Medicines & Healthcare products Regulatory Agency

MHRA

MHRA GDP Symposium

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#GMDPevents

Medicines & Healthcare products Regulatory Agency

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Questions and Answers

Question:

If major Pharmaceutical Manufacturers don't provide original copies of their licenses as part of the Supplier Approval process, is it considered acceptable to have carried out a risk-assessment on those suppliers to justify the absence, and to have records evidencing due diligence checks (such as financials, Eudra checks, website info etc, statement requests asking site to confirm what their license scope is) to mitigate the lack of original licenses? The GDP guidelines state these databases should not be relied upon as a method of approval as they don't contain all details however it is hard to know what to do if major Pharma companies won't provide the information requested.

Answer:

Yes alternative methods of supply qualification can be relied upon. In accordance with local procedures and risk assessments.

Question:

Why when EU Guidelines 343/01 state in Chapter 1.2 that 'the size, structure and complexity of distributor's activities should be taken into consideration when developing or modifying the quality system', are MHRA Inspectors inconsistently placing onerous burdens on small wholesalers, with very small numbers of staff and limited and straightforward operations, unless they are seeking to drive smaller companies out of the business, which leaves less choice, less competition, and ultimately higher costs for the people and organisations wishing to procure medicines.

Answer:

No, the guidelines are written that the QMS is commensurate to the size and nature of the business.

Question:

In discussions with other professionals, it is apparent that MHRA Inspectors are inconsistently placing an unrealistic burden of oversight on Contract Responsible Persons, named on the licences of largely small wholesalers, who do not wish or are unable to provide the experience, knowledge and expertise in house. It is apparent that some Inspectors in some companies are expecting Contract RPs to demonstrate the same detailed level of knowledge of a wholesaler's day to day business as they would of a full time employee. This again is inconsistent with a previous approach where the MHRA were reluctant to allow Managers and Directors of companies to act as their own RPs as there was a conflict of duties, responsibilities and targets. Can the MHRA GDP Inspectorate give clear, consistent guidelines to Contract RPs as to their expectations in the application of their interpretation of the implementation of the EU Guidelines, and associated legislation.

Answer:

The MHRA do not differentiate between the standard of a contract RP's and those RP's directly employed at the company.

Question:

If a warehouse location wants to receive 5°C cold chain stock into their site but they will only 'handle' the stock at the site by unloading it from one temperature controlled trailer directly onto another, without storing or holding the stock, would they still need a WDA licence to perform this function because it is cold chain and not ambient product?

Answer:

If they are not actively changing or providing or adjusting the cooling methods then no WDA is required.

Question:

Why does the MHRA specifically limit ambient goods to a storage time of 36hrs at a warehouse location before a WDA licence is required and prohibit any dwell time for cold chain goods without the WDA, yet in the EU the EMA allows a storage time of 72hrs for both ambient and cold chain goods to be held prior to any WDA being required? Why is there not a harmonised approach across the EU?

Answer:

The UK policy position has been 36 hours for many years. As time it is not covered by any regulation EU member states are free to set their own time limits.

Question:

What is the proposed timeline for MHRA to implement licensing and routine Inspection of Active Substance sites, in order for UK to apply for whitelisting as a Third Country under 2001/83 Article 111b, or to allow the provision by MHRA of written confirmations under Article 46b?

Answer:

The MHRA already requires registration of UK based API manufacturing, distribution and importation sites. A programme of routine inspections of UK based API sites is already in place and has been in operation for a number of years.

Question:

If a European customer is collecting purchased stock (paid for on proforma) from a UK WDA Holder and has signed a TA to take responsibility for this, what does the UK WDA holder then require to see regarding temperature validation during transport?

Answer:

The supplying WDA holder should ensure that due diligence is applied to ensure transport mythology is GDP complaint.

Question:

If a pharmacy has applied for a WDA and has begun to ensure that the storage areas and audit trails are GDP compliant, is there any way that stock originally purchased in and stored under the pharmacy during this time, which is not able to be used by the pharmacy could be passed over to the wholesale side of the business once the licence was granted? Could the RP in this case assess approved supplier, storage etc and make a decision, or is it the case that the stock was purchased before the licence was granted and can not therefore pass over to the wholesale side of the business?

Answer:

No, it has been stored outside of the controlled supply chain.

