Important Notice Regarding International Shipments of Biological Research Materials, Including Expression/Packaging Plasmids and Vectors

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To all PIs, Lab Assistants and Contacts,

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Who should read this notice?

Anyone who ships biological research materials (including plasmids and vectors) internationally or who directs other researchers to do so. Administrative staff cannot ship these materials. Note: The shipment of tangible biological materials is NOT covered by the Fundamental Research Exclusion.

Why does it matter?

Failure to comply with federal regulations on shipping research materials can result in loss of research funding, significant penalties and fines (up to $300,000 per occurrence) for the University and/or for the responsible University employee, even for unintentional errors. Individuals who intentionally evade such regulations can face criminal penalties, including jail time. Non-compliant shipments can also lead to significant delays in delivery, seizure by customs authorities, loss or damage by carriers, injury to shipping and laboratory personnel, and harm to U.S. national security.

What do I need to know?

U.S. export and transportation regulations impose strict licensing, packaging, and labeling requirements on international shipments of a wide variety of materials, including certain biological research materials. The regulations are not always intuitive, are broader and apply to more pathogens than domestic rules regarding "Select Agents" (pathogens determined by the Centers for Disease Control and Prevention (CDC) and/or the US Department of Agriculture to pose a severe threat to heath) and may apply to materials that you might not think of as sensitive or dangerous.

Among other things, U.S. export controls apply to international shipments of human, animal, and plant pathogens (bacteria, viruses, fungi and toxins). The controlled pathogens are listed under Export Control Classification Numbers (ECCN) 1C351 and 1C354 of the Commerce Control List. ***Importantly, this list includes organisms that are not on the list of Select Agents. Further, as detailed below, the controls in 1C353 extend even to genetic elements of these pathogens, such as expression plasmids containing the G-gene from Vesicular stomatitis virus***.

Examples of export-controlled pathogens include: Chikungunya virus, Cholera toxin, *Coxiella burnetii*, Ebolavirus, Enterohaemorrhagic *E. coli* (EHEC), Pseudorabies virus, *Salmonella typhi*, Saxitoxin, Tetrodotoxin, Vesicular stomatitis virus, *Vibrio cholerae*, etc. The current version of the full lists can be found on the Department of Commerce Regulations website. (scroll down to the 1C351 section, found on pages 65 to 72).

International shipment of export-controlled organisms, *even in attenuated form*, requires a license for all international destinations. Vaccines in an FDA-approved, pharmaceutical formulation are subject to less stringent controls, but may still require a license to certain recipients/destinations; other forms of attenuation generally do not change the level of control.

Significantly for biological researchers, **export controls not only apply to complete, wild-type organisms, but also to genes of listed organisms and subunits of listed toxins, including genetically modified organisms that contain, and genetic elements that code for, those genes**. "Genetic elements" include (but are not limited to) chromosomes, genomes, plasmids, transposons, vectors, and inactivated organisms containing recoverable nucleic acid fragments.

Notably, while there are some exclusions for bacterial and fungal genes that do not represent a significant health hazard, ***genetic material of controlled viruses is presumed harmful*** by the regulators, ***such that plasmids, vectors, etc., containing any genes specific to a 1C351 virus will require an export license in almost all circumstances***, with limited exclusions (that must be carefully analyzed in every case) for situations in which the gene at issue also occurs in a non-controlled organism, or is incomplete or has been modified, for example by deletion or substitution, so that it no longer has the same sequence and function as the gene in the controlled virus.

Please be aware that, contrary to what you may hear from certain plasmid suppliers or possibly even from researchers at other institutions, Yale has confirmed with the regulators that ***expression/packaging plasmids containing the VSV-G gene are strictly controlled and require a license for export to all destinations****, notwithstanding their widespread international use and availability.*

What do I need to do?

(1) Process all research materials shipments through eShipGlobal. Never transport research materials in a personal vehicle (unless approved by EHS to do so), on the Yale Shuttle or public transport, or by hand on an aircraft, train, or vessel. The eShipGlobal system is designed to identify shipments that may require an export license or other permits, and to escalate such shipments to experienced EHS personnel who can conduct further review, determine the applicable level of control and, if an export license is required, apply to the Department of Commerce on behalf of the PI. (The licensing process may take several weeks or more, so it is important to plan ahead.) The University has recently implemented a series of enhancements to the eShipGlobal system and expects to implement further refinements to make the process more efficient and easier for shippers, towards the end of the first quarter of 2019, so watch out for changes.

(2) If applicable, take revised training. In particular, effective January 2019, faculty and staff registered as shippers in eShipGlobal will be unable to make further shipments until they complete revised training. When the revised training is available, all impacted shippers will receive a notification identifying updated training requirements from the Training Management System (TMS) or via eShipGlobal. Your updated training requirements will be based on your current shipping level. You may continue to ship under your current training credentials until you are notified that the revised training is available. All Principal Investigators who have not taken Category A, Category B, Dry Ice or General Awareness training previously will receive a notification from TMS prompting them to complete mandatory General Awareness training.

Compliance with these important U.S. laws is everyone's responsibility and the University appreciates your careful attention to this information. If you have any questions about the rules and regulations referenced in this letter, please feel free to contact me at any time.

Thank you, in advance, for your careful review of this important information.

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