

MHRA public consultation on Advanced Therapy Medicinal Products

September 2008

The Medicines and Healthcare products Regulatory Agency (MHRA) has launched a public consultation to gain public and industry input on the UK's "hospital exemption" scheme under the 2007 European Advanced Therapy Medicinal Products Regulation. The MHRA is also consulting on changes to the "Specials" regime in connection with Advanced Therapy Medicinal Products.

What is an ATMP and why is it important?

An Advanced Therapy Medicinal Product (ATMP) is one of, or a combination, of a "gene therapy medicinal product", a "somatic cell therapy medicinal product" and a "tissue engineered product". The Regulation sweeps all these sophisticated products into a European legal regime that is primarily concerned with pharmaceutical products; that of the 2001 Medicinal Products Directive. However, the scientific, regulatory and economic issues concerning ATMPs mean introduce issues which go far beyond those which are relevant to conventional pharmaceutical products, or even biosimilars. One effect of the Regulation is therefore to make significant amendments to the Medicinal Products Directive.

The "hospital exemption"

As science accelerates into the future, the law which regulates it is often left languishing in its tail lights. The exemption under Article 28 (2) of the ATMP Regulation aims to provide some flexibility from general regulatory requirements so as to accommodate small scale and developmental research in hospitals.

Under the Regulation, there is an exemption for ATMPs which are prepared on a non routine basis and used within the same Member State in a hospital under the professional responsibility of a medical practitioner in order to comply with an individual prescription for an individual patient.

The hospital exemption applies only to ATMPs prepared on non-routine basis and used within the same Member State, according to specific quality standards and used in a hospital under the professional responsibility of a medical practitioner in order to comply with individual prescription for a specific patient.

ATMP manufacturers must be authorised by the competent authority of the relevant Member State: in the UK, this is the MHRA. As such, the MHRA is required to “*ensure that national traceability and pharmacovigilance requirements as well as the specific quality standards...equivalent to those provided for at Community level*” are met.

When the Regulation comes into force at the end of this year, applications for marketing authorisations for ATMPs will be brought under a centralised procedure in which a centralised European authorisation is granted by the European Commission following assessment by the European Medicines Agency (“EMA”). Under the exemption, therefore, traceability and pharmacovigilance need to be equivalent to ATMPs for which a centralised marketing authorisation would be granted by the European Medical Agency.

The “Specials” scheme

“Specials” are unlicensed medicinal products ordered and used by an authorised healthcare professional to meet the special needs of specific patients, supplied in response to a *bona fide* unsolicited order. They are permitted, as a derogation from the general law on medicinal products, by Article 5(1) of the Medicinal Products Directive. As such, the “Specials” scheme is similar to, but distinct from, the “hospital exemption”. Specials that are not ATMPs will not be affected by the new proposals.

The MHRA’s proposals for the hospital exemption and specials scheme

Although Regulations are directly effective in each Member State (i.e. they need no implementing legislation), states are required to implement the hospital exemption using domestic arrangements. In the UK, responsibility is again placed on the shoulders of the MHRA. It is therefore consulting stakeholders to formulate how best to implement the exemption here. Here are some of its proposals.

Good Manufacturing Practice (GMP) – GMP plays an important role in the hospital exemption, as the ATMPs must be manufactured to a particular standard under licence from the MHRA. The role of the MHRA would be granting manufacturer’s licences for unlicensed products and inspection for compliance with GMP standards.

Pharmacovigilance – It is proposed that the pharmacovigilance requirements for the hospital exemption would cover notification of adverse reactions. It may provide the MHRA with the ability to ask for a risk management plan. Such a request may be made at the time the manufacturer seeks a licence from the MHRA.

Traceability – It is proposed that there must be traceable records of donors to the point of dispatch to the organisation using the ATMPs. The end user would be required to keep records of the receipt of the materials until its destruction.

Patient information/labelling/advertising – The proposals are aimed to reflect the potentially high risk nature of ATMPs.

Ethical issues – It is proposed that, provided that the treatment does not involve xenotransplantation, it would not require the approval of a research ethics committee. Clinical ethical issues would be governed by the particular NHS trusts' clinical governance arrangements. The Gene Therapy Advisory Committee ("GTAC") may also be called upon to provide ethical advice to medical practitioners on the use of gene therapy and stem cell-derived products.

Additional requirements – The Regulation sets minimum standards, but Member States may set a higher bar. The MHRA suggests that the test for such additional requirements would be if the measure was:

- necessary to protect the public,
- consistent with the purpose of the hospital exemption
- necessary on the grounds of ensuring clarity of the regulatory arrangements

What next?

The ATMP Regulation enters into force on 30 December 2008. It is envisaged that the exemption will be implemented on the same date.

The deadline to submit a response to the consultation is 15 October 2008.

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