pci CLINICAL TRIAL SERVICES

Water Cooler Chat

European Compassionate Use Programs: What are the Quality and Distribution Considerations?

RECORDED APRIL 9, 2020

YOUR BRIDGE BETWEEN LIFE-CHANGING THERAPIES AND PATIENTS




PCI Clinical Trial Services hosts a weekly virtual ***Water Cooler Chat*** series, where our subject matter experts host informal discussions around a number of clinical supply hot topics.

European Compassionate Use Programs: What are the Quality and Distribution Considerations?

Our experts – Tris Evans, VP of Global Clinical Quality, Gavin Morgan, Senior Manager of Global Logistics and Uday Pathapati, Senior Manager of Clinical Project Management – recently discussed what factors need to be considered from a quality, packaging and labeling, logistical and risk management perspectives when planning an EU Compassionate Use Program.

Compassionate use supplies in Europe are unlicensed medicines and not traditional clinical trial supply. As such the quality and distribution considerations are different for compassionate use supplies in Europe. This article will provide an overview on:

- QP requirements & expectations
- Importing compassionate use medicines into the UK & EU
- Relabeling of compassionate use material
- The role of the healthcare physician
- Bona Fide checks
- Compassionate use supply distribution

QP REQUIREMENTS & EXPECTATIONS

Is QP release needed for compassionate use supplies in the UK?

It is not, as there is no QP named on the MHRA "Manufacturer Specials" license used for importation. For compassionate use that falls under the "Named Patient category," the physician takes the responsibility for quality of that medicine ultimately, therefore negating the need for QP supply chain assessments (audits), QP GMP declaration, and QP release of supplies.

However, Compassionate or Named Patient Use medicines do need to be manufactured according to GMP standards. If there is a clinical trial already running with the same material, that means the audits may have been completed and the GMP standards are already deemed compliant. If it is a new product, then the sponsor company and the clinical trial service provider will need to work together to understand the level of supply chain oversight that is in place.

What about for the rest of Europe?

The requirements for these unlicensed compassionate use supplies is locally controlled within each European country

and therefore the standards differ across Europe. Some countries might expect a QP release on this type of supply, but many do not. This is where working with an experienced clinical trial services provider would prove useful as there is no central EU directive to govern these unlicensed supplies, and each country in Europe presents a different set of rules and regulations that need to be followed.

What are the QP requirements if the compassionate use supply needs to be exported outside of Europe?
To export these unlicensed compassionate use medicines out of Europe, there would be a GMP QP release required because they are exported utilizing a Manufacturers Import Authorization (MIA), which does include a named QP on it.

Importing Compassionate Use Medicines into the EU

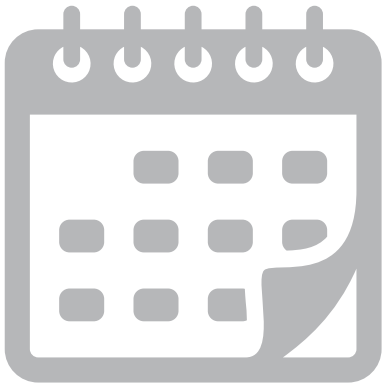
What is the first thing that needs to be considered when looking to import unlicensed medicine into the EU?
If it is already within the EU, was it previously imported as an IMP? If this is the case, then it can be brought in under the importers standard MHRA MIA IMP licenses.

If it is a product that is already in its final state and will not be labeled, the unlicensed material will need to be imported under the importers MHRA "specials" license and will require MHRA approval for each individual import.

How long does it take to get the MHRA's approval and what is required?
It can typically take up to 28 days to obtain the MHRA's approval, but in the circumstance where it is an urgent need, an explanation can be sent to the MHRA to hopefully expedite this timeline.

The information needed to get the MHRA's approval include:

- Default spreadsheet to be completed and submitted via email to the MHRA
- Explanation of what is being imported, including a quantity that should not exceed 25 doses
- The reason the material is being imported



2-3 WEEKS

This is the time required for an MHRA approval. If you are importing final labeled compassionate use material into the EU and will just need it to be distributed, received, QC approved, and released – keep this timeline in mind.

Can you ship from the US directly to an EU hospital/ pharmacy without it going to a UK or European depot first?
Material coming from the US into an EU state will be required to go through customs clearance. Even though that country may not have a specific import license requirement, it is material that will be imported for free circulation within the European Union, therefore it has to go through a customs clearance. The drug product owner will need an Importer of Record (IOR) and unless the site or healthcare physician in question within the country concerned has the appropriate license, it would have to come to a clinical trial services provider with a "specials" license (if UK is the site of EU import) before being distributed.

TIP

If a hospital or pharmacy is able to apply for an import license and get regulatory approval, the compassionate drug provider could ship directly to the site.

Relabeling of Compassionate Use Material

What are the guidelines for labeling of compassionate use material?
In terms of labeling, there are no specific guidelines like there are for clinical trials. Each country has their own regulations. Country-specific guidelines will depend on the type of approval and the prescribing physician request. It is recommended to follow the EU GMP Annex 13 labeling requirements to ensure you capture all key items such as:

- The lot number
- The expiry date
- The description

It is important that the label does not contain any references to a clinical trial or EudraCT numbers. It should not contain any clinical trial caution statements either. The clinical trial caution statement will need to be replaced with a caution statement for compassionate use material.

