Succeeding Mother Margaret George, Sisters Joseph Harvey and Regina Mattingly led the Community from 1859 to 1887. During this period the Community assisted in founding the Sisters of Charity of St. Elizabeth in Newark, New Jersey (1859), and the Sisters of Charity of Seton Hill in Greensburg, Pennsylvania (1870). Mount St. Joseph motherhouse, including the Chapel of the Immaculate Conception, was completed in 1901. In the 1920s internal changes resulted from the Community changing its canonical status from diocesan to pontifical, and beginning in 1929 the Sisters of Charity absorbed more than 40 hearing-impaired members of the Pious Union of Our Lady of Good Counsel.

The Sisters and Daughters of Charity formed the Mother Seton Conference in 1947 to work for the canonization of their founder. Their efforts were rewarded when Elizabeth Seton was declared venerable by the Church in 1957 and beatified in 1963. In the 1950s a house of studies for temporary professed Sisters, part of the Church-wide Sister Formation movement, was established at the motherhouse to provide new members with an extensive spiritual and educational experience before beginning their ministries. This helped prepare the Congregation for the renewal that was to come.