Medicines & Healthcare products Regulatory Agency

Regulator's Update

NHS QATS Symposium 2025

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September 2025

1

Putting patients first

The MHRA published its Business Plan for 2025-26. This is the final year of the three-year Corporate Plan 2023–26.

Our priorities were set out as follows:

- Protecting public safety and maintaining public trust
- Delivering efficient predictable services through regulatory excellence
- Being an agile organisation that drives innovation

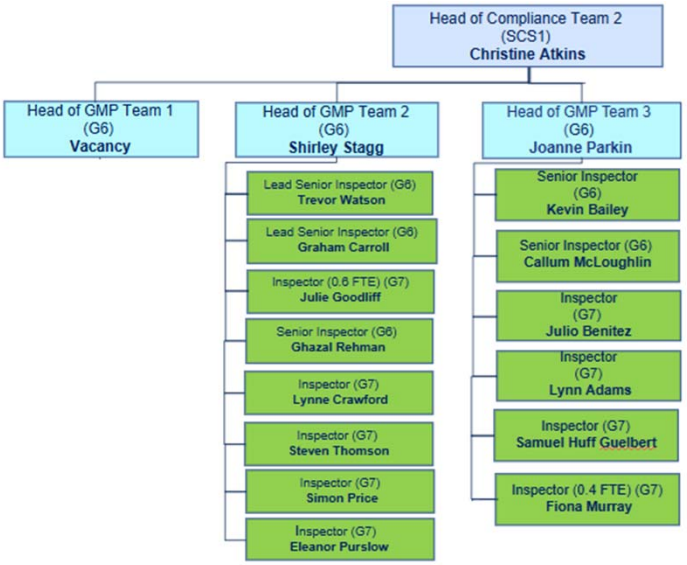
2

Outline

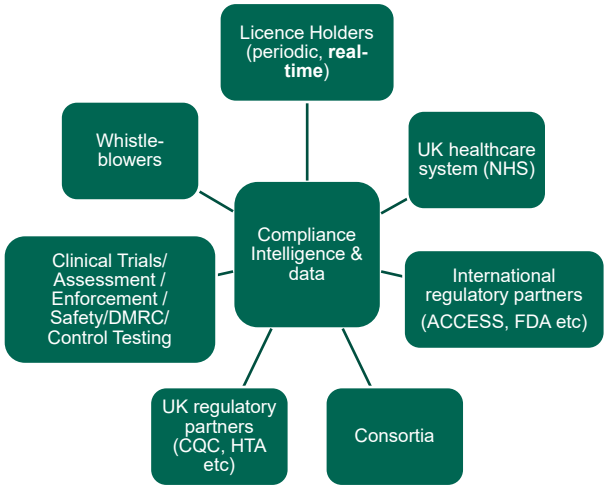
- GMP Inspectorate
  - Inspectorate team for Unlicensed Medicines
  - Inspection programme / focus
- Collaboration
- Inspection Hot Topics and findings

GMP Inspectorate team

A subset of this team support sites that handle 'Unlicensed' Medicines



Enhanced use of data



Optimal access and use of intelligence and data is critical to our ability to use risk to drive our compliance programme and an Outcome Based Collaborative Regulation (OBCR) model for regulatory oversight. Better use of data will also better inform inspectors during the conduct of inspections.

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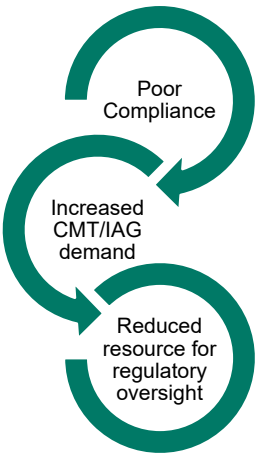
Upstream intervention



Poor compliance results in significant downstream impact on patients, the supply chain and the resources of the regulator (CMT, IAG). By increasing our upstream engagement across the product lifecycle with stakeholders we can inform and educate and reduce the cost of poor compliance

6

6

UK Collaboration – The future?

Information sharing on sites within the UK

- NHS QA Regional Assurance – Section 10 Facilities
- MHRA Inspectorate – MS licenced facilities

- Common systems?
- Common findings?
- Impact onto alternative services?

