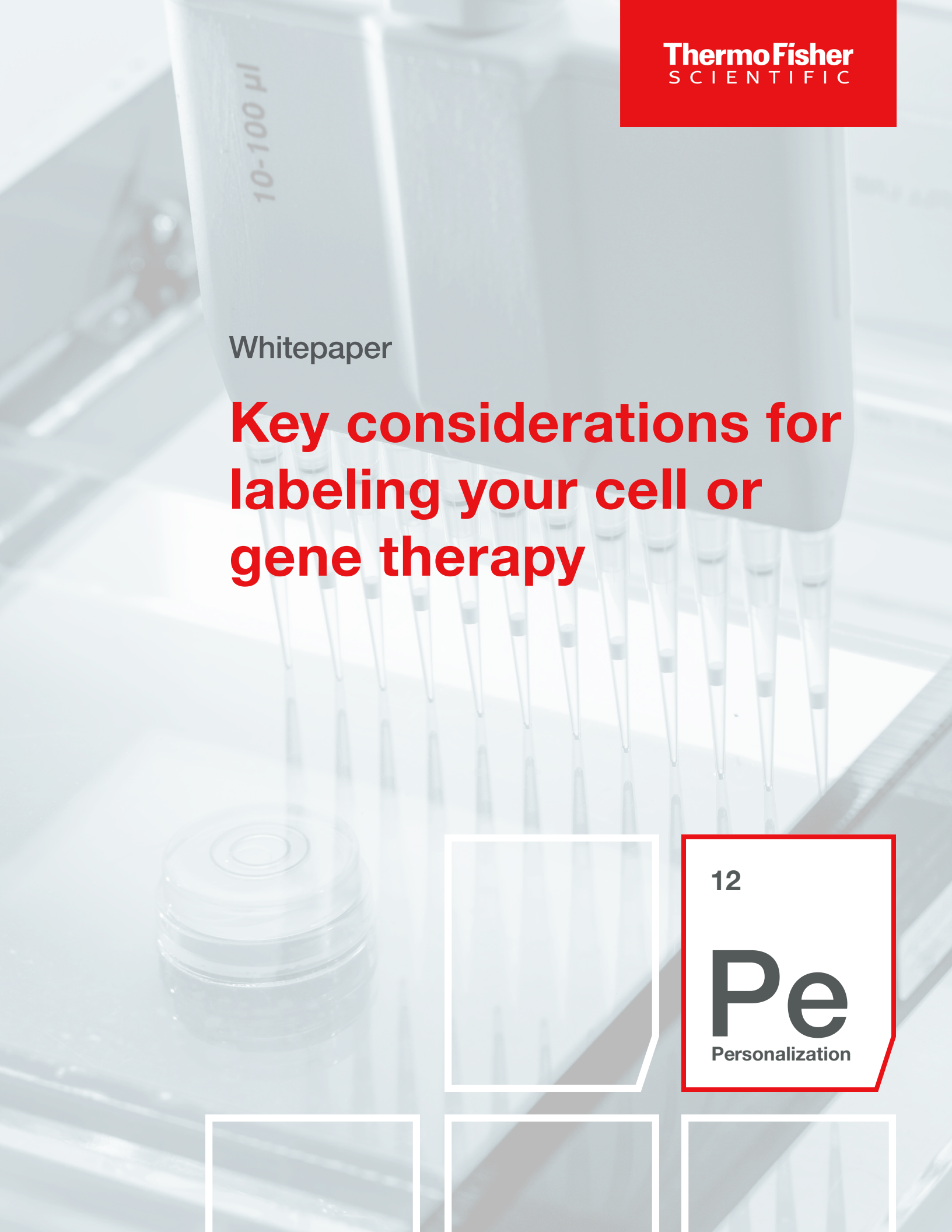


ThermoFisher SCIENTIFIC

Whitepaper

Key considerations for labeling your cell or gene therapy

12

Pe

Personalization

Executive summary

With the continued expansion of the pharmaceutical industry's global footprint and the growing complexity of today's drug products, ensuring their safe delivery to patients is becoming more challenging than ever before.

Not only must a sponsor secure a supply chain that can support their commercial goals, but they must also safeguard their products using viable packaging and labeling strategies. Without them, they run the risk of their drug being delivered outside of its specifications and/or without the information necessary for it to be properly identified and used during clinical trials.

This can be particularly difficult for those products shipped within the cryogenic temperature range of -150° to -196° C, such as cell and gene therapies. Time out of environment can have a major impact on the efficacy of the therapy and, ultimately, its clinical outcomes. As sponsors focus on maintaining the temperature range required for these therapies, they must also keep in mind the challenges these temperatures can present when properly labeling personalized therapies for clinical trial distribution.

