Advanced Therapy Treatment Centres

Northern Alliance Advanced Therapies Treatment Centre

Version 1 | October 2021

The role of a Qualified Person (QP) within Advanced Therapy Medicinal Products (ATMPs)

Written by: Anne Black | Regional QA Specialist Pharmacist, North East & North Cumbria
David Caulfield | Assistant Director of Pharmacy, QA Newcastle upon Tyne Hospitals NHS Foundation Trust

Funded by

UK Research and Innovation

Coordinated by

CATAPULT Cell and Gene Therapy

Introduction

The role of the Qualified Person (QP) is poorly understood in healthcare and beyond. This has led to confusion and uncertainty around the requirement for a QP in the delivery of ATMPs.

The aim of this document is to bust the myths and clarify when a QP is required in relation to the supply chain of ATMPs.

A QP is the person named on a manufacturer's authorisation with the legal responsibility for certifying that a medicinal product has been manufactured and tested in line with the requirements of the appropriate authorisation i.e. Marketing Authorisation for marketed (licensed) medicines; Investigational Medicinal Product Dossier (IMPD) for Investigational Medicinal Products (IMPs). QPs have other responsibilities in relation to the manufacture of ATMPs, many of these may be delegated. Legally the certification of batches of manufactured ATMP must be performed personally by the QP. It is key that sponsors, manufacturers and healthcare providers understand this.

The legal basis for a QP is a requirement specific to the UK and EU as follows:

- For Marketed Medicines: Regulation 41, paragraph 9 of The Human Medicines Regulation 2012 (as amended), UKSI 2012:1916. In the EU by directive 2001/83/EC, Article 48.
- For Clinical Trials: Regulation 43, paragraph 6 of The Medicines for Humans Use (Clinical Trials) Regulations 2004 (as amended), UKSI 2004/1031. In the EU by directive 2001/20/EC, Article 13.

What is the role of a QP in the certification of an ATMP?

All licenced medicines manufactured in the UK must be certified by a UK QP. Medicines manufactured in the EEA (MHRA listed countries) are certified by EU QPs. This certification is currently recognised in the UK. Medicines manufactured in third countries (currently any country outside of the EEA) must be certified by a UK QP on importation.

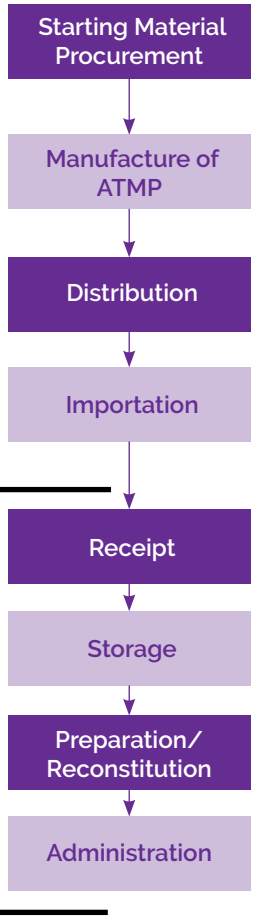
All Investigational medicinal products or comparators (IMPs) manufactured in the UK must be certified by a UK QP. IMPs manufactured in the EEA (Listed Countries) are certified by EEA QPs; this certification is recognised in the UK. However, as part of the importation process a UK QP must ensure a suitable system is in place to verify that an appropriate QP certification has occurred in the EEA. IMPs manufactured in third countries (countries outside of the EEA) must be certified by a UK QP following importation even if they are designated as an Approved country (a third country which holds a Mutual Recognition Agreement giving Medicines Health Regulations Authority (MHRA) recognition that the holder country has equivalent standards of GMP). See Figure 1 for further clarification.

Figure 1: The Regulatory and QP Requirements for the ATMP Product Journey

NB: Unlicensed medicines manufactured under an MHRA Specials Manufacturing Licence are approved by a named Head of Quality in line with the specification. They do not require QP certification. * SPS Institutional Readiness documents are available at **https://www.sps.nhs.uk/networks/pan-uk-pharmacy-working-group-for-atmps/**

KEY

HTA - Human Tissue Authority
EEA – European Economic Area
GMP - Good Manufacturing Practice
GDP - Good Distribution Practice
QP - Qualified Person
IMP - Investigational Medicinal Product
ULM - Unlicensed Medicine
RPi - Responsible Person (import)
RP - Responsible Person
GCP - Good Clinical Practice
MA - Marketing Authorisation
MS - MHRA Manufacturers Specials Licence
GPP - Good Preparation Practice



Specialist Pharmacy Service (SPS) Institutional Readiness Guidance is available to facilitate implementation*

QP Involvement is not required for these stages

UK ATMP Manufacturer	EEA (Listed) Country Manufacturer	Third Country Manufacturer
HTA Licence with tissue / cell type approved	As for UK, with Export approved in addition	As for EEA (Listed) Country
UK GMP or equivalent **with UK QP Certification**	UK GMP or equivalent with certification by EEA (listed) country QP	UK GMP or equivalent with certification by Approved country QP equivalent
UK GDP	UK GDP or equivalent	UK GDP or equivalent
N/A	**Oversight by: UK QP if IMP** RPi if MA RP if ULM	**UK QP certification if IMP or MA** For ULM MS Licence required
GDP	As UK	As UK
GCP if IMP GDP if MA	As UK	As UK
GCP if IMP GPP if MA	As UK	As UK

Q&As

How is Manufacture different from Preparation or Reconstitution of Medicines?

