2.3.A Adventitious Agents Safety Evaluation

The safety of the KN035 has been ensured through its DS and DP manufacturing process and raw materials controls. The manufacturing of KN035 is conducted in a strict cGMP environment to minimize the introduction of adventitious agents during the manufacturing process.

No animal sourced materials were used during the manufacturing process of KN035 DS and DP. The only animal sourced materials used during the host cell line CHOK1 adaptation to generate the host cell bank CHOK1S were bovine virus serum and trypsin. The CoAs of these materials are provided in 3.2.A.4.1 and 3.2.A.4.2 to ensure the low risk of BSE/TSE. In addition, the host cell line CHOK1S WCB was tested for porcine viruses, Bornavirus, and bovine/porcine circovirus (PCV), and the MCB was extensively tested for adventitious viruses, retrovirus, mycoplasma, bovine virus and sterility.

Viral clearance studies were performed using validated small scale model for low pH inactivation step, anion exchange chromatography and the nanofiltration step in the DS downstream processing. Two model viruses used are xMuLV and MMV. The results of viral log reduction factor is presented in Table 2.18

Table 2.18 Log reduction factor summary

TABLE 1A – LOG REDUCTION FACTORS		
LOW pH TREATMENT	**RUN 1**	**RUN 2**
MLV	4.51 ± 0.39 $\log_{10}$	4.89 ± 0.44 $\log_{10}$
ANION EXCHANGE CHROMATOGRAPHY		
MLV	≥5.42 ± 0.33 $\log_{10}$	≥5.41 ± 0.31 $\log_{10}$
MMV	5.29 ± 0.36 $\log_{10}$	6.07 ± 0.36 $\log_{10}$
VIRUS REDUCTION FILTRATION		
MLV	≥3.79 ± 0.33 $\log_{10}$	≥3.53 ± 0.32 $\log_{10}$
MMV	≥6.84 ± 0.29 $\log_{10}$	6.25 ± 0.44 $\log_{10}$

TABLE 1B – OVERALL LOG REDUCTION FACTORS	
MLV	≥13.45 ± 0.59 $\log_{10}$
MMV	11.54 ± 0.57 $\log_{10}$

The safety margin is calculated to be less than 1 viral particle per 35145 doses.