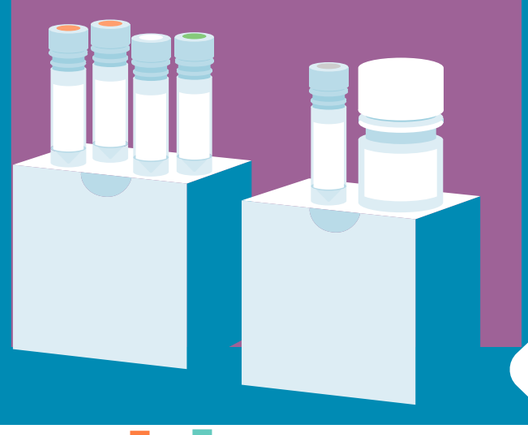
RESIDUAL DNA TESTING:
Homebrew vs off-the-shelf solutions

To verify product quality, the amount of residual DNA in a drug's final dosage form must meet guidelines established by multiple regulatory agencies. Each regulatory agency has specific guidelines for acceptable limits depending on the product and therapeutic modality.

Companies that produce biopharmaceutical products must verify the quantity of residual DNA impurities throughout the purification process, and in the final drug product.

Commercial kits for residual DNA testing can shorten process development time and reduce in-house staffing, overheads, and expertise requirements. This lowers risk and results in a cost-effective solution overall.



STEPS TO SETTING UP YOUR OWN RESIDUAL DNA TESTING SOLUTION

CREATE A QUALIFIED METHOD FOR TESTING A MANUFACTURED BIOLOGIC FOR RELEASE

Do you have the right in-house expertise?

Identify target sequence	Bioinformatics expert or Molecular Biologist with bioinformatics expertise
Design primers & probe	Molecular Biologist
Optimize concentration of primers & probes (Statistical software can help to design a shorter experimental plan)	Molecular Biologist with Design of Experiments (DoE) & biostatistics skills
Characterization & qualification of DNA controls/standard (Have you got a reliable source for your DNA controls?)	Molecular Biologist and regulatory expert
Source and qualify reagents • Source reagents • Qualification of reagents (Do you have a procedure for qualifying critical reagents? / What process is in place for dealing with delays from raw materials suppliers? / Have you defined a process to QC raw materials? / cGMP reagents can take up to a week to produce)	
Ensure process conforms to regulatory requirements (Do you have the in-house expertise to un-derstand regulatory requirements?)	Regulatory expert
Create test method • Draft • Review • For commercial product: update method for own site	Molecular Biologist with technical writing skills
Qualification/validation of the analytical method • Draft qualification method • Review • Qualification & execution • Report • Draft validation method • Execution of the validation • Validation report	Molecular Biologist, regulatory expert (knowledge of FDA and other regulatory agency requirements), industry expert

At this point, you have a qualified method that can be used to test a manufactured biologic for release

CREATING THE QUALIFIED METHOD IS ONLY THE FIRST HURDLE...

Staffing requirements and overheads are much greater for an in-house solution

METHOD MAINTENANCE IN-HOUSE

The in-house method requires routine testing and health evaluation

- Method health evaluation
- Inventory management
  Maintain an inventory of critical primers, probes and DNA controls
- Dedicated team to support the method in-house
- Re-qualification of each new lot of primer/probe mixes

TROUBLE-SHOOTING

Do you have the resources in-house to troubleshoot the issue when something goes wrong with the test method?

- Have you got a process in-house to identify the issue when the assay starts to fail?
- Do you have the in-house resources to troubleshoot the issue?
- Can you afford the time to get back on-line? It can take a week or more to check all parts of the process and get back online.

It can take a week or longer to get back online.

RISK MITIGATION

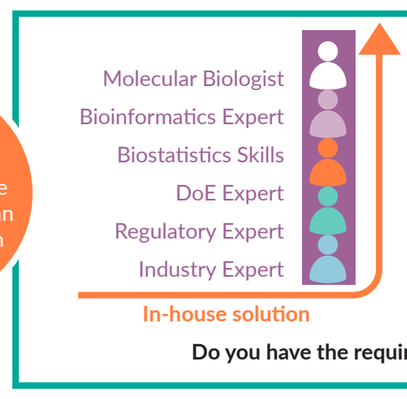
Are you able to afford a failed assay to delay batch release?

