' are 'fake medicines that pass themselves off as real, authorised medicines', according to the European Medicines Agency (EMA).³ They may contain incorrect ingredients, low-grade ingredients or incorrect doses and may have suspicious distribution histories or unofficial packaging.⁴ These products may be mislabelled, misleading and dangerous to the consumer.

In recent years, there has been an increase in falsified and counterfeit medicines, which increases the risk of inadvertent administration and can result in detrimental patient effects. Such effects include failed treatment, adverse side effects and, in some cases, death.^{5–7}

The distribution of falsified medicine is not restricted to on-line purchases or developing countries; the problem spans the entire global market and a variety of distribution chains, from medicines sourced online to treatments supplied through the UK National Health Service (NHS)^{1–5–7} (table 1).

In response to this growing problem, the European Parliament and the Council of the European Union have published the EU FMD (Directive 2011/62/EU), which requires complete implementation by 2018.⁸ The Directive states that each eligible medicinal product must have a unique identifier and tamper-evident seal to allow for the authentication of each medicine pack at the point of dispensing (table 2).

EXPIRED AND RECALLED MEDICINES

Medicine authentication systems should not only identify falsified medicines but also expired and recalled medicines. Current recall methods depend on regulatory authority alerts and removal of recalled medicines at a variety of stages in the drug distribution cycle. An alert to identify a recalled medicine at the authentication stage of dispensing will act as a further safety measure.

AUTHENTICATION AND VERIFICATION

New authentication services must verify and authenticate medicinal products. Verification of authenticity, recalled status and expiry must occur multiple times at a variety of stages in the drug distribution cycle. However, authentication will occur only once at the point of dispense, ensuring that medicines are not reintroduced into the drug distribution chain after dispensing. The hospital pharmacist is positively positioned to carry out the task of authentication, and has become the key healthcare professional in the fight against falsified medication.⁹

SECONDARY CARE AUTHENTICATION

Based on preliminary, practice-based research in a UK NHS Teaching Hospital, using the Aegate Ltd (Melbourn, UK) authentication service,¹⁰ it has become evident that authentication in secondary care presents unique challenges. The following GAP guidelines are proposed to alleviate such challenges:

1. Each individual hospital must decide on the optimum point for medicines authentication. According to the draft FMD delegated acts,^{11–12} in certain circumstances the point of authentication can be earlier than the time the medicinal product is supplied to the public. However, preliminary research at the pilot site has indicated that authentication by an accredited pharmacy technician or pharmacist as the last step in the checking process would be most valuable. Authentication at the very final stage ensures safety directly before leaving the dispensary.
2. Robotic authentication should be favoured over manual where possible using 2D data matrix scanners to reduce the risk of dispensing without authentication while facilitating lean working. Scanning each individual medicinal product can be a time-consuming process if not correctly integrated with dispensary workflow and adds a step to an already lengthy process. Robotic authentication removes the risk of human error. However, only robotic dispensing systems with suitable built-in scanners would appear to have the capability of robotic authentication at the point of dispensing.
3. Medicines identified as falsified or recalled should be quarantined for the inspection of suitably qualified professionals to investigate. These professionals include the medicines safety team, medicines information department or quality control team.

Table 1 Examples of recent global incidents of falsified medicine use^{5 6}

Falsified medicine (indication)	Country/Year	Report
Avastin (anticancer)	USA/2012	Drug lacked active ingredient. Used in 19 medical practices
Viagra and Cialis (erectile dysfunction)	UK/2012	Smuggled into the UK. Contained undeclared active ingredients, compromising patient safety
Zidolam-N (anti-HIV/AIDS)	Kenya/2011	Three thousand people affected by falsified batch
Glibenclamide (antidiabetic medicine)	China/2009	Contained six times the normal dose of active ingredient. Two deaths and nine hospitalisations
Seretide Evohaler (asthma)	UK/2009	Batch recalled due to EU Customs Intelligence

- Medicines should be dispensed in full packs and only be removed from original containers for administration to the patient.

This ensures that medicines remain in a container with a 2D data matrix at all times allowing for verification at any stage. It also ensures that any medicines returned to pharmacy can be verified for future redispensing.

- If dispensing from split packs does occur, the original container should not leave the dispensary until its entire contents are used.

Although medicine packs can only be authenticated once, this method ensures that medicines dispensed from split packs can still be verified before each dispensing.

- Medicines that are removed from split packs should be verified by scanning the 2D data matrix on the original container and transferred into a suitable container.

Although a packet can only be authenticated once, this method allows for each dispense to be verified each time.

- Medicines authentication services should have an option to differentiate between a product dispensed elsewhere and a product dispensed in-house.

This option would ensure products 'Dispensed Elsewhere' are identified as suspicious and those 'Dispensed Here' can safely be reused in-house.

- Once a national medicines serial code repository is established and in operation, any medicine returned to pharmacy, intended for reuse and outside of their original container should be reverified by contacting the medicines authentication service citing the product batch number and expiry date.

Table 2 Summary of the Falsified Medicines Directive⁸

1	All European pharmacies will be affected by this directive
2	Over-the-counter medicines (unless deemed vulnerable) will not require authentication
3	All prescription-only medicines (unless excluded via risk assessment) will require authentication
4	Tamper-evident seals will be required for all products covered by the FMD
5	Serial numbers and 2D barcodes are to be attached at manufacture
6	Manufacturers are responsible for the cost of the medicines authentication service

Products returned from wards outside of original containers will not contain a 2D barcode. This makes authentication of such a product very difficult. It would appear that only through direct communication with the medicines authentication service provider will authentication or reverification of these products be possible.

- If a medicine has been authenticated but is no longer required for the current dispensing process, there should be an option to highlight the medicine on screen and click undo to return the product to stock.

An undo button would allow the medicine to be returned to stock unauthenticated, permitting the product to be authenticated when next dispensed.

- Authentication should be incorporated into departmental procedures. Incidents where medicinal products leave a dispensary without authentication should be classed as a dispensing error.

It is advised that departments incorporate the authentication of medicines into daily processes to ensure compliance with the FMD.

- Authentication of extemporaneously prepared medicines should occur at product assembly before final product preparation by a qualified member of staff.

The preparation of extemporaneous products is often a lengthy process performed on an individual patient basis. Detection of falsified, expired or recalled ingredients before production is a time-efficient approach which reduces the need to remake products due to unsuitable ingredients.

- Authentication procedures must include checking that the tamper-evident seal has not been altered.

Medicines authentication includes examination of the tamper-evident seal as well as product scanning.

CONCLUSIONS

Adopting these guidelines will aid a smooth transition to the implementation of an authentication and verification system in secondary care, minimising risks to patient safety and facilitating pharmacy compliance.

LIMITATIONS

These guidelines are subject to change based on the FMD delegated acts. Authentication of medicines in secondary care is at an early stage of development and best practices may change with experience and research.

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LTD (Oxford UK). It must be stressed that this publication was created purely for practice and academic interest. DAB is a stockholder in IP Assett Ventures and Translation Ventures Ltd (Charlbury, Oxfordshire, UK), a company that among other services provides cell therapy biomanufacturing, regulatory and financial advice to clients in the cell therapy sector. DAB is subject to the Chartered Financial Analyst Institute (CFA) Institute's Codes, Standards, and Guidelines, and as such, this author must stress that this piece is provided for academic interest only and must not be construed in any way as an investment recommendation.

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