Nothing is fixed, however conversations and consideration for this remain ongoing

7

7

GMP Inspections of MS licenced facilities – hot topics

- Compliance with general Pharmaceutical Quality System requirements
- Understanding staffing requirements and proactive monitoring of capacity
- Release processes
- Sterility assurance controls
  - Material transfer controls and sanitisation

8

8

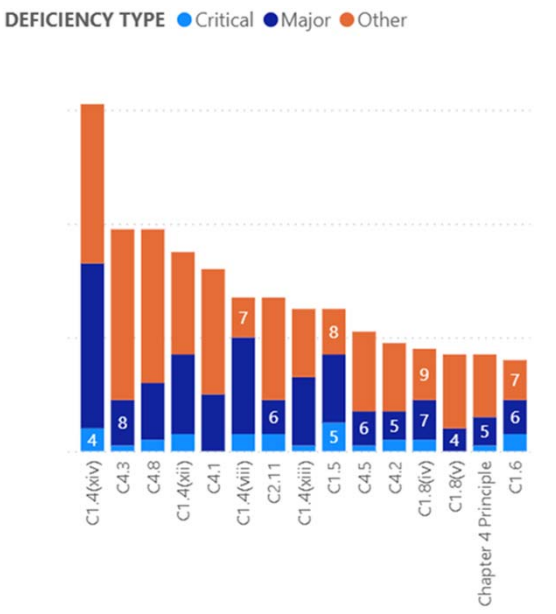
Deficiency data Aug.2024 to now

Excluding Annex 1 references and references to other guidance documents, the top 15 cited references for MS licenced sites are shown here.

Key areas:

- Chapter 1 – Pharmaceutical Quality System
- Chapter 4 – Documentation

The bars reflect the number of times that specific reference has been cited in the past year



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Pharmaceutical Quality systems

- Deviations
  - Robustness of assessment and investigation
  - Assignment of criticality
- Change control management
  - Prospective assessments of changes in advance of implementation
  - Consideration of impact to the licence and also capacity
  - Appropriate effectiveness checks
- Recalls
  - Anything that has left the MS licenced unit is a recall (even if still on the same NHS trust)
  - Recalls should be rapid and timely
  - Recalls are still needed even after administration, if information acquired after this occurs
  - Recalls must be reported to the DMRC

10

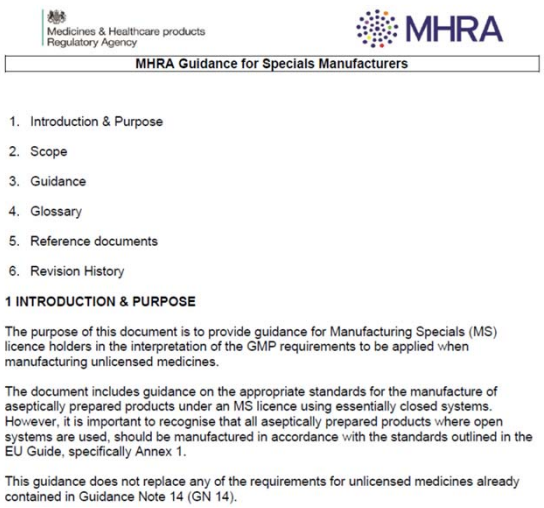
10

Specials Specific references

Nearly every inspection finding letter will include a reference to the
MHRA Guidance for 'Specials' manufacturers

This includes information for example on:

- Capacity Planning
- Order management
- Batch release and Releasing Officers
- Production aspects, including:
  - Auto-compounders
  - Aseptic controls
  - Contamination controls inc. Sanitisation
  - Monitoring – Particulate, EM
  - Labelling



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MHRA

MHRA Guidance for Specials Manufacturers

1. Introduction & Purpose
2. Scope
3. Guidance
4. Glossary
5. Reference documents
6. Revision History

1 INTRODUCTION & PURPOSE

The purpose of this document is to provide guidance for Manufacturing Specials (MS) licence holders in the interpretation of the GMP requirements to be applied when manufacturing unlicensed medicines.

The document includes guidance on the appropriate standards for the manufacture of aseptically prepared products under an MS licence using essentially closed systems. However, it is important to recognise that all aseptically prepared products where open systems are used, should be manufactured in accordance with the standards outlined in the EU Guide, specifically Annex 1.

This guidance does not replace any of the requirements for unlicensed medicines already contained in Guidance Note 14 (GN 14).

Specials Specific Aspects - Capacity (section 3.1.3)

- A capacity plan should be in place, to ensure adequate resourcing for the expected demand.
- There should be a thorough understanding of production demand and supply constraints, and appropriate strategies to highlight imbalances in a timely manner to ensure appropriate action is taken.
- Capacity plans should also address associated essential tasks such as maintenance of the quality management system, order entry, surface sanitisation, preparation activities, and product release and any other relevant activities so that a company clearly understands any bottlenecks in its process.
- A unit's defined capacity should only be exceeded infrequently. If it is exceeded, approval from QA must be sought through the use of the planned deviation system.
- Compliance with the capacity plan should be assessed at a minimum monthly during management review and reviewed at least annually. Any changes should be evaluated through the change control system.