- Have you factored in delays for reagents failing qualification?
- Do you have a process in place to deal with delays and issues with your raw materials?

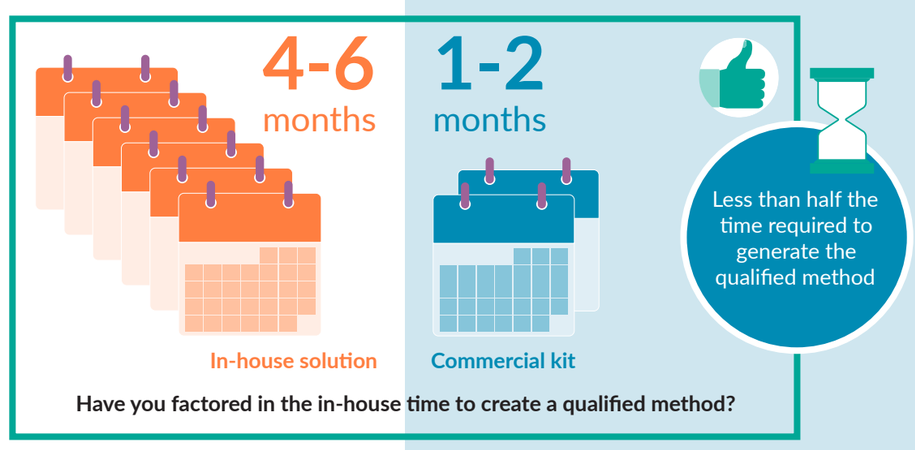
REGULATORY ISSUES

Do you have a dedicated person who can respond to questions coming from regulatory authorities?

- Do you have someone in-house to can answer regulatory questions regarding assay design and how it was validated?



Do you have the required expertise in-house?



Have you factored in the in-house time to create a qualified method?

"For those convinced that creating their own assays saves money, it's time to consider the hidden expenses. Troubleshooting DIY assays can become a time-consuming and costly endeavor. Commercial DNA quantitation kits offer a reliable, ready-to-use solution, ensuring accurate results without the unexpected financial detours of assay troubleshooting."

– James Baus

STEPS TO SETTING UP A COMMERCIAL RESIDUAL DNA TESTING SOLUTION

The Applied Biosystems™ resDNASEQ™ Quantitative DNA Kits utilize a quantitative PCR (qPCR)-based system to detect plasmid DNA and host cell DNA from various cell types commonly employed in the development of gene therapies, cell-based vaccines, and similar biotherapeutics.

With the resDNASEQ system, you can achieve both sensitive and specific quantitation, ensuring a high level of confidence in the data obtained from a diverse range of sample types. This includes in-process samples with different sample matrices, as well as purified final products

The overall performance of the resDNASEQ method, including sensitivity, accuracy, precision, range, and linearity meets or exceeds the example described in USP <509>.

The resDNASEQ system offers a sample to result solution.

No requirement for assay component procurement

No requirement to qualify critical reagents

Lab technician	Qualification/validation of the analytical method • Adapt qualification method (provided) • Review • Qualification & execution • Report • Draft validation method • Execution of the validation • Validation report

At this point, you have a qualified method that can be used to test a manufactured biologic for release

Support services include access to a team of experts including molecular biologists and regulatory experts meaning that you can run the process in-house with a Lab Technician. Thus reducing staffing and overheads costs.

When you use a commercial kit, you are covered from sample to result and everything in between. These risks are not your issue.

Access to a team of Regulatory Experts comes as part of the commercial kit.

BENEFITS OF THE THERMO FISHER COMMERCIAL KIT

Reduced staffing and overheads in-house	Dedicated team of experts	Access to a team of experts including regulatory specialists
Lower risk	Support from sample to result	No unexpected delays or costs
Eliminated time needed to develop assay in-house	Cost effective	Method creation and maintenance is handled for you

ThermoFisher SCIENTIFIC