Question:

Is the designation on a WDA(H) of 3.1.3 Immunological Medicinal Products, intended to cover vaccinations such as pneumococcal vaccine? Or are such products considered to be Prescription Only Medicines without any additional requirements?

Answer:

An immunological product is a biological product that has an immunological mode of action. Article 1 of Directive 2001/83/EC defines an immunological medicinal product as: Any medicinal product consisting of vaccines, toxins, serums or allergen products: (a) vaccines, toxins and serums shall cover in particular:
(i) agents used to produce active immunity, such as cholera vaccine, BCG, polio vaccines, smallpox vaccine; (ii) agents used to diagnose the state of immunity, including in particular tuberculin and tuberculin PPD, toxins for the Schick and Dick Tests, brucellin; (iii) agents used to produce passive immunity, such as diphtheria antitoxin, anti-smallpox globulin, antilymphocytic globulin; (b) 'allergen product' shall mean any medicinal product which is intended to identify or induce a specific acquired alteration in the immunological response to an allergizing agent.

Question:

After receiving feedback and recommendation from an inspection, is there a set time period for an inspector to issue GDP certificate?

Answer:

The GDP certificate is automatically generated and issued upon closure of the inspection case folder following appropriate CAPA from the company.

Question:

What to do if the inspection deficiency report points refers to a wrong EU Guideline section, as this may help to action appropriate remedial action pertaining to the deficiency.

Answer:

Please refer back to your inspector.

Question:

When a UK MAH also holds a UK WDA is permissible to use the MAH connection to the EMVS to decommission serialised product (damages, returns etc) or must this be done through a WDA connection to the UKMVS.

Answer:

Advice should be sought from EMVO on the functionality of the system. The decommissioning of damages and returns would be done at the physical location holding the stock concerned and as such this would ordinarily be done via the relevant NMVS.

Question:

Do non-UK storage sites need to be listed on a UK WDA(H) licence?

Answer:

No they cannot be listed on a UK WDA.

Question:

If you are considering charging more for complicated inspections associated with additional hours, will you be reducing the fees for compliant and non-complicated inspections?

Answer:

Compliant and non complicated organisations benefit through the application of our risk based inspection programme with longer intervals between inspections.

Question:

Can the MHRA share their change control for their office move from Victoria to canary wharf please.

Answer:

No GDP are not able to but it may be available via an FOI request.

Question:

A CMR is a transport document and is used for the movement of goods by road whether to/from/within the EU or not.

Answer:

Need further information to be able to answer the question.

Question:

Where does an NHS Trust stand with the WDA and changes in the episode role and requirements

Answer:

Need further information to be able to answer the question.

Question:

How can you define and detail a change when you don’t know what you are changing to and the regulatory framework is not defined.

Answer:

Need further information to be able to answer the question.

Question:

What is the agencies stance on the use of curtain side lorries for medication? There seems to be conflicting feedback.

Answer:

Regardless of the mode of transport, it should be possible to demonstrate that the medicines have not been exposed to conditions that may compromise their quality and integrity. A risk based approach should be utilised when planning transportation.

Question:

Is the expectation that the Responsible Person approves each change regardless of what that change is, or should this be managed based on risk?

Answer:

A change control system should be in place. The system should incorporate quality risk management principles, and be proportionate and effective.

Question:

We are awaiting MHRA decision on listing sites on licence who store goods in transit e.g. refrigerated goods over a weekend. Is there any guidance available yet?

Answer:

All sites storing cold chain medicinal products should hold a WDA.

Question:

Is there a scenario in which temperature monitors are not required for transport of product given the requirement (9.4). If requested, customers should be provided with information to demonstrate that products have complied with the temperature storage conditions?

Answer:

Regardless of the mode of transport, it should be possible to demonstrate that the medicines have not been exposed to conditions that may compromise their quality and integrity. A risk based approach should be utilised when planning transportation.

Question:

Customer Qualification - what is the recommended way to perform the GDP customer qualification check when the customer is in a country that doesn't have a national database and isn't covered by Eudra database? Also what is the recommended process when there are no local regulations for wholesale distribution of medicinal products in the customer country?

