Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

MHRA GMP Inspections

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MHRA
Regulating Medicines and Medical Devices

How MHRA select GMP inspection sites

MHRA GMP inspection method

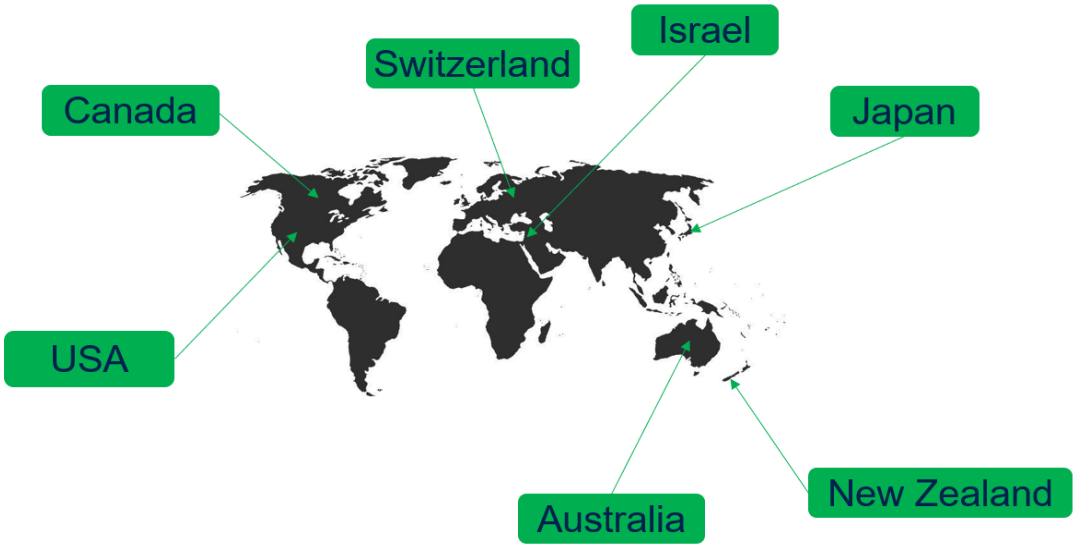
Typical GMP inspection duration

GMP inspection frequencies

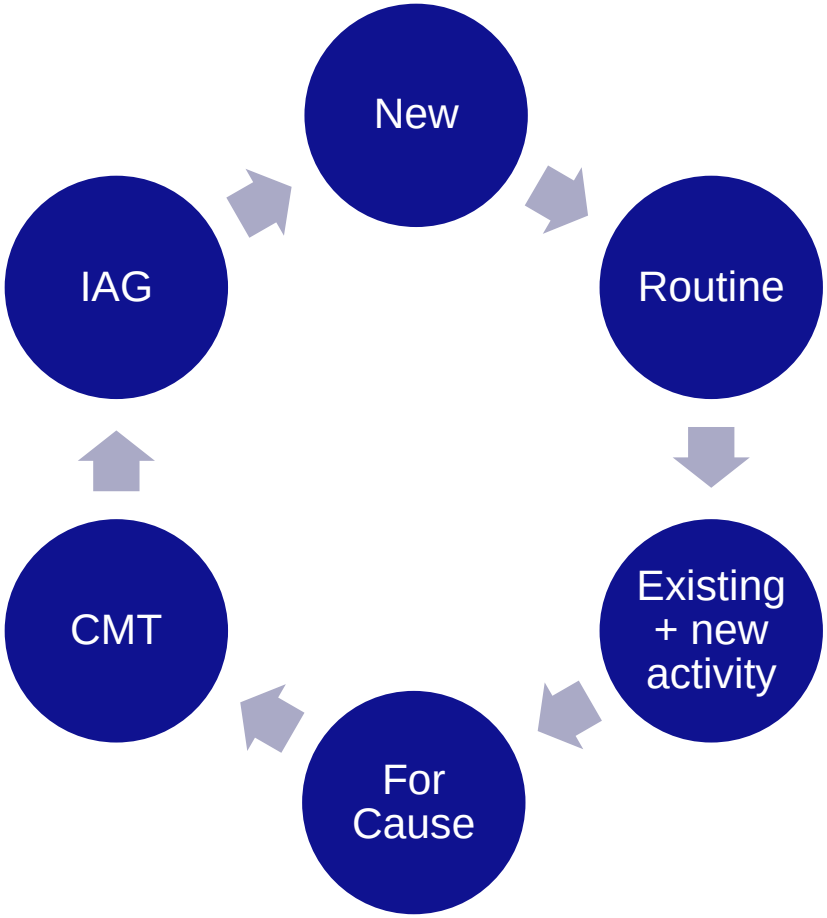
Annual number of GMP inspections

How MHRA select GMP inspection sites

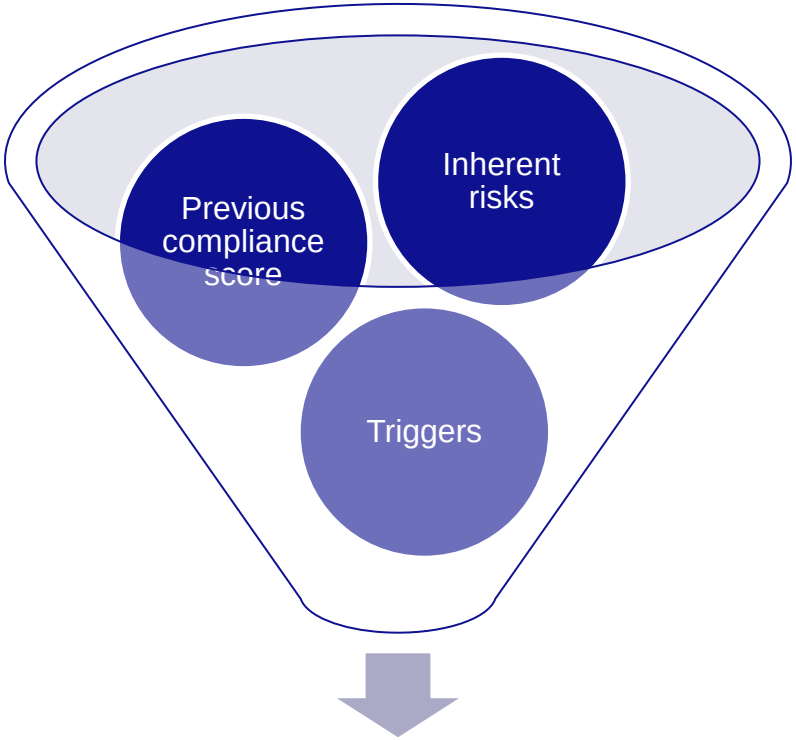
UK & Rest of World*



How MHRA select GMP inspection sites



How MHRA select GMP inspection sites



Risk Based Inspection Process

Pre-Inspection Compliance Report

Shift in Performance	Key Personnel	Company Ownership /Structure or Status	Processes /Products	Facilities/ Equipment	Data Integrity Policy	Computerised systems
Assurance of QMS and site under control (i.e. metrics for deviations/ complaints/ recalls)	Changes to organisation and numbers	Details	Changes in type and number of products and outsourcing GMP issues with API suppliers Rejected batches, sterility test and media fill failures	Changes to buildings/ equipment/ contract laboratories	Do you have one?	Listed out SMEs to be available

GMP Inspection Method

What happens on site

Deficiency classifications

Compliance Management process

Inspection Action Group

What happens on site

- Opening meeting
- Review of changes
- High risk to low risk
- Process detail
- Not process order!
- Pause & regroup
- Closing meeting

Deficiency Classifications

Other Major Critical

Compliance Management process

Who

- Non-statutory process
- Senior Inspectorate staff

When

- Significant poor / marginal compliance
- Large number of Major deficiencies
- Persistent poor compliance
- Inadequate responses to inspection
- Following IAG for closer monitoring
- Not formal regulatory action

How

- New referrals via e-correspondence and meetings as required
- Deficiencies referred to a CMT representative
- Review and discuss with site Inspector
- Post inspection letter signed by Senior* Inspectorate staff member

Why

- Escalate case management and direct companies to a state of compliance
- Protect public health and try to avoid the need for regulatory action
- Maintain supply of medicines

Inspection Action Group

Who

- Regulatory Unit Manager (chair)
- Medical Assessor
- Pharmaceutical Assessor
- Solicitor (DH Legal Services)
- IAG Secretariat Member
- Referring Inspector(s)
- Enforcement representative
- Expert / Lead Senior Inspector from respective GXP
- VMD representative as applicable

When

- Usually if one or more Critical deficiencies identified during inspection
- Unable to contact licence holder
- Refusal to accept inspection
- Unacceptable applications or variations (e.g. refusal to name a QP)