Specials Specific Aspects – Capacity deficiency examples

- Senior Executive Management had not ensured that an adequate number of experienced personnel were available to implement and maintain the quality system and support manufacturing operations
- General levels of staff absence due to annual leave, sickness, training requirements or staff attrition were not factored into the prospective management of capacity plans.
- Projected Capacity frequently exceeded the procedural 80% limit, with weekly capacity figures for up to 125%
- The quality system was not adequately resourced and did not ensure that there were sufficient trained personnel and resources available for the handling, assessment, investigation and review of complaints and quality defects
- Corrective and preventative actions, document review, supplier review, nonconformances, change controls and self-inspection actions were found to be overdue.
- There was no formal capacity plan in place, and data was not routinely reported or trended.
- The Capacity Planning SOP lacked detail on recording and escalating breaches of capacity

Specials Specific Aspects – Labelling (sections 3.5.14 & 3.12.9)

3.12.9 BP labelling requirements for unlicensed medicine.

Unlicensed medicines should be labelled as per the BP general monograph for unlicensed medicines (part II and V) and in accordance with the general monograph for the specific dosage form. The monograph lists critical information which must appear on the label

Labelling is not simply for internal identification. The following should be included:

- The MS licence number if manufactured on site (but cannot be on any S10 or blood labelling products)
- Route of administration
- Excipients of known effect or all excipients for injectable, topical or ophthalmic products

This list is not exhaustive

Specials Specific Aspects – Release (sections 3.1.6 & 3.2.1)

- Batch release must include an independent check against the original order (or prescription if manufactured as a bespoke product for an individual patient).
- For Internal batch orders, release should be against a specification or equivalent document in anticipation of supply.
  - These are at the time of product release, not pre-check
- Releasing officers should be named within the Quality System and be approved for batch release activities by the person named on the licence for QC
- A releasing officer should typically have at least 2 years post-qualification relevant GMP experience

Sterility Assurance and Material Transfer

- In March 2025 a letter was sent to all Manufacturer's "Specials" (MS) Licence holders who were involved in the manufacture of sterile products.
- This was then supported by a Blog post: MHRA Letter to MS licence holders – Aseptic operations – MHRA Inspectorate
- This was part of the continued focus on the control of aseptic operations, linked to the expectations for the sanitisation of components and equipment being transferred into the grade A working zone, and also activities linked to the preparation of pooled bulk products (pooling) or intermediate products.

Sterility Assurance and Material Transfer deficiency examples

- Operators failed to overlap wipe strokes when transferring items or on work surfaces
- Operators failed to wipe the top of a vial, and the edges of an infusion bag, when transferring into the grade A Laminar Air Flow (LAF) cabinet.
- Unidirectional wiping was inconsistent, and wipes were not folded to a flat unused surface for each subsequent item.
- Triple wrapped sterile items were not being transferred in the intended manner to reduce contamination and were being manually transferred via spray and wipe process.
- Hold times of consumables in grade C was not controlled in any procedure
- Generic binbag liners for waste were transferred for use within the Grade B rooms, and large trays used for transfer had notches and handles which were difficult to sanitise
- The material transfer process from controlled unclassified to Grade B did not consider the risk of the length of time taken between sporicidal wipe and movement of items into the grade B, when these items were exposed to an unclassified environment in the set-up area which had frequent foot traffic

17

Material Transfer Verification deficiency examples

- The qualification did not ensure a robust verification challenge was in place as only 1 out of 10 items was required to have >0 colonies pre-sanitisation.
- The protocol for transfer validation did not offer robust assurance of the process as the bioburden of the items before the process was not known.
- Each item was tested using a single contact plate and did not ensure the most challenging areas such as the end flaps on syringe wrapping were sampled.
- Transfer qualification was not carried out using two duplicate sets of samples to separate pre and post sanitisation sampling, negating the challenge conditions where monitoring / testing action has a cleaning effect in itself.
- The protocol for transfer validation did not adequately stipulate a representative number or type of relevant items
- Verification qualification criteria did not demonstrate robust and effective sanitisation as operators alert and action limits allowed for growth post sanitisation without justification.
- Manual Material Transfer qualification for operators had not been carried out routinely and as such an effective transfer disinfection was not currently assured.

18

Other thoughts

- Environmental Monitoring
- Process Validation / Aseptic Process simulation and Operator assessments
- Aging Sites

19

Key message

- Good controls will help manage the overall compliance and Patient Safety
  - Robust and timely Quality systems
  - Focus on sterility assurance and prevention of contamination
  - Appropriate qualified staffing levels
- Use the available information and support systems
  - Learn from each other
  - Share information between units and the SPS or Regional Leads
  - Share information with the MHRA – via Interim Compliance reports and DMRC reporting
  - Use the published information
    - EU GMP chapters and Annexes
    - MHRA guidance and blogs
    - NHS publications (Aseptic Services)

20

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Thank you

21

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22

22