Answer:

Checks should be performed to ensure that supplies are only made to persons who are authorised or entitled to receive medicinal products for wholesale distribution or supply to the public in accordance with the applicable legal and administrative provisions of the country concerned. The wholesaler should take reasonable steps to verify any information they have been supplied, this may involve making additional checks with the regulatory authority for medicines for the country concerned.

Question:

What's the MHRA's recommendation for verifying customers in countries where public registers are not available?

Answer:

Checks should be performed to ensure that supplies are only made to persons who are authorised or entitled to receive medicinal products for wholesale distribution or supply to the public in accordance with the applicable legal and administrative provisions of the country concerned. The wholesaler should take reasonable steps to verify any information they have been supplied, this may involve making additional checks with the regulatory authority for medicines for the country concerned.

Question:

Customer Qualification - should the licence check be completed for the end delivery address (physical customer) or the company buying the goods (financial customer)? Or both?

Answer:

Both.

Question:

Would the MHRA consider making it a requirement if the WDA licence that all sales data is submitted annually to help tackle organised crime?

Answer:

MHRA will not be making it a requirement to submit sales data but will continue to seek sales data on a voluntary basis from a range of wholesalers to tackle crime. The assistance WDA holders provide here is appreciated.

Question:

Will the MHRA consider taking a stronger line to prevent unlicensed services such as Royal Mail from being used to deliver all levels of medicine? Surely it would be the next step to ensure the supply chain is safer from falsified medicines?

Answer:

Regardless of the mode of transport, it should be possible to demonstrate that the medicines have not been exposed to conditions that may compromise their quality and integrity. A risk based approach should be utilised when planning transportation.

Question:

Has any comparing and contrasting been done against the rise of deficiencies compared to the rise of the use of consultant/contractor RP's?

Answer:

No. Each inspection and associated RP is assessed on a case by case basis.

Question:

Would the MHRA consider setting up a CPD area for all responsible people on their website so CPD and learning plans can be logged and monitored? IOSH do this for their H&S professionals which is successful.

Answer:

This is something that is currently being considered.

Question:

Do non-UK storage sites need to be listed on a UK WDA(H) licence?

Answer:

No, non UK sites cannot be listed on a UK WDA.

Question:

How do you recommend A customer should be qualified and independently verified in addition to the licence provided, where they are not within the EU?

Answer:

Checks should be performed to ensure that supplies are only made to persons who are authorised or entitled to receive medicinal products for wholesale distribution or supply to the public in accordance with the applicable legal and administrative provisions of the country concerned. The wholesaler should take reasonable steps to verify any information they have been supplied, this may involve making additional checks with the regulatory authority for medicines for the country concerned.

Question:

When will the finalised slide decks be available on line?

Answer:

All presentations that can be published are available in the delegate area.

Question:

For companies applying for the online selling logo what expectations in terms of compliance are you looking for?

Answer:

Please refer to the publish guidelines at https://www.gov.uk/guidance/register-for-the-distance-selling-logo

Question:

Regarding controlled drugs licensing would there be any possibility to enhance the partnership between the MHRA and HO and improve the licensing process? The HO process is particularly challenging and frequently has impacts on our customer supply chain due to delayed licenses.

Answer:

The MHRA and Home Office currently work in partnership, however the licensing processes are completely separate and will remain so.

Question:

How patent regime would be maintained - separate from EU?

Answer:

The MHRA don't maintain patents. This maybe a question to raise with the intellectual property office.

Question:

Please define legal presence. Does this mean a registered UK business to hold MAs after 2020?

Answer:

More information is required in order to answer this question.

Question:

Will the slides from today's presentations be made available?

Answer:

Yes, all presentations that can be published are available in the delegate area.

Question:

Can we bring introduction products to UK and sell to EEA under WDA and vice versa?

Answer:

No. Introduced products are for purchase and sale between third countries only.

Question:

Do WDA holders have to document all complaints if they export the products under ex-works?

Answer:

Ex works is not recognised under GDP. All shipments must be made according to due diligence and shipping ex works does not fulfil the diligence requirements under GDP as certain customs formalities are required to be performed by the exporter. All complaints made to the WDA(H) holder must be recorded and processed in accordance with Chapter 6.2 of the EU GDP Guidelines

Question:

If as a wholesaler we receive product that is going to be shipped onwards for use in a clinical trial (but the products will be shipped to a site within Europe with a WDA or a repacker on their behalf who also has a WDA or manufacturing licence) who is responsible for decommissioning? We, the wholesaler, are not involved in the clinical trial and therefore we are of the opinion that the company receiving the products from us must verify and decommission, whether this be the company responsible for the trial or the repacker that we ship to on the company's behalf. However, our European customers are asking us if they give us evidence that the products will be used in a trial, can we be responsible for the decommissioning?