Manufacture relates to the process which creates (and tests) the medicinal product. Preparation (often termed Reconstitution) relates to any steps that are required post manufacture in order to make the medicinal product ready to administer to a patient. This may involve a thaw or a dilution step, for example.

In the ATMP arena it is often difficult to define whether or not a finishing step is a manufacturing or a preparation step. One way to differentiate between the two is that a manufacturing step typically involves a chemical, biological or structural change. If you are uncertain, the Pan UK Pharmacy Working Group for ATMPs may be able to advise. Contact the Working Group via Anne Black **anne.black7@nhs.net**

Is a QP required for preparation steps before administration of an ATMP?

No, not if it is truly a preparation step. QP certification will occur at the point of release of the medicinal product. A QP is not required for a preparation step. However, as ATMPs are medicinal products, then for clinical trials it is important that the clinical trials pharmacist ensures that preparation occurs in line with the requirements of the protocol and of any pharmacy manual / processing manual. Pharmacy oversight is required for the preparation of marketed medicines to ensure that it is undertaken in line with the requirements of the SmPC. Further information can be found here: **https://www.sps.nhs.uk/articles/pharmacy-oversight-and-supervision-requirements-for-preparation-of-licensed-atmps/**

Why does a Sponsor of a clinical trial engage with a QP routinely?

- Vendor assurance audits (i.e. technical audits of IMP manufacturing facilities).
- QP certification following manufacture
- Assessment of the impact of deviations on IMP quality attributes post certification (such as temperature deviations)

As a consequence of EU exit, for what additional reasons would a Sponsor of a clinical trial engage with a QP?

Where a product is manufactured in Europe for use in a clinical site in the UK, a sponsor will need to engage with a MIA (IMP) holder with a QP named on the licence and with suitable authorisations in order to obtain QP certification following importation of the IMP (see figure 1 above).

Does a clinical site need a QP to be involved in the delivery of a clinical trial?

The expectation of clinical sites is to undertake the preparation; as such no manufacturing steps are expected and a QP is not required.

Is the role of a QP different for ATMPs compared to conventional medicines?

A QP's role in ATMPs is more resource intensive, in particular for autologous products where the manufacture of one batch provides treatment to only one patient. This differs from conventional medicines where a QP would release sufficient medicines to treat thousands of patients in a single batch certification. As such the manufacture of ATMPs creates an unprecedented demand for QP resource.

Q&As

Is a QP required for distributed manufacture?
If it is manufacture then a QP is currently required. However, the Innovative Licencing and Access Pathway (ILAP) initiative is exploring innovative ways for the QP to remain responsible but without being physically present. Watch this space, e.g. point of care manufacturing.

Out of specification (OOS) ATMPs - Does this need a QP?
For autologous cell or tissue based ATMPs a QP cannot certify the batch if it does not comply with the Marketing Authorisation or the Investigational Medicinal Product Dossier (IMPD). However, there are occasions in which it might be in the best interest of the patient to receive this medicine. In these situations, OOS are not certified by the QP. However, QP verification is performed during which the QP verifies that the product has been manufactured in compliance with Good Manufacturing Practice and provides an evaluation of any risks associated with the product. This information can then be used in the Hospital's local governance approval process, which may authorise the use of the product for the individual patient (via the treating physician). Further information can be found here: **https://www.sps.nhs.uk/articles/out-of- specification-advanced-therapy-medicinal-products-guidance-for-healthcare-organisations/**

Is a QP involved in reviewing deviations during transportation of an ATMP?
Deviations during transport are required to be assessed by the manufacturer and, behind the scenes, this information is reviewed and agreed in accordance with SOPs approved by the manufacturer's QP. QPs at clinical centres may be able to give advice, however they aren't legally entitled to make this judgement as they are not named on the manufacturers' Manufacturing Authorisation and do not have access to stability data needed to support any decision.

Is there a lack of QPs in the NHS?
Yes, there is a lack of QPs in the NHS because of the expensive and complex training required and the associated difficulties in retaining QPs in the NHS.

Is the lack of QPs in the NHS a barrier to delivery of ATMP clinical trials?
This could be a barrier to the manufacturing pipeline of Advanced Therapy IMPs however this is not a barrier to delivery of ATMP clinical trials in an NHS setting. N.B. a QP is not required for the collection and transportation of starting materials.

How do I become a QP?
In the UK, individuals who fulfil the expectation of the QP study guide as having the necessary education and practical experience, are assessed by the Joint Professional Bodies on behalf of the MHRA. Successful candidates are added to registers held by the Joint Professional bodies and are issued certificates indicating they are eligible to act as a Qualified Person. Only once named on an MHRA manufacturing licence for marketed medicines (MIA) or investigational medicinal products (MIA(IMP)), are these individuals known as Qualified Persons.

For further information, contact the Joint professional bodies- The Royal Pharmaceutical Society, The Royal Society of Biology and The Royal Society of Chemistry. Further information can be found here:

https://www.rpharms.com/development/education-training/training/qualified-persons-a-guide