Mr Nicolas Rossignol
European Commission
Directorate-General Enterprise and Industry
Unit F2 Pharmaceuticals
45 Avenue d'Auderghem, Office 10/128
B-1049 Brussels
Belgium

[Date]

Sent by email and by post

Comments on the Proposals to Amend Annex I to Directive 2001/83 As Regards Advanced Therapy Medicinal Products

Dear Mr Rossignol

Action Duchenne welcomes the opportunity to provide the Commission with our comments on the proposals to amend Annex I to Directive 2001/83. Action Duchenne is a charity organisation based in the United Kingdom. Action Duchenne has the mission to exclusively fund research for a cure, and to promote campaigns for better medical care for Duchenne and Becker Muscular Dystrophy. We also work closely with our sister organisations in the other Member States of the European Union to foster greater awareness of these diseases at a European level. Our organisation has received tremendous support (including financial support) from the general public including parents of the sufferers who so desperately would like to find a cure for their loved ones.

Duchenne Muscular Dystrophy is a devastatingly severe disease in that young men are totally paralysed by late teens and die young from respiratory or heart failure. The disease affects one in 3500 males, thus making it the most prevalent form of muscular dystrophies. The disorder is caused by a mutation in the dystrophin (DMD) gene, located in the X chromosome. This gene codes for the protein dystrophin, an important structural protein that stabilises the dystroglycan complex located on the cell membrane. In the case of Duchenne muscular dystrophy, a mutation may occur as a result of a missing base or codon through nonsense, premature stop signal, out-of-frame and duplication. These mutations result in a biologically dysfunctional protein being produced in muscle cells.

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Currently, there is no known cure for this disease. Although there is little commercial interest in developing treatments for this group of patients, Action Duchenne has provided research grants to a number of academic groups to research new treatment approaches. Researchers have focussed their efforts primarily on exploring use of antisense oligonucleotides to induce specific exon skipping. Such an approach has been shown to be capable of restoring the reading frame and expression of functional dystrophin in certain experimental settings. These findings may form a good basis for clinical application of this technology to the treatment of Duchenne and Becker Muscular Dystrophies.

Against this factual background, we wish to make the following observations on the Commission's proposals.

We understand Annex I to Directive 2001/83 relates to the specific information that an applicant for a marketing authorisation is required to submit to the competent authorities for them to assess the safety, quality and efficacy of a medicinal product. The current regulatory approach to evaluating safety, quality and efficacy of a medicinal product is based upon a defined product which can used to assess its risk/benefit balance in a patient population sharing similar clinical characteristics. However, this conventional approach may not be applicable or relevant to medicines which are produced specifically to address the clinical need of a specific patient, i.e. "personalised medicine".

We believe that the amendment to this Annex should take account of the technological advances in using "platform medicine" to treat a disease like Duchenne. In that we mean use of a technological platform to generate patient-specific individualised medicine. As explained above, Action Duchenne is funding academic groups to research the potential clinical application of effective exon skipping to restore dystrophin expression in various gene mutations. These mutations may vary from patient to patient. Therefore, the anti-sense oligonucleotides must be chemically synthesised to target the specific mutation found in the individual patient. Such an approach will present new challenges as regards evaluation of pre-clinical and clinical safety and efficacy of these patient-specific oligonucleotides.

In the case of exon skipping, there is not a single defined medicinal product that can be used in all sufferers of Duchenne muscular dystrophy. Instead, the composition of the medicinal product is individualised. **We believe that there is a need to provide greater clarity and guidance as to how safety, quality and efficacy of "personalised medicines" will be assessed**.

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We believe that there is already a body of evidence to support use of anti-sense oligonucleotides to induce specific exon skipping as a viable therapeutic approach to treating Duchenne children. In that regard, it should be recognised in Community law that therapeutic interventions based upon platform technologies cannot be treated in the same way as conventional pharmaceutical products. Unless Annex I to Directive 2001/83 is amended to address specifically these new approaches, then it would be impossible (1) to attract commercial partners to develop personalised products and (2) to progress through the regulatory process in time to realise their therapeutic potential in treating Duchenne. For many of the Duchenne sufferers, unless a viable cure (such as exon skipping) is available, sadly the reality is that they will not live beyond their teens.

In line with the broader European policy to innovate and to develop new therapeutic approaches to treat diseases where there is an unmet medical need (and particularly in the case of Duchenne, one deals with the vulnerable paediatric populations), we urge the Commission to take this opportunity to recognise the need to adopt a new approach to assessing risk/benefit balance of platform technologies intended for delivering individualised or personalised medicines.

In conclusion, we agree that grant of an approval should be firmly based upon an assessment of risk/benefit. However, we believe that the process for assessing risk/benefit (and accordingly the data requirements) for personalised or individualised medicines ought to be clarified in the current amendment to Annex I. For Duchenne children, timely access to these life-saving medicines is critically important before it is too late for them.

Thank you for your attention.

Yours sincerely

Nick Catlin
Chief Executive
Action Duchenne