Answer:

Verification & decommissioning of marketed packs for use in Clinical Trials must be performed at last point in the chain holding the MIA or WDA(H) authorisation.

Question:

What authorisation would be required to import introduction products and sell them to UK WDA holder for export to 3rd country?

Answer:

An MIA although the questioner here appears to be confused between the differentials between 'introduction' and' import' the two functions are very different.

Question:

Technical notes stated EU qualified person could certify product from EU For UK without need for recertification. Providing they were named in MIA. Does new Responsible person import role provide alternate to this approach. Also how does naming of a EU qualified Person on MIA look.

Answer:

https://www.gov.uk/government/publications/further-guidance-note-on-the-regulation-of-medicines-medical-devices-and-clinical-trials-if-theres-no-brexit-deal/further-guidance-note-on-the-regulation-of-medicines-medical-devices-and-clinical-trials-if-theres-no-brexit-deal

Question:

If a wholesaler does not disclose if they have a contract in place with a manufacturer how do you decide if they are designated wholesaler and therefore won't have to authenticate?

Answer:

The designated status is determined by the MAH and will be visible on NMVS - further legal advice indicates that designation will be restricted to pre-wholesalers.

Question:

If a 3PL adds a subcontracted storage facility to their WDA and the change aligns with chapter 7 (i.e. audits, comprehensive technical agreements, notification and acceptance of the additional site by the MAHs that the 3PL serve and supplier review mechanisms) is there a need for the MAH's to list the 3PL's subcontracted storage site on their WDA? If so is there still the need for MAH to conduct a full audit and have a separate TA?

Answer:

The MAH needs to name the subcontracted site but does not need to audit it. Provisions for audit of the sub contracted site should be included in the technical agreement between the MAH and the original 3PL provider.

Question:

Re GDP example. Do the MHRA not have to confirm RPs before addition to a WDL?

Answer:

Yes.

Question:

In June 2018 the EMA published a Q&A regarding the transportation and storage of medicinal products with no labelling statements (i.e. no labelled storage conditions) whereby it summarised that the temperature of the same should be monitored during transportation. What are the MHRA's expectations regarding? Please included confirmation of monitoring of all shipments versus a sample based on risk.

Answer:

The guidelines require all products to be shipped within the defined limits as described by the manufacturers or on the outer packaging. If there are no storage requirements forthcoming from either source, no temperature monitoring is required.

Question:

The term ‘introduced product’ was used in Cheryl Blake’s presentation. Please can the term be explained?

Answer:

For a medicinal product to be an introduced medicinal product it has to be sourced from a non-EEA country by a licenced wholesale dealer and re-exported back to a non-EEA country by the same licenced wholesale dealer. An introduced medicinal product will not have a marketing authorisation for the UK or another EEA country. Such products can be held on a licenced site in a free zone or in a bonded warehouse under an appropriate customs processing procedure. This is very different to Import.

Question:

What kind of verification would be required for 3rd country customer beyond verification of license from local issuing authority.

Answer:

Verification that the licence and information provided by the customer is accurate and meets the criteria of the county in question, transcription may be required. This may also involve making additional checks with the regulatory authority for medicines in the country concerned where possible and documenting the outcome as evidence. Any licences obtained should be translated into English and authenticated by a notary with appropriate due diligence carried out. MHRA's expectation is that an authorised wholesale dealer should have oversight of the export of the product and have all the appropriate documentation to evidence it. Please also refer to p170 and p170 of the 2017 edition of the Green Guide.

Question:

Can you write a blog on introduced medicines?

Answer:

Yes, a blog will be published in the coming months.

Question:

If a hospital has added a new premises on their WDA (which we have been sent a copy of), but the site is yet to be inspected by the MHRA, can we send product to this new address?

Answer:

No the site would need to be inspected.

