

## Issues to Consider When Selecting Primary Human Hepatocytes

Primary human hepatocytes are essential tools for drug discovery, ADME/DMPK, and toxicology studies – but it is important to remember that not all lots are the same. Taking time to ask key questions up front about donor history, histopathology, hepatocyte function, and other issues can help researchers get the best match for each project. Here are a few issues to consider:

- **Plateability**, which describes the attachment efficiency of each batch of cells. “Not all batches will attach well to standard plasticware or collagen-coated 96-well plates, which is probably the most commonly used platform among most hepatocyte users,” said LifeNet Health Chief Scientist Ed LeCluyse, PhD. Issues to consider include proper handling during thawing, assessing optimal seeding density, morphological features and hepatic functions over time, and whether a lot is designated for suspension vs. plateable applications.
- **Tissue and cell sourcing**. Access to quality human cells from both healthy and diseased donors is crucial for toxicity testing, ADME, and disease modeling. While there are well established guidelines for tissue banks, these standards often do not cover all aspects related to preclinical applications. This lack of universal protocols for recovering, processing, preserving, documenting, and qualifying tissues can make it challenging for researchers to determine the best provider to work with. One solution is to look for a vertically integrated organization that can offer more assurances and information across the donation continuum – including consent, recovery, preservation, isolation, characterization, and quality control.
- **The breadth and depth of donor information**. While it is understood that hepatocyte lots will vary based on a donor’s life stage and health status, other demographics can also come into play when it comes to ensuring a good fit for a given study. Researchers should look for detailed information, including medical history and exposure to infectious diseases.
- **Pathology assessment**. Researchers should ensure ratings are available for fibrosis, inflammatory activity, steatosis, hepatocellular ballooning, non-alcoholic fatty liver disease, and nonalcoholic steatohepatitis. Pathology notes can also be helpful.
- **Viability and yield of recovered hepatocytes**. This points to cell survival after cryopreservation. “The viability that you’re looking for generally is batches of hepatocytes that are greater than 70%, if not higher,” Dr. LeCluyse said. A typical yield is 5 to 10 million viable cells per vial, but with today’s technologies, that number can go even higher.
- **Enzyme profiling**. Researchers should look for information about major CYP enzymes, which are important in drug metabolism and drug-drug interactions, as well as 7-ethoxycoumarin, the industry standard for phase 2 metabolism. “Make sure you’re asking about the enzyme profiling data and whether it represents normal or average values, as well as indications of polymorphic alleles,” Dr. LeCluyse said.
- **Assessment of induction potential**. While this has evolved over the years, the latest recommendations from working groups call for a ten-fold mRNA expression relative to a positive control.
- **Optional or custom data**. Researchers may find it helpful to have additional information to assess whether a hepatocyte lot will fit their purpose. This can include transporter expression or functional activity, or other pathways of interest such as FMOs or AOs. The willingness of a cell provider to partner to provide this information is a crucial factor.

Taking time up front to consider the many factors that can influence hepatocyte performance can pay off over the course of a project. LifeNet Health LifeSciences is committed to offering unparalleled partnership and service, starting with expert help with lot selection. We also offer post-purchase follow-up, including troubleshooting advice from our world-class scientists.