PUBLIC CONSULTATION PAPER ON THE REGULATION ON ADVACED THERAPY MEDICINAL PRODUCTS

Comments by

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2.1 Marketing Authorisation

Marketing authorisation can only be applicable to products involving batch production.

Autologous products cannot be marketed. They are only produced for one single patient, therfore they are worthless to any other person in the world. Hence, there is **no market** for such products! Autologous cells belong to the patient and cannot be subject to commercial interests.

2.2 Combined products

The regulation regulates

-somatic cell therapy

-genetic therapy

-tissue engineering

Tissue Engineering is always, per definition, involving combined products. This is basically the nature of tissue engineering. So there is no need to stress this fact further.

Today, most of the tissue engineering products are combinations of autologous cells and medical devices having already a marketing authorization. As concluded above, there is no market for such products, hence there cannot be any marketing authorisation

For all other products, regulations for medicinal products or medical devices should apply, depending on the mode of action.

2.3 Hospital Exemption

The overwhelming majority of ATMP´s are tailor-made therapies for individual patients. These therapies have been developed in hospitals under the responsibility of a physician within the last 30 years and have been successfully used to treat thousands of patients

The very nature of the these therapies render them practically insufficient for traditional centralised industrial pharmaceutical production, since:

-they are mainly autologous procedures requiring at least two surgical/medical interventions

-there is no batch production

-physicians and laboratories are required to stay in close contact with each other throughout the whole production process in order to plan for the consequent surgical/medical intervention

-transport imposes a high risk on the quality of cells: as longer transport distances are more likely to influence the quality of cells or increase the possibility of the product being lost . This may have dramatic impacts on an individual patients.If a product is lost, a patient must undergo surgery again fo tissue harvesting, or a patient is already in the operating theater under anesthesia and cannot receice his necessary treatment.

The current legislation with an unclear article 28 (2) is a real threat to the tratment of patients who are in neeed of ATMP´s, since competent authorities in different EU member states execute it differently. Especially, it is unclear

-whether or not full GMP - as requried for pharmaceutical batch production - is necessary for the production of individulised therapies in hospitals

-is there a restriction on numbers of treated patients

-can parts of the production process be out sourced to other authorized laboratories.

From our long experience in treating patients with autologous cells (since 1989, see literature), we conclude:

-Individualised autologous therapies must stay as close as possible to the patient and the responsible physician in order to minimize risks associated to long distances and logistic problems. Furthermore, they cannot be seen as traditional pharmaceutical products which can be bought and sold on commercial grounds.

-Quality standards for these treatments must be high and authorization by a compentent authority must be issued, however pharmaceutical GMP is not applicable. It imposes an enormous financial burden on public health budgets without further increasing quality.

-restriction in numbers are unethical, every patient in need must have the same access to these treatments.

-industrial companies will never meet the demand of all necessary treatments as they only will focus on therapies which will guarantee a high return on investment. By hindering hospitals to meet this demand, patients will not get the treatment they need.

In general, products involving cells are so different in theire nature, that they can be hardly regulated under one single set of requirements. ATMP´s range from simple cultured autologous adult mesenchymal cells to autologous immunomodulating cells or homologous genically altered cells and homologous stem cells. As in the medical devices regulation, requirements should be defined by risk classes.

Autologous cultured cells should be regulated throghout the European Union under Directive 2004/23/EC as already commenced by several member states. This would guarantee high quality levels, high ethical standards,local availibility and cost effectivness for public health budgets.

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