Question:

I’m an MIA Holder, MA holder virtual company. I procure API from UK and third country and ship direct to CMOs - do I need an API registration for this. If I store the API at a third party UK API registered site do I need an API registration for onward supply?

Answer:

The flow chart identifying if registration is required for API related activities can be found in the 2017 Orange Guide on page 489. Based on the information provided a registration would be required.

Question:

Can you expand on the term ‘actors’ in supply chain.

Answer:

Actors' is just a way of defining people or a company involved in a section of the supply chain. It does not infer anything derogatory.

Question:

Will this FMD presentation be made available?

Answer:

Yes but watermarked?

Question:

What is the difference between parallel import and parallel distribution?

Answer:

Please refer to pages 173 - 175 of the 2017 Green guide.

Question:

If a product is licensed but not launched in the UK and we source it from within EEA is this parallel import or parallel distribution?

Answer:

Depends if it is authorised via national route =parallel import or centrally authorised =parallel distribution.

Question:

Is use of Mean kinetic temp (MKT) when assessing the impact of an unexpected temperature deviation on the stability of the product, appropriate? If not what would be appropriate?

Answer:

The application of MKT to temperature monitoring of wholesale products is only appropriate where an acceptable MKT value is provided by the MA holder for a specific product, and the recording of the temperature can be confirmed to be consistent and complete from the moment of leaving the manufacturers premises. In practice the application of MKT fails where a complete chain of temperature recording cannot be allocated to a specific consignment of product. Attempts to apply MKT have been proposed by wholesalers as an alternative to having adequate temperature control within warehouses or during transportation and to downgrade the impact of temperature excursions. The use of MKT in the wholesale environment without robust supporting information and methodology is therefore discouraged.

Question:

If wholesaler supplying medicines to a clinical trial organization who perform the repackaging before the product goes to the clinical trials who has responsibility for decommissioning of products - the clinical trial organization or the wholesaler supplying the product?

Answer:

Verification & decommissioning of marketed packs for use in Clinical Trials must be performed at last point in the chain holding the MIA or WDA(H) authorisation.

Question:

If a product is P item in EU, POM in UK, how it will work on EUHub?

Answer:

The MAH will load the products on to the relevant NMVS in accordance with the legal classification in the Member State concerned. The EMVS is linked to each NMVS acting as a central repository.

Question:

Richard Andrews states that more and more sites are being referred to IAG and CMT: do you have a root cause identified for this? Is industry compliance falling or is inspection rigour increasing?

Answer:

This is likely to be a combination but no investigative work has been performed to verify this. Each referral is made on a case by case basis.

Question:

Last year you discussed the diversion of certain medicines including Pregabalin and Gabapentin. This year, no reference was made to these drugs. Can we have an update on this? I had assumed, on last years presentation, that this was a real growing issue and that focus of attention needed to be on these two drugs. Has this now changed?

Answer:

We have not had significant incidents of these two reported to us. A lack on reported incidents however can not be taken to indicate an absence of attempts to divert. The products are well known as medicines of abuse. Hopefully our highlighting of the matter has kept wholesalers alert. Also note the reclassification of pregabalin and gabapentin to controlled drugs – changes come into force this April. https://www.gov.uk/government/news/pregabalin-and-gabapentin-to-be-controlled-as-class-c-drugs

Question:

As a specials manufacturer where we supply small pharmacies with a host of different supply routes which vary on a day to day basis. Do we have to verify each and every route? Or, is it enough to validate our packaging and using a transportation service that has a WDA licence?

Answer:

If anything, as a specials manufacturer, it is more important that you hold data for your chosen transportation methods. The requirement is that you verify and risk assess your chosen transport methodology. MHRA would expect that data is available to show that you are transporting the products according to the product requirements.

Question:

If alternate warehouse being used and RP can demonstrate GDP compliance in all areas other than notifying MHRA of additional site, is that positive?

Answer:

No, any site used for storage must be named on a WDA(H).

Question:

Which training providers are recommended to comply with the Gold Standards. Who is accepted as Gold Standard training for RPs?

Answer:

Currently the only accredited RP training provider for the Gold Standard is Seer Pharma Ltd.

Question:

How can we not apply for export if no deal we will be stuck?

Answer:

You can apply to vary your WDA to add export at anytime.

Question:

What about products going FROM the UK to Europe?

Answer:

This will be export after Brexit.