Tissue biopsy has for the longest time been the gold-standard in cancer research and patient management. However, in the age of precision and personalized medicine, a shift is being made towards the employment of liquid biopsies and further analysis by NGS technology. While both the genetic and epigenetic markers of cell-free DNA (cfDNA) reflect the molecular status of its tissue-of-origin it is known that preanalytical procedures impact the downstream results. Calls for greater standardization are continuously being made, yet studies that comprehensively assess the impact of different methods on downstream diagnostic parameters, including NGS, are lacking. An analysis of blood plasma is presented with the aim to assess the variability of their respective cfDNA diagnostic parameters. The most popular methods of cfDNA isolation were assessed. Quantification of cfDNA was performed by qPCR as well as cfDNA fragment analysis. cfDNA methylation was analysed by pyrosequencing, the first next-generation sequencing instrument which is still a gold-standard in DNA methylation research. Different isolation methods gave a wide range of cfDNA yields. cfDNA fragmentation was also impacted with different methods producing different fragmentation indexes. Still, cfDNA methylation data have remained consistent across different methods used. While both cfDNA yield and cfDNA fragmentation are highly impacted by preanalytical methods employed, cfDNA methylation analysed by pyrosequencing has remained unchanged. cfDNA methylation has been shown as a stable biomarker that could reduce pressure of method and protocol inter-lab standardization and help cfDNA find clinical use sooner rather than later.