Basis for each recommendation:

Start → Only very dissimilar sequences? — Yes → Try adding more homologous sequences

Accuracy can often be improved considerably by including closely related sequences, which can then be removed after alignment. The additional sequences act as "stepping stones" between distantly-related sequences.

Only very dissimilar sequences? — No → Type of input sequences?

Type of input sequences? → Amino acids / ncRNA / DNA/mRNA

ncRNA → Input as an `RNAStringSet`

DNA/mRNA → All protein coding?

Amino acids → Use `AlignSeqs`

Input as an `RNAStringSet` → Use `AlignSeqs`

All protein coding? — Yes → Use `AlignTranslation`

Alignment of amino acid and non-coding RNA sequences can be improved by making use of their conserved secondary structure. `DECIPHER` will automatically predict secondary structures if the input is an `AAStringSet` or `RNAStringSet`. For coding (nucleotide) sequences, `AlignTranslation` will align the sequences in amino acid space.

Use `AlignSeqs` / Use `AlignTranslation` → Using the alignment for phylogenetics?

Staggering the alignment decreases false positive homologies by separating independent insertions.

Using the alignment for phylogenetics? — No → Aligning more than 46k sequences?

Using the alignment for phylogenetics? — Yes → After alignment run `StaggerAlignment`

Aligning more than 46k sequences? — Yes → Consider using a chained guide tree

Aligning more than 46k sequences? — No → Only extremely similar sequences?

After alignment run `StaggerAlignment` → Only extremely similar sequences?

Chained guide trees offer a viable alternative when aligning more than 46,340 sequences, which is the maximum for the default guide tree. Refer to the section of this vignette entitled "Building a Guide Tree".

Consider using a chained guide tree → Specify arguments: `iterations=0` `refinements=0`

Only extremely similar sequences? — Yes → Specify arguments: `iterations=0` `refinements=0`

Iteration and refinement steps are unnecessary when all of the sequences are very similar or when a chained guide tree is being used.

Only extremely similar sequences? — No → Many sequences much shorter than others (fragments)?

Specify arguments: `iterations=0` `refinements=0` → Many sequences much shorter than others (fragments)?

Many sequences much shorter than others (fragments)? — Yes → Specify argument: `normPower=0`

Many sequences much shorter than others (fragments)? — No → **Ready to align!**

Specify argument: `normPower=0` → **Ready to align!**

Setting `normPower` to zero will weigh all columns of the alignment equally, regardless of column occupancy. This helps with aligning partial-length sequences because many columns of the alignment are expected to have low occupancy.