Getting started

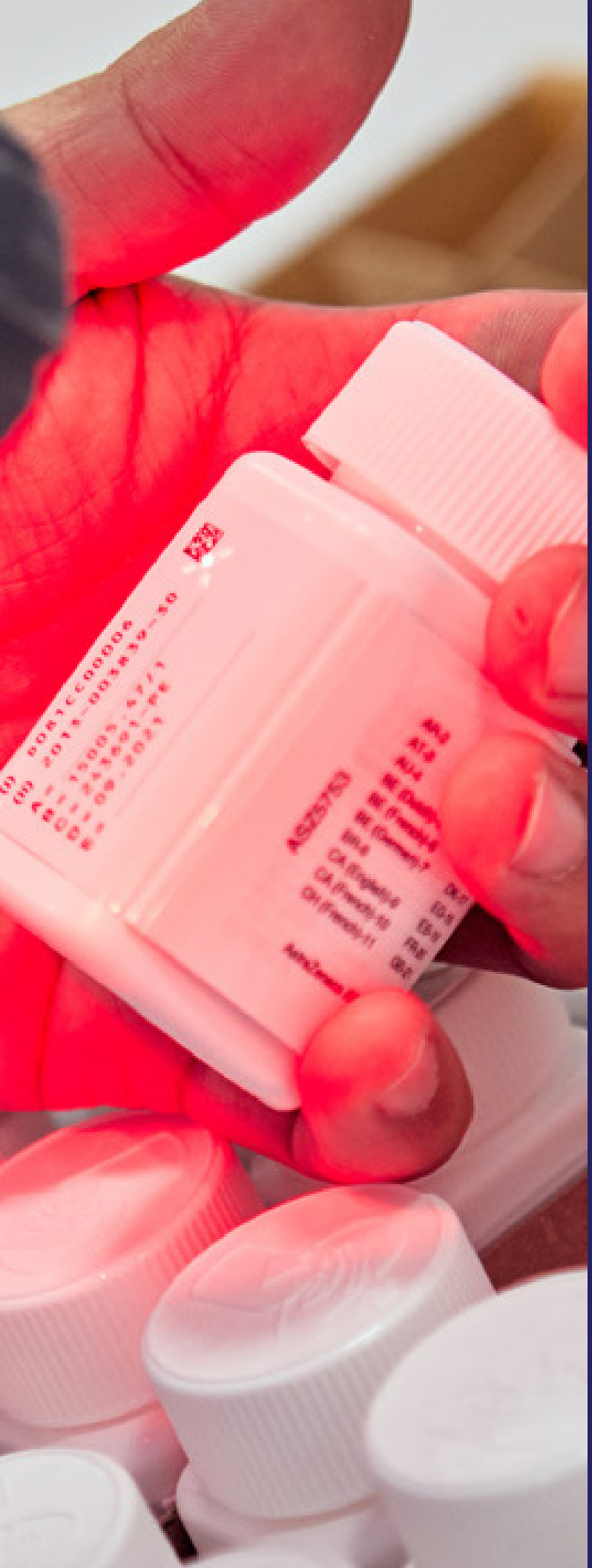
The inherent nature of biologic cells makes them susceptible to deterioration over time, which is why cell and gene therapies must be stored at ultracold or cryogenic temperatures to maintain their integrity until the patient is ready to be dosed. As such, the freshly frozen or cryopreserved drug will then need to be placed in packaging with a label that can withstand subzero temperatures.

It is important to understand all of the factors you should consider about your label before it is applied, since over-labeling or relabeling is particularly difficult at cryogenic temperatures, due to the lack of adherence of the label to the container after cryopreservation.

Working with a qualified labeling team to determine what factors you should consider about your label and what it should include can help you avoid costly issues once your clinical trial is underway. Some of the information your labeling partner will need to get started includes:

- **Container type:** Cryovial or cryobag, as well as the volume of the container, will impact your options for the label type, as well as the amount of information that can be included on the primary label.
- **Label application procedure:** Will it be applied manually or by a machine? What type of environment will the label activities take place? Ambient, cold, or over dry-ice? Machine labeling often leads to more consistent results but may not be part of the process when manufacturing a single dose. Additionally, the ambient temperature and temperature of the product are important to understand for label adherence.
- **Desired label type:** A label may be a standard, single-panel label or a booklet label. It is important to note that there are several components involved in manufacturing a booklet label and not all are optimized for cryogenic conditions, such as the type of paper used to make up the inner pages of a booklet and the hot melt used to bind the pages together.
- **How the drug will be packaged during shipment:** It is important to know the size of the carton the drug will be shipped in, in order to make sure the label connections or the labeled material can fit inside.
- **Target countries for your clinical activities:** Regulatory requirements vary by country and what may be allowed in one country may not be acceptable to another.
- **Basic required information:** This includes details related to the sponsor, the clinical trial's protocol, dosing instructions, etc.
- **Final storage temperature:** It's important to always select labels that are indicated for the desired storage temperatures.

