Public Consultation Paper on the Regulation on Advanced Therapy Medicinal Products

European Commission

Response by EGAN, 27th March 2013

Introduction

EGAN represents the views of patients with inherited disease in Europe. The vast majority of genetic conditions affecting patients in Europe today lack a cure or effective treatment. This field of unmet need is characterised by severe conditions often affecting multiple systems in the body, for which therapies are usually targeted mainly at limiting the impact of symptoms, rather than prevention of disease progression. Patients and their families look towards research and innovation as the source of a therapy for their condition.

Advanced Therapy Medicinal Products (ATMPs) comprising stem cell therapies, tissue therapies, gene therapies and combined therapies comprise some of the most promising types of innovative therapy, from which much is expected from the European patient community.

At the time of its implementation, EGAN regarded the ATMP regulation as a major asset to the European legislative framework. The central regulation of ATMPs should provide a high Europe-wide standard of safety, and a normalised licensing procedure. This common landscape across the European Union when combined with incentives provided by the regulation should encourage investment in the development of ATMPs. It is unfortunate that, to date, the benefits to European patients arising from the regulation have been extremely sparse.

In the context of marketing authorisations, there have been just three positive opinions (in regard to only two products) from the Committee for Advanced Therapies (CAT) over its four year operating period, there have been only nine applications, and just two market authorisations. This is an extremely low turnover rate, which compares poorly to the number of clinical trials on products within the scope of the legislation. In the UK alone there have been more than 100 investigation medicinal products which fall within scope.

The current number of market authorisations should, in theory, include all products which were on the market when the regulation came into force; and which benefited from a transitional moratorium, which ended at the end of 2012.

When uptake of other the other services that the regulation provides for are examined, it is again clear that the final step towards a market authorisation is not being taken for whatever reason. There have been 64 products classified as ATMPs, and 125 scientific advice procedures. There is clearly much ongoing work on the development of products which fall within the scope of the regulation.

It is clear then, that the ATMP regulation is not what it could be, and is not doing the job that we hoped for when it was implemented. We therefore welcome this review of the application of the regulation.

Alastair Kent OBE and Nick Meade both represented EGAN as a patient member and alternate member respectively on the Committee for Advanced Therapies from its inception until October 2011. This response is written with the benefit of their experience of the committee in action.

EGAN Secretariat
Koninginnelaan 23
3762 DA Soest
The Netherlands

P. + 31 35 6034040
F. + 31 35 6027440
E. egan@egan.eu

Marketing authorisation application requirements for advanced therapy medicinal products

The evidence of activity of the CAT discussed in our introduction is stark. There is a great deal of work being carried out on development of ATMPs in Europe. There have been two market authorisations, one of which was the result of an extremely protracted procedure. Clearly the final hurdle is too high, too difficult or too onerous to get over for potential applicants.

We therefore urge the Commission to take account of the practical experience of applicants, previous and potential, submitted to this consultation, with a view to giving the CAT a mandate to apply the regulations in as flexible an approach as possible. This is not to say that we believe a lowering of safety standards are required, but that the regulatory standards should be applied with a greater acknowledgement of the state of the art, and the practicalities of meeting the requirements for a marketing authorisation.

Hospital exemption

The Hospital exemption is a positive stimulus to innovation. It has also allowed the continued supply of locally delivered therapies which fall within the scope of the ATMP regulation. This continued availability benefits patients and benefits innovation by providing an arena in which innovative therapies can be provided to patients outside the scope of a clinical trial to build knowledge.

Though there are risks that a broad application of this exemption, which may allow for example products from a hospital to travel across Europe or for a hospital to be defined as a multisite entity, may create the possibility of circumvention of the requirement for market authorisation, the exemption should be preserved as much as possible. We do not see it as a barrier to bringing ATMPs to market.

We believe attention should be paid to developing a regulatory route for products to make the leap from hospital use to European market authorisation. This is currently a very large step for a hospital based provider to take.

Incentives for the development of advanced therapy medicinal products

A brief examination of the incentives contained within the ATMP regulation shows that two incentives are benefiting from a reasonable take up rate: the provision of scientific advice, and the classification process. These are both provided to all potential applicants. The provision of certification of quality and non-clinical data is limited to small and medium-size enterprises and has been taken up twice in four years.

We do not doubt the value of CAT approval of the data set on which a marketing authorisation is based. We note however that this is the only assistance which is limited to a subset of potential applicants. We suggest therefore that the expansion of this incentive to all applicants should be piloted.

Assessment of and adaption to the innovation landscape

It is clear from our participation in the regulatory process to date and from our discussions with stakeholders that the ATMP field is different to the traditional drug development pathway. In the main, innovation in the field of ATMPs arises from pure research, most often in laboratories which have previously never produced therapeutic products. Those enterprises, hospitals, or laboratories that find themselves with intellectual property which has the potential to provide the basis for a future ATMP are not experienced in dealing with the regulatory world.

This situation leads to two issues which we believe limits the rate of application for ATMP market authorisations. First, the initial development is not carried out according to usual product development standards, which would be the default approach for traditional therapy development; a situation which may damage the quality of any potential application. Second, the potential applicants are unwilling to engage with the European Medicines Agency due to the complexity of the processes involved.

Given the clear potential for these issues to prevent or limit applications, we believe serious attention should be paid to their potential mitigation, and to the mitigation of any other issues that are presented during this consultation.

Attention should be paid for example, to the potential to split intellectual property contained within a market authorisation using an approach similar to the drug master file concept. This would allow innovators to keep their knowledge confidential while allowing a partner organisation to develop the concept into a marketable therapy.

The operation and personnel of the Committee for Advanced Therapies

Article 21 1c and 1d mandates that the membership of the CAT should include representatives of the patient and clinician community. Representatives of EGAN performed this role on behalf of the patient community until the well known conflicts of interest issue arose which led to some of the membership of the CAT stepping down.

We would like to take this opportunity to particularly highlight the value of those members representing clinicians, and of the academic members nominated by member states, to the functioning of the committee.

Those members who had direct experience of working in the field of ATMP development served a dual role as experts with a cutting-edge knowledge of the treatments under discussion, and as the members that could regularly bring a reality check to the proceedings. It is these members who would explain to the committee that the requirements being proposed are, for example, inappropriate for an ATMP, or simply not possible. The members with practical experience played a vital role in ensuring that the regulatory process followed biology rather than trying to force biology to follow the regulations.

It is our understanding that these four seats, two clinicians and two patients, have now remained unfilled for almost eighteen months, while academic members nominated by member states have been replaced by others. The CAT is now clearly less heterogeneous than it was at its inception, and we believe less able to do the difficult job of regulating emerging technologies. With all due to respect to the eminent regulators on the CAT, we believe they would agree with us that their deliberations would be enhanced if the presence of leading academic experts in the field could be permitted.

We urge the Commission to find a way to bring those with current, active, and high-quality knowledge of the field of ATMP back to regular membership of the CAT. We believe their interests should be made abundantly clear, and that they should be accepted and allowed to continue to shape the future of therapies for unmet needs in Europe.

We are grateful for the opportunity to comment on this consultation and would be happy to discuss any of these issues further at the Commission's convenience.

Alastair Kent OBE
President
EGAN

alastair@geneticalliance.org.uk