- Inadequate responses to post inspection letter
- CMT case escalation
- Result of product recall / DMRC
- Issues raised by EU Member States
- Outcome of Enforcement activity

How

- Confirm referral to IAG during closing meeting
- Included in post inspection letter signed by Senior* Inspectorate staff member
- All correspondence from that point via IAG Secretariat
- Other trigger: letter only

Inspection Action Group

Gather information

- Will want to know the potential impact of supply issues on the patient
- What markets are supplied, All EU and MRA partners?

Possible outcomes (UK)

- Refusal to grant licence or variation
- Revoke, vary or suspension of licence (proposed or immediate)
- Statement of non-compliance with GMP (for finished product or API site)
- Restricted GMP certificate (for finished product or API site)
- Removal of QP/RP from the licence
- Cease and desist order for BEA
- Request QP for justification of actions or refer to professional body
- Request company to attend a meeting at MHRA offices
- Referral to Enforcement

Possible outcomes (Non-UK)

- Refusal to name a site on a Marketing Authorisation
- Recommend removal from a Marketing Authorisation
- [Conditioned] Statement of non-compliance with GMP
- Restricted GMP certificate
- Triggered API inspection – removal of site from Marketing Authorisation
- Triggered IMP inspection – suspension of clinical trial

Typical GMP Inspection duration

Follows EU COUP

From 1-10 days

~800 sites, overseas >350

GMP inspection frequencies

Follows EU COUP

0 - 3 years*

Flexibility

	Intrinsic		
Compliance Risk	Low	Medium	High
Low	Risk Rating = A	Risk Rating = A	Risk Rating = B
Medium	Risk Rating = A	Risk Rating = B	Risk Rating = C
High	Risk Rating = B	Risk Rating = C	Risk Rating = C

Risk Rating	Suggested Inspection Frequency
A	Reduced Frequency, 2 to 3 yrs
B	Moderate Frequency, 1 to 2 yrs
C	Increased Frequency, < 1 yr

Annual number of GMP inspections

Conducted over 1200 inspections during the year with over 183 being performed at overseas companies.

Issued over 5,550 export certificates (including 1,615 requests within 48 hours).

Issued over 2,075 licences (a combination of Wholesale, Manufacturing and Active Pharmaceutical Ingredients), supporting those conducting processing activities.

315 GMP UK inspections performed, equating to 667 man days

An additional 64 sites overseas where inspected for GMP consisting another 670 man days

Continued to develop the Inspectorate blog: we now have 10,471 subscribers and our most popular posts have received over 43,000 hits.

Organised major symposia on all aspects of inspections which were attended by around 3,000 delegates.

We spoke at over 30 conference events.

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