## 2.3.S.7 Stability

Stability studies are designed to support the long-term storage of the drug substance at -40℃±5℃ and identify the stability indicating assays under accelerated conditions (-20℃±2℃). The containers used for stability studies are small Nalgene LDPE bottles which are representative of the DS storage container. 36 months long term stability study and at least 6 months of accelerated study are planned. The stability specification is same as that used for release of the DS. The stability protocol is presented in Table 2.10.

**Table 2.10 Experiment design for accelerated and long-term stability test of KN035DS**

| Experiment condition | Test point (month) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 6 | 9 | 12 | 18 | 24 | 36 |
| Accelerated (-20℃±2℃) | △ | √ | √ | √ | △ | √√ | -- | -- | -- | -- |
| Long-term (-40℃±5℃) | △ | -- | -- | √ | △ | √ | △ | √ | △ | △ |

△. Appearance, pI, peptide mapping,Western blot, SE-HPLC, WCX-HPLC, CE-SDS (reducing), HCP, host cell DNA, potency (binding and blocking assays), endotoxin, bioburden and protein content.

√√ Stability testing will continue if no significant differences in the test results were observed after 6 months.

√SE-HPLC, WCX-HPLC, CE-SDS (reducing), and protein content.

Nine months of long term stability data are available for 3 lots of DS. No significant change of any quality attributes tested was noted in either lot. The DS is stable for at least 9 month under long term. Accelerated stability testing of KN035 DS was conducted at -20±2℃. No significant change or trend is noted except aggregate tested by SE-HPLC. Aggregate% for all 3 DS lots showed slightly trending up under accelerated conditions. It is not clear the noted trends are caused by method variation or it is a real trend. We will continuously monitor the stability, identify the degradation pathways and stability indicating assays. If accelerated stability study cannot conclude any changes for DS quality, we will perform stability studies under stressed conditions in the future. The updated stability data will be reported in the annual report. All the long term stability data are presented in section 3.2.S.7.3 Tables 3.48 to 3.50. The accelerated stability data are presented in 3.2.S.7.3Tables 3.51 to 3.53.