ATTACHMENT A

Amino Acid Sequences of the Variable Domains of Bevacizumab

Variable Heavy

```
A.4.6.1     EIQLVQSGPELKQPGETVRISCKASGYTFTNYGMNWVKQAPGKGLKWMG
            *   *  ** *   *** *  *               *        * *
F(ab)-12    EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVRQAPGKGLEWVG
                                        *  ** * *            *
humIII      EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS
            1        10        20        30        40

A.4.6.1     WINTYTGEPTYAADFKRRFTFSLETSASTAYLQISNLKNDDTATYFCAK
                                      *  *      *** ***   * *
F(ab)-12    WINTYTGEPTYAADFKRRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCAK
            * **** ***  *** *   * * *  * *                  *
humIII      VISGDGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
           50  a      60        70        80  abc      90

A.4.6.1     YPHYYGSSHWYFDVWGAGITVTVSS
                              *  *
F(ab)-12    YPHYYGSSHWYFDVWGQGTLVTVSS
            *            *
humIII      G----------FDYWGQGTLVTVSS
                            110
```

Variable Light

```
A.4.6.1     DIQMTQTTSSLSASLGDRVIISCSASQDISNYLNWYQQKPDGTVKVLIY
                 **      *    * *                 ****
F(ab)-12    DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAPKVLIY
                                    *   *     *           *
humKI       DIQMTQSPSSLSASVGDRVTITCRASQSISNYLAWYQQKPGKAPKLLIY
            1        10        20        30        40

A.4.6.1     FTSSLHSGVPSRFSGSGSGTDYSLTISNLEPEDIATYYCQQYSTVPWTF
                                 **    * *   *
F(ab)-12    FTSSLHSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYSTVPWTF
            **   *                                      ***
humKI       AASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSLPWTF
           50        60        70        80        90

A.4.6.1     GGGTKLEIKR
            *   *
F(ab)-12    GQGTKVEIKR

humKI       GQGTKVEIKR
           100
```

Fig. 1. Amino acid sequence of variable heavy and light domains of muMAbVEGF A.4.6.1, humanized F(ab) with optimal VEGF binding [F(ab)-12] and human consensus frameworks (*humIII*, heavy subgroup III; *humκI*, light κ subgroup I). *Asterisks*, differences between humanized F(ab)-12 and the murine MAb or between F(ab)-12 and the human framework. CDRs are *underlined*.