1. The sponsor proposes the following Indications for Use (IFU):

> *The FSYX™ Ocular Pressure Adjusting Pump (FSYX OPAP) is indicated as adjunctive therapy for the* ***reduction of intraocular pressure*** *during use* ***nightly use*** *in adult patients with open-angle glaucoma and intraocular pressure ≤ 21 mmHg.*

The conventional IOP measurement is defined by the pressure difference between the inside of the anterior segment of the eye and the environment immediately outside, as measured by applanating the cornea. Conventionally, this immediate outside environment is atmospheric pressure. However, when applying negative pressure using the FSYX OPAP device, this environment is below atmospheric pressure. An alternative IOP parameter was devised by Equinox to measure IOP while the device is in use (i.e., with negative pressure [NP] on), as the Goldmann applanator cannot be used while a patient is wearing the goggles. This parameter was found to be lowered only while the device is in use (i.e., with NP on) and the reduction ended once the device was turned off. However, Equinox defines this alternative parameter as TCPD relative to atmospheric pressure without accounting for the NP microenvironment. Although the data demonstrated that this alternative IOP is lowered temporarily when the device is in use, Equinox acknowledges that conventional IOP actually increases by 21.7% - 26.9% with MPD use. Hence, IOP defined in one way increases, while IOP defined in another way decreases.

Do you believe there is clinical benefit to the lowering of this alternative IOP parameter and increasing of TCPD on a daily basis for several hours?

2. In support of the demonstration of effectiveness, the sponsor has submitted data from the CP-X19 pivotal trial and 21 additional studies (see Section 8 - Report of Prior Investigations in FDAs executive summary).

In CP-X19 pivotal trial, the pre-specified primary and secondary effectiveness endpoints were met:

- 58.1% (54/93) of study eyes and 1.1% (1/93) of control eyes demonstrated a ≥20% reduction of IOP (by excursion tonometry) at the Week-52 clinic visit.
- 63.4% (59/93) of study eyes and 3.2% (3/93) of control eyes demonstrated a ≥20% reduction of IOP (by excursion tonometry) at the Week-52 sleep lab visit.

Measurements by Goldmann applanation tonometry show that after cessation of device use, the IOP reverts closely to the IOP measured before device use.

Do you believe the IOP lowering as measured by excursion tonometry during use of the device observed in CP-X19 pivotal trial, in combination with data from the other

supportive additional studies demonstrates a reasonable assurance of effectiveness as an adjunctive therapy for the reduction of intraocular pressure during use in adult patients with open-angle glaucoma and IOP ≤ 21 mmHg? If not, what additional assessments do you recommend?

3. In CP-X19 pivotal trial, the following were the key safety findings at one year:

- Ocular adverse events (most frequently reported):
  - eyelid edema (11.8%),
  - signs and symptoms of dry eye (5.4%),
  - conjunctival hyperemia (4.3%),
  - eye pain (3.2%), eyelid erythema (2.2%),
  - loss of best-corrected distance visual acuity ≥10 letters from baseline (2.2%), and
  - posterior vitreous detachment (2.2%).

- Periorbital adverse events:
  - periorbital edema (12.9%),
  - periorbital contact dermatitis (4.3%), and
  - periorbital pain (2.2%)

- The *post hoc* analysis of visual field conducted by a third-party reading center revealed mean deviation worsening ≥2.5 dB in four study eyes (6.5%) at Weeks 26 and three study eyes (4.8%) at Week 52.

- Optical coherence tomography (OCT) examinations were collected from 62 participants at the Week 26 and Week 52 and evaluated *post hoc* by a third party reading center. No formal quantitative analysis of OCT data had been planned or was conducted.

a. Do you believe the available data demonstrates reasonable assurance of safety at 1 year?

b. Do you believe the available data demonstrates reasonable assurance of long-term safety?

c. If not, what additional data do you do you recommend?

4. The currently proposed device labeling recommends: 1) Range of programmable negative pressure (NP) between -5 to -20 mm Hg; and 2) Range of wear time between 1 to 8 hours

The following data is available for range of programmable NP:

- CP-X19 trial:
    - 93 participants with a range of mean NP between -10.0 mm Hg to -12.1 mm Hg.
    - 8 participants who used the device with NP between -17 mm Hg to -20 mm Hg for at least 26 weeks during the trial. Of these eight, three (37.5%) experienced ocular and/or periorbital AEs.
    - 53 participants used devices programmed >-12 mm Hg at some point during the trial. 38 of these 53 completed the trial while 15 discontinued early. Of these 38, 18 were reported with a device-related AE.
- CP-X10 trial:
    - 64 participants with a range of mean NP between -10.59 mm Hg to -11.46 mm Hg.

The following data is available for range of wear time:

- CP-X19 trial
    - 93 participants with average daily wear time ranging from 5.44 to 5.63 hours
    - 61 participants with average wear time at the Week-52 sleep lab visit of 2.9±0.3 hours 11:00 pm – 2:00 am and 2.6±0.5 hours 2:00 am – 5:00 am.
- CP-X10 trial
    - 64 participants with average daily wear time ranging from 3.74 to 4.38 hours (average 4.4)

a. Do you believe the available data supports the proposed range of programmable NP;

b. Do you believe the available data supports the proposed range of wear time?

c. If not, what do you recommend?

5. The sponsor proposed the following IFU:

The FSYX™ Ocular Pressure Adjusting Pump (FSYX OPAP) is indicated as adjunctive therapy for the reduction of intraocular pressure during use in adult patients with open-angle glaucoma and IOP ≤ 21 mmHg.

In the CP-X19 pivotal trial, IOP was measured via pneumotonometry with the excursion goggles, before and during NP application, during in-clinic visits. The proportion of study eyes with at least 20% IOP reduction (relative to atmospheric pressure) was 58.1% (at Week 52) and the mean IOP changed from 18.0 mm Hg to 11.4 mm Hg. The mean transcorneal pressure difference (TCPD) increased (i.e., relative to the microenvironment surrounding the eye that is created by the goggles) in the study eye to 23.4 mmHg).

Does the proposed IFU statement use the appropriate nomenclature and language to accurately describe the function of the device with regard to IOP? If not, how should the IFU statement describe the function of the device?

6. **Do the probable benefits of the FSYX OPAP device outweigh the probable risks for use in patients who meet the criteria specified in the proposed IFU?**