Annex 1 – Amendments to EP760

1. An *in vitro* or *ex vivo* method for cleaving a target DNA in a mammalian cell, inducing a targeted mutagenesis in a mammalian cell or genome editing in a mammalian cell, the method comprising the steps of

(a) providing a composition comprising a single-chain guide RNA (sgRNA) and a Cas9 protein, and wherein the sgRNA and the Cas9 protein are present in a mass ratio ranging from 100:225 to 100:22.5, and

(b) transferring the composition into the cell,

wherein the Cas9 protein is a *Streptococcus pyogenes* Cas9 protein

2. An *in vitro* or *ex vivo* method of preparing a mammalian cell, the method comprising the steps of

(a) providing a composition comprising a single-chain guide RNA (sgRNA) and a Cas9 protein, and wherein the sgRNA and the Cas9 protein are present in a mass ratio ranging from 100:225 to 100:22.5, and

(b) transferring the composition into the cell,

wherein the Cas9 protein is a *Streptococcus pyogenes* Cas9 protein

4. An *in vitro* or *ex vivo* use of a sgRNA and a Cas9 protein for transfer into a mammalian cell for cleaving a target DNA in said mammalian cell, inducing a targeted mutagenesis in said mammalian cell or genome editing in said mammalian cell, wherein the sgRNA and the Cas9 protein are provided in a composition and wherein the sgRNA and the Cas9 protein are present in a mass ratio ranging from 100:225 to 100:22.5, and the composition is transferred into the cell, and wherein the Cas9 protein is a *Streptococcus pyogenes* Cas9 protein.

5. An *in vitro* or *ex vivo* use of a Cas9 protein complexed with a sgRNA for transfer into a mammalian cell for cleaving a target DNA in said mammalian cell, inducing a targeted mutagenesis in said mammalian cell or genome editing in said mammalian cell, and

wherein the sgRNA and the Cas9 protein are present in a mass ratio ranging from 100:225 to 100:22.5, and wherein the Cas9 protein is a *Streptococcus pyogenes* Cas9 protein.