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June 7, 2018 CN #18-003

Dear Valued Customer,

Charles River strives to provide the highest level of support to our global customers by delivering industry-leading scientific and technological advances. As part of our ongoing effort to better serve our customers, we want to inform you of upcoming changes associated with the product codes identified below, which includes all available sensitivities of Endosafe® Limulus Amebocyte Lysate (LAL) reagents.

PRODUCT CODE	PRODUCT DESCRIPTION
R110	Licensed Gel-Clot LAL (50-Test vial), including customer reorder codes R11012 and R11025
R120	Licensed Gel-Clot LAL (10-Test vial), including customer reorder codes R12003, R12006, R12012, and R12025
R130	Licensed Gel-Clot LAL (Single-Test vial), including customer reorder codes R13003, R13006, R13012, and R13025
R150	Licensed Kinetic Turbidimetric LAL (KTA 50-Test Vial), including customer reorder codes R15003, R15006, and R15015
R160	Licensed Coatest LAL (Endochrome Vial), including customer reorder code R160K
R170	Licensed Kinetic Chromogenic LAL (KCA Endochrome-K™), including customer reorder codes R1708K, R1710K, and R17100K
R1900	Licensed Kinetic Turbidimetric LAL (KTA^2 50-Test Vial), including customer reorder code R19000
PTS11F	Licensed PTS™ cartridges (ten cartridges/pouch), including customer reorder codes PTS1101F, and PTS1105F
PTS20F	Licensed PTS™ cartridges (one cartridge/pouch), including customer reorder codes PTS201F, PTS2001F, PTS2005F, and PTS20005F
PTS55F	Licensed PTS™ cartridges (five cartridges/pouch), including customer reorder codes PTS551F, PTS5501F, PTS5505F, and PTS55005F

As indicated in the Customer Notification, **CN #18-001**, dated February 26, 2018, we communicated our plan to implement shipping changes that would apply to the LAL products listed above. We have now received approval from the FDA, on May 17, 2018, to implement these changes based on the execution of previously approved protocols. This notification is intended to provide further details to our customers regarding each of the listed changes below, and the implementation schedule.

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Description of Changes:

There are two (2) related shipping changes and one (1) associated label change that are scheduled to be implemented. The details of these changes and the associated LAL products impacted are provided below.

Shipping:

Charles River will be removing cool packs from containers during shipping of all product codes listed in the above table. Shipping studies, consistent with those executed for other products, and approved by the FDA in May 2016, have been performed using the new shipping containers without the polystyrene foam inserts (detailed below). Results have proven that the performance of our products are not impacted when shipped without cool packs. This change is to harmonize the conditions in which all of our LAL products can be shipped, which will reduce the risk of potential shipping discrepancies, lower the weight of shipping containers, and reduce the customer burden of disposing the cool packs upon receipt.

Additionally, the polystyrene foam inserts used in our shipping containers will be eliminated. This change is being made in recognition of the impact polystyrene is known to have on the environment along with reducing the level of packaging that our customers would need to dispose of upon arrival. Charles River has evaluated new shipping containers and performed studies to support removal of these inserts. The results of this testing established that the new shipping containers are equivalent in their functionality to the current containers.

Labeling:

As a result of the changes above, the labeling associated with the R110, R120, R130, and R160 LAL products will be modified. The product labels for the box, vial, and package insert for these four (4) product codes will be changed to reflect product storage at a range of 2°–25°C prior to reconstitution. This change in labeling is to harmonize the storage conditions for all of Charles River's licensed products and to allow for alternative storage by our customers with limited resources. Real-time long-term stability studies detailed under protocol to support this change are consistent with those executed for Charles River's other products, which were approved by the FDA in May 2016. We are currently working with labeling suppliers to make this change. Once production schedules can be coordinated, and a receipt date identified, we will issue separate notification providing customers with a date for implementation for the modified labels.

Implementation Date:

Charles River will implement the two (2) changes related to shipping described above beginning on **August 15, 2018** for all of our global customers. Any Charles River products shipped on or after August 15, 2018 will be shipped in these new containers without polystyrene foam inserts, or the use of cool packs. Upon receipt, customers can continue to store products labeled 2–8°C under

refrigerated conditions. Once the label change is made to reflect the storage condition of 2–25°C prior to reconstitution, customers will then have the option to store at the wider temperature range.

The products listed continue to be formulated, filled, freeze-dried, labeled, and packaged using the same equipment, and the same raw materials provided by the same approved suppliers, and documented on the same batch records as previously approved. The methods and procedures used for Quality Control testing of each product and process used by Quality Assurance to perform final release also remain unchanged.

There are many factors that contribute to our overall decision-making process regarding changes, including technology advancements, constantly evolving standards of care and maintenance, and regulatory compliance mandates. If you should have any questions, please contact the Charles River Technical Services team at endosafe-support@crl.com.

Sincerely,

Allen M. Rudis

Allen M. Rudis
Associate Director, Regulatory Compliance