



## Liver Disease Capabilities

### Nonalcoholic fatty liver diseases & non-alcoholic steatohepatitis (NAFLD & NASH)

Non-Alcoholic Fatty Liver Disease (NAFLD) is a chronic liver disease, affecting up to 30% of the world population. Its effects range from simple fat accumulation (steatosis) to inflammatory-mediated fibrosis or cirrhosis – the most severe form of the disease called Non-Alcoholic Steato-Hepatitis (NASH). It is estimated that 20-25% of NAFLD patients will advance to NASH during their lifetime, placing them at significantly increased risk for liver failure or liver cancer.

#### Scientific expertise

Our scientific experts include pathologists and scientific advisors in liver disease, infectious disease, translational genomics, and soluble protein biomarkers. Our expert team integrates therapeutic insights, state-of-the-art technologies, best-in-class methods and quality systems to optimize your NAFLD/NASH study design, assuring high-quality data delivery and regulatory approval. We have participated in more than 25 hepatology studies in various capacities, and we provide custom product-specific assay support.

#### NASH and NAFLD team of experts

In collaboration with our parent organization, IQVIA, we have a cross-company NASH and NAFLD team with solid experience, global CRO expertise, and multiple reference testing services. This includes a Center of Excellence (CoE) in NASH that includes experienced operations, data management, laboratory, scientific, regulatory and medical teams. Globally, we have a vetted NASH network of proven investigators. Innovations in patient identification using proprietary algorithms and data resources assure the completion of a NASH clinical trial on time and within budget.

#### Experience

We offer an extensive test menu of liver function tests – both standard and custom tests – and provide strategic guidance to address your study goals to drive better outcomes and regulatory approvals.

#### Liver biopsy – the gold standard

Tissue biopsy diagnosis remains still the gold standard for the assessment of NAFLD and NASH. The staging of the most critical component of NASH – fibrosis – is still best done at the microscope with the help of hematoxylin and eosin (H&E) and two special histochemical stains, Masson's trichrome and a reticulin (silver) stain. Both of these stains are validated at our laboratories worldwide.

In addition, Q<sup>2</sup> Solutions has validated a variety of other special histochemical stains including orcein, Prussian blue, and PAS (with and without diastase) to help screen for and exclude non-NASH disease entities that may confound study results. Most patients come to a clinical trial with an outside diagnosis and staging of NASH. Due to inter-observer variability, these archival tissues often need to be re-evaluated at the central lab to confirm the outside diagnosis. We have several liver-specialized pathologists who have reviewed tens of thousands of NASH cases over the last five years, and we also have deep academic expertise.

In the context of the FDA's recommendation for enhanced quality assurance and adjudicatory reviews of liver biopsies in clinical trials, Q<sup>2</sup> Solutions offers our "2+1" adjudication pathology reviews. This means that each biopsy is reviewed at least twice by two independent Q<sup>2</sup> Solutions pathologists. If there is any discordance on the endpoints of the analysis, a third independent pathologist reviews the case and renders the definitive summary diagnosis. This "2+1" arrangement can be tailored to the sponsor and may include clinical site pathologists (e.g., hospital) or expert academic pathologists.

#### Non-invasive biomarkers for NASH

We offer several of the composite biomarker tests to evaluate for NAFLD/NASH. The heritability and inter-ethnic variations in susceptibility suggest that genetic factors may play an important role in determining the phenotypic manifestation and overall risk for NAFLD. Gene clusters in families with certain genetic variants on or near TM6SF2 and PNPLA3 genes can increase the heritability of NAFLD by up to 27% within families. We perform the testing for these genetic markers. We offer the Enhanced Liver Fibrosis (ELF™) Test, a non-invasive blood test that measures three direct markers of fibrosis and assesses the risk of NAFLD/NASH progression and liver-related events. In addition, we recently validated the NIS4® assay in collaboration with Genfit, another noninvasive diagnostic marker for measuring NASH and fibrosis. NIS4 assigns a continuous score (0.0 to 1.0) based on quantification of four circulating biomarkers: miR-34a, alpha-2-macroglobulin, YKL-40 and hemoglobin A1c. Furthermore, we offer other NASH biomarkers such as hyaluronic acid, PIIINP, TIMP-1, retinol binding protein-4, and more (see list on reverse). Contact us for more details on our testing services.

## Global capabilities

We have global anatomic pathology and central laboratory capabilities, and a streamlined operational management structure that assures continuity and process alignment. We provide state-of-the-art technologies, quality management systems, high capacity, and have a high-quality infrastructure to address the full spectrum of your testing needs. This includes project management, sample processing and long-term sample storage.

## Digital pathology

Q<sup>2</sup> Solutions works with several AI-supported, NASH-specialized image analysis vendors to provide both internal quality assurance data as well as to generate exploratory data in parallel with our pathologists supporting clinical trials.

## Project management

We take pride in our experienced project management staff that supports the highest level of delivery quality. To simplify the entire study process and maximize quality and efficiency, we offer a highly trained project manager who functions as a single source of information on your clinical trial. From study set-up, kit creation, budget monitoring, database design and site communication to sample handling, reporting and database lock, our project manager proactively identifies and manages every risk to help assure our clients receive consistent, meticulous results.

## Sample processing

We take a proven approach to specimen handling. Through our global network, we share sponsor requirements, best practices, and study-specific information with our regional laboratories. By applying the latest knowledge and experience to our global standard operating procedures (SOPs), we protect the integrity of your laboratory samples and reduce pre-analytic variability. We process samples upon receipt in the laboratory seven days a week. Samples are tracked until either the laboratory testing has been completed or the sample has been assigned a permanent storage location. Specimen processing personnel routinely provide feedback to the project management team.

## Sample storage

We have a broad range of biobanking services and technologies to align with your protocol and storage needs. With 100,000+ samples shipping every month, we know what it takes to effectively manage biospecimens. We have a dedicated team of specimen management and storage personnel in global locations – including the US, Europe, and Asia – with oversight of all storage sample handling, from receipt to storage. Our global long-term management and storage system can handle all sample types.

## Standard assays for liver function

### Liver function/test method

- Aspartate aminotransferase level (AST)
- Alanine aminotransferase level (AST)
- GGT
- Apolipoprotein
- Glucose levels
- Alkaline phosphatase (ALP)

### Specialized liver function tests

- Hyaluronic acid (HA)
- PIIINP
- TIMP-1
- Retinol binding protein-4 (RBP-4)
- Proc-3
- GAL-3
- YKL-40
- CK-18 Caspase cleaved (MN-65, MN-30)
- Masson trichrome

- Reticulin
- Periodic acid-Schiff (with and without diastase)
- Prussian blue (iron)
- Orcein (copper)

### Composite noninvasive biomarker tests

- Fibrosis-4 score (FIB4)
- NAFLD Fibrosis score (NFS)
- Enhanced Liver Fibrosis (ELF) Score
- Fibro test
- NIS4

### Genetic markers for NAFLD predisposition

- PNPLA3 – Single nucleotide polymorphism (SNP)
- TMS6SF2 – Single nucleotide polymorphism (SNP)

### Measurement of liver-specific miRNA levels

- miR-122
- miR-34a

## Contact us

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