TIP

It is important that the label does not contain any references to a clinical trial or EudraCT numbers. It should not contain any clinical trial caution statements either. The clinical trial caution statement will need to be replaced with a caution statement for compassionate use material.

Are there any language requirements to consider for the label text?
In terms of label text language requirements, some countries require the label text to be in the local language while others do not. Historically, the label text language requirements depend on:

- The treatment indication
- How urgent the medicine is
- Regulatory approval received from authority

An experienced clinical trial services provider would be able to assist you with the label text to ensure all required information is captured in the format stated by the guidelines of the specific country in question.

Is it common to overlabel Clinical Trial Material that is already labeled for a particular clinical trial protocol, or is complete relabeling for dedicated compassionate use recommended?
Both methods are valid. In the case where a kit from an active trial is utilized, the label text is reviewed to ensure it captures all the necessary information. A block-out label is used to remove trial specific information such as the protocol, the EudraCT number, and the clinical trial caution statement.

If the hospital or clinic requesting the compassionate use supply is managing a clinical trial using the same supply, they must be able to differentiate between the kit(s) that is for compassionate use and those that are for the clinical trial.

TIP

Avoid mixing compassionate use supplies with clinical trial supplies. It is crucial for a hospital to be able to differentiate between a clinical trial kit and a compassionate use kit if they are running a clinical trial at that site. There are labeling practices that make this differentiation clear.

The Role of the Healthcare Physician

What needs to be considered in terms of the healthcare physician in the UK/EU?
Before compassionate use unlicensed supply can be distributed to the responsible healthcare physician, the credentials of that healthcare physician concerned will need to be verified. There needs to be an unsolicited order from a doctor, a pharmacist, or a dentist as this is typically the person who is ordering the drug and who the supply will be sent to.

Bona fide checks

What is a Bona Fide Check and what is the process?
As per the MHRA guidelines, the bona fide check is key before a compassionate use kit is delivered to the patient, a third-party vendor or directly to the hospitals. The address on the shipment request must match the address of the hospital or pharmacy, or in the case of shipping to a third-party vendor, match the address shown on their license. If the addresses do not match, then an explanation from the sponsor is needed to complete the bona fide checks.

Distribution of Compassionate Use Medicines

Are there any countries with more involved regulatory processes required?
Yes, there are a few EU countries that have their own rules regarding compassionate use material, and it is a good idea to check with your regulatory group before distributing supplies. For example, Italy has the Nulla Osta, an approval document that the courier is expected to have on file prior to the shipment entering the country. It is a very straight-forward document obtained by the physician or investigative site that is going to be receiving this compassionate use drug supply. France is another great example where at the moment there is no import license required, but they also require a document, similar to the Nulla Osta, to be on file.

How long does it take to distribute compassionate use supply in the EU?
Typically, for compassionate use supply that is to be imported in its final labeled state, the time needed to import, set up the project, release and distribute the material is approximately 2 to 4 weeks once the required MHRA Import Authorization for Specials Use is in place. If a labeling operation is expected to take place within an EU clinical trial service provider, the IMP supply can then be manufactured, released and ready for distribution within approximately 4 to 6 weeks.

*If you are interested in learning about PCI's **Water Cooler Chat** series where our experts answer clinical hot topic questions in real-time, please visit us **here** to see the schedule and register for this complimentary series.*

ABOUT OUR PCI CLINICAL TRIAL SERVICES STAFF MEMBERS

Tristram Evans

Vice President, Global Quality - Clinical Services

Tris leads the Clinical Quality teams across PCI. In Tris' 6 years with PCI, he has been successful leading and building a well-recognized Global Clinical Quality team, ensuring harmonization of Clinical Quality standards globally. Tris has worked in the pharma industry within various Quality roles for 20 years with experience in commercial, investigational and unlicensed medicine manufacture, release and supply. Tris is an EU Qualified Person (QP), qualifying in 2011 and is named on PCI commercial and clinical licences in the UK and Ireland with experience in multiple product dosage forms.

Gavin Morgan

Senior Manager, Global Logistics - Clinical Services

Since 2009, Gavin has been leading the clinical distribution team at PCI's Bridgend facility. His main responsibilities include the overseeing of all activities associated with UK imports along with supporting the full supply chain of clinical trial supplies including the selection and management of 3rd party couriers and depots. Gavin has over 20 years of experience within the clinical trial industry, with a focus on the distribution of clinical materials globally. Previously, Gavin worked at Bilcare Global Clinical Services.

Uday Pathapati

Senior Manager, Clinical Project Management - Clinical Services

Uday currently leads one of the Clinical Project Management teams at PCI Bridgend, responsible for training and mentoring Project Managers and Associate project managers to ensure they are providing the industry leading customer experience. Since joining PCI in 2011 Uday has worked for 9 years on clinical projects from early Phase I to Phase III with a key focus on management of Compassionate Use (CU), Named Patient Supply (NPP) and Early Access Programs (EAP) in the EU.

*If you are interested in learning about PCI's **Water Cooler Chat** series where our experts answer questions in real-time, please visit us **here** to see the schedule and register for this complimentary series.*