Working with a qualified labeling team to determine what factors you should consider about your label and what it should include can help you avoid costly issues once your clinical trial is underway.



Planning for global scalability

Packaging cannot begin, labels cannot be printed, and label design activities cannot start until you have the proper translations and regulatory information for each country. Usually, it is an afterthought, but the standard industry timeline for these activities can be anywhere from three to six months just to get label text. You must have a proper strategy in place to source this content, and your label partner should be able to manage this entire process, develop a streamlined strategy to minimize cost and delays, and allow for quick changes in case a country is added or dropped late in the process.

As mentioned above, a key consideration specific to global trials is the countries in which a clinical trial will be conducted. Some countries may also have requirements for labeling that need to be considered during label design. The label must be printed in the local language of any countries where it will be administered. One way to maximize flexibility of the labeled material is to use a booklet label with multiple translations. Ideally, your labeling partner will offer full translation and regulatory services, in order to provide appropriate guidance on what needs to be on the label for each country.

By taking the time to understand your global activities, your labeling partner can gain the information necessary to properly and efficiently design the best label for your product and its specific needs. For growing biotechs, the advantage of working with experts who can create a comprehensive labeling plan based on the clinical trial protocol, from generating the master text to working through regulatory hurdles, is immeasurable in an increasingly competitive market. For example, expiry dates may require updates, so they must be designed in a way that they can be easily relabeled. Other information, such as manufacturer and contract research organization address and sponsor name and address, could change over time, so the ability to quickly update labels is necessary.

Flexibility in labeling is essential for cell and gene therapies

The demands of a clinical trial can change over time, which can result in the need to de- and relabel a product to ensure the label accurately reflects current dosing instructions, patient information, etc. However, secondary labels are often used to denote any patient specific or variable dosing information because it can be challenging to make changes to a label adhered to a product stored at cryogenic temperatures.

For example, primary labels applied at the time of manufacture can include generic information, such as the sponsor's name, the clinical trial protocol, manufacturing date, and expiry date. These labels are placed directly on the vial or bag that will be cryopreserved. Secondary labels should be used for information that is variable, such as randomization or kit ID, patient specific information, dosage, and dosing instructions (as these are often variable in early phase trials). These labels are placed on secondary packaging, which protects the product in transit and holds the secondary label. The secondary package and label must both still be indicated for the final storage temperature.

The approach of using generic information on a primary label and more customized details on a secondary label is particularly useful for allogeneic cell and gene therapies, as they target a wider patient population. Secondary labeling can also be used to accommodate just-in-time labeling, which is a frequently requested service for cell and gene therapies.

It is important to keep in mind, though, that labels will adhere differently to different packaging, so just because you have used a specific label in the past, that does not mean it will work on other containers in the future. To ensure the longevity of a label on primary packaging, your labeling partner can conduct label validation studies.

This strategy offers unique insight into the viability of a label by exposing it to environmental testing that accelerates aging and assesses how it performs over time, likely preventing costly recalls and/or the difficulty and expense of having to de- and/or relabel a cryopreserved cell or gene therapy.

Choose the right partner

Be skeptical of labeling partners who are too quick to agree to whatever labeling requests you make, as they should also be able to demonstrate a clear plan with examples to prove the label will work as intended (in the case of customized labels) and/or not peel or deteriorate during shipment.

If the latter occurs, you will lose the information essential for your drug's proper use and distribution, threatening the successful execution of your clinical trial and your overall timeline to market.

A competent labeling partner will be one that has remained abreast of current labeling and cold chain shipping innovations, so they can explore all possible options to accommodate your drug and its labeling needs

They will work tirelessly to develop alternatives to today's traditional labeling approaches in an ongoing effort to facilitate what can be a dauting task in clinical trial planning.

Working through these critical details with an experienced labeling partner helps them develop a suitable packaging and labeling plan, giving you the confidence that he integrity and efficacy of your product will be maintained throughout its journey, from the lab to the patient.

About us

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 65 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services and commercial manufacturing and packaging. We give pharma and biotech companies of all sizes instant access to a global network of facilities and technical experts across the Americas, Europe, Asia and Australia. Our global leadership is built on a reputation for scientific and technical excellence. We offer integrated drug development and clinical services tailored to fit your drug development journey through our Quick to CareTM program. As a leading pharma services provider, we deliver unrivaled quality, reliability and compliance. Together with our customers, we're rapidly turning pharmaceutical possibilities into realities.

ThermoFisher SCIENTIFIC

12

Pe

Personalization

Find your missing element with Thermo Fisher Scientific.

+1 919 226 3200 • thermofisher.com/patheon • pharmaservices@thermofisher.com