University Children's Hospital Würzburg
Laboratory for Stem Cell Processing & Cellular Therapy

From: [redacted]
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Follow Up Flag: Follow up
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PUBLIC CONSULTATION ON THE REGULATION ON ADVANCED THERAPY MEDICINAL PRODUCTS

As a manufacturer of ATMPS in an academic institution (big University Medical Center in Germany) I would like to briefly comment on the current state of ATMP development, application to patients and speed of progress in that field.

1. The EU-regulation of ATMPs mainly targets commercial medicinal drug development and market authorization. However, this is in contrast to reality since most innovation and development in cellular therapy comes from academic institution which have neither the intention nor the capacities to apply for a marketing authorization. Their intention is to develop and optimize cellular products and offer them to as many patients as possible on an individual basis. A revised EU-regulation on ATMPs has to be tailored to meet the needs of these drug developers and not big industrial companies.

2. With a very few exceptions, the majority of AMTPS have to be manufactured on a highly individualized basis. Production of these products is cost- and labour-intensive and has to be carried out in a close-to-the-patient situation (classical bench-to-bedside scenario). For example, for cancer vaccines the GMP-manufacturing site has to be closely related to the operation theatre, when tumour material is used as antigen source for vaccine production. Many attemps of early commercialization have already failed, as there are usually only few patients falling into the inclusion criteria of a product application, the personell manufacturing and applying the ATMP has to be highly specialized in both GMP-production and medical care, and the costs are high with no appropriate reimbursement by insurance companies on the horizont.

3. Hospital exemption is an invaluable tool, however, it's realization in different countries is highly diverse. For example, in Germany almost no treatments on the basis of the hospital exemption have been realized by the competent authorities. In addition, since the HE regulation is in some contrast to clinical trials, it does not fit the spirit of academic institutions, which have a genuine interest in subjecting their products to scientific evaluation.

4. The realization of clinical trials with a ATMPs has reached an effort which is not manageable anymore even for larger institutions of patient care. We have applied now for funding of a DC-vaccination trial in 50 patients using a product, where lot of clinical experience is available worldwide already. The pure costs for management and monitoring (only a minor scientific byprogramme) were in the range of € 700,000.-, not included the medical costs for production and patient care. Who will finance these amounts and how can scientific progress in this field will be possible with these sums?

As possible solutions for the future the following proposals are conceivable:

- medicinal products produced for individual patients must fall under a different regulation than off-the-shelf mass products. The institutions of specialised medical care are must be equipped with the appropriate rights to guarantee a close-to-the patient product manufacturing. Of course, standards like GMP-production, holding of an appropriate license etc. must be met by the individual institution.

- a production license for an ATMP should be associated with the obligation to use these products only in a scientific context. At the same time, the conditions for clinical evaluation of ATMPs in an academic institution must be brought back to manageable levels. Such an approach could also prevent mis- or uncontrolled use of ATMPs in questionable institution with no public commission for patient care.
Furthermore, instead of focussing of a narrowly defined products, one could define an advanced therapy medinical process, e.g. "cancer vaccines" or "T-cell therapy of refractory viral diseases" which would enable institutions to develop their early phase products more flexible under the supervision of one competent authority.

- it should be aknowledges that data from animal studies are of limited informativity in ATMPs. Regulators tend to insist on the conduct of animal studies despite the fact that profound clinical experience with an ATMP is already existing. This is scientifically not justified and in sharp ethical contrast to animal rights.

- in an early phase of development of a product, the requirements regarding certificates for reagents and additives should be lowered and then adapted to higher levels as the phase of clinical testing advances

- funding possibilities should be ameliorate for clinical trials with ATMPs, e.g. in the Horizon 2020 program

I appreciate very much the intention of the European Commission to approve the unsatisfactory situation in the field of ATMPs and to promote the safe use of these promissing products for the welfare of patients with desperate diseases.

Sincerely yours,

Matthias Eyrich

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Prof. Dr. med. Matthias Eyrich, MD
University Children's Hospital Würzburg
Laboratory for Stem Cell Processing & Cellular Therapy
Josef-Schneider-Strasse 2
D-97080 Würzburg
Germany
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