Supplementary file 2

Definitions of Adverse Events

An adverse event (AE) is defined as any untoward medical occurrence in a patient or clinical trial patient administered a medicinal product, which does not necessarily have a causal relationship with the study treatment (Directive 2001/20/EC). An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

Non-Serious Adverse Event (SAE)

A non-serious AE is defined as any untoward change in a patient's medical conditions that does not meet serious criteria noted below (e.g., is not fatal, is not life-threatening, does not require hospitalization, does not prolong a current hospitalization, is not disabling, etc.).

Serious Adverse Event (SAE)

A serious adverse event (SAE) is defined in line with Directive 2001/20/EC as any adverse experience that meets any of the following criteria:

- results in death
- is life-threatening
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- results in a congenital anomaly/birth defect
- is an important medical event

Serious Unexpected Adverse Event/Reaction Definition

An adverse event/reaction, the nature or severity of which is not consistent with the applicable product information (e.g. investigator's brochure for an unauthorised investigational product).

Adverse Events of Special Interest (Sight-threatening Events)

The following adverse events are considered to be of special interest and by default shall be reported as SAEs (medically important criteria):

- Adverse Events that caused a decrease in visual acuity of >30 ETDRS letters or > +0.6 LogMAR (compared with the last assessment of visual acuity at the last visit) lasting >1 hour
- Adverse Events that caused a decrease in visual acuity to the level of Light Perception or worse lasting >1 hour
- Adverse Events that required surgical intervention (e.g., conventional surgery, vitreous tap or biopsy with intravitreal injection of anti-infectives, or laser or retinal cryopexy with gas) to prevent permanent loss of sight
- Adverse Events associated with severe intraocular inflammation (i.e., 4+ anterior chamber cell/flare or 4+ vitritis)
- Adverse Events that, in the opinion of the investigator, may require medical intervention to prevent permanent loss of sight.

Intensity Assessments

For every AE, the intensity (severity) has been assessed. Specifically, the intensity of events has been classified as:

- Mild **:** Does not interfere with patient’s usual function (awareness of symptoms or signs, but easily tolerated [acceptable]).
- Moderate **:** Interferes to some extent with patient’s usual function (enough discomfort to interfere with usual activity [disturbing]).
- Severe**:** Interferes significantly with patient’s usual function (incapacity to work or to do usual activities [unacceptable])