17, 1326−1335, or Kauffman, K. J. et al. Nano Lett. 2015, 15, 7300−7306; see also WO2019077053). Syringe pumps generate flow that has relatively low pulsation and the mixing ratio of two or more solutions can be well-controlled. However, normal syringes do not offer a closed, aseptic boundary outside of a Grade A cleanroom environment because the inside of the syringe barrel is exposed to the ambient environment before the syringe plunger is pulled to load fluid into the syringe barrel. This is particularly critical for systems in which the liposomes and/or lipoplex are too big to pass through a sterilizing grade filter and cannot be terminally sterilized without significant degradation. Peristaltic pumps, by contrast, can be used with fully closed fluid paths that do not require operation in a Grade A cleanroom environment to maintain aseptic processing and sterility assurance. This is a large advantage, because Grade A cleanroom environments are costly to maintain and require time-consuming environmental monitoring controls. Accordingly, Applicants have discovered methods and systems using peristaltic pumps that includes a dampener to drastically reduce the pulsations or oscillations from peristaltic pumps useful to produce, mix, transfer, and/or manufacture pharmaceutical compositions and formulations, including, e.g., compositions and formulations comprising RNA and lipids, including lipoplexes or liposomes, e.g., RNA vaccines. Although the dampeners disclosed herein are discussed in combination with peristaltic pumps, the pump system does not necessarily have to be a peristaltic pump system, as dampeners could be combined with any pumping system that generates pulses as part of its mechanism of action (including, e.g., membrane, piston, etc.). For example, a syringe pump system can use the dampeners disclosed herein. In some examples, these methods and systems using peristaltic pumps that includes a dampener are suitable to ensure smooth or consistent flow rate to produce, mix, transfer and/or manufacture pharmaceutical compositions comprising RNA and lipids (including lipoplexes or liposomes), including, e.g., RNA vaccines.

[0008] In one aspect, the present disclosure refers to a tubing kit for forming a mixture comprising: a first portion of tubing configured to be fluidly connected to a container containing a first composition; a second portion of tubing configured to be fluidly connected to a container containing a second composition; a dampener fluidly connected to the first portion of tubing and fluidly connected to the second portion of tubing; a mixer for mixing the first composition from the first portion of tubing and the second composition from the second portion of tubing; a first dampener connector that fluidly connects the first portion of tubing to the dampener and to the mixer, a second dampener connector that fluidly connects the second portion of tubing to the dampener and to the mixer, a mixture container for collecting the mixed first composition and second composition from the mixer, wherein the first portion of tubing is configured to be connected to a first peristaltic pump head for pumping the first composition from the container containing the first composition to the mixture container, and the second portion of tubing is configured to be connected to a second peristaltic pump head for pumping the second composition from the container containing the second composition to the mixture container. In some examples, a tubing kit for forming a mixture includes: a first portion of tubing configured to be fluidly connected to a container containing a first composition; a second portion of tubing configured to be fluidly connected to a container containing a second composition; a dampener fluidly connected to the first portion of tubing and fluidly connected to the second portion of tubing; a mixer for mixing the first composition from the first portion of tubing and the second composition from the second portion of tubing; a mixture container for collecting the mixed first composition and second composition from the mixer, wherein the first portion of tubing is configured to be connected to at least one peristaltic pump head for pumping the first composition from the container containing the first

composition to the mixture container, and the second portion of tubing is configured to be connected to at least one peristaltic pump head for pumping the second composition from the container containing the second composition to the mixture container. In some examples, the dampener comprises an enclosed volume of fluid. In some examples, the fluid is air. In some examples, the dampener is a tubing dampener. In some examples, the dampener comprises a flexible membrane. In some examples, the tubing kit includes a first tee connector that fluidly connects the dampener, the first portion of tubing, and a first mixer input portion of tubing, wherein the first mixer input portion of tubing fluidly connects to the mixer. In some examples, the tubing kit includes a second tee connector that fluidly connects the dampener, the second portion of tubing, and a second mixer input portion of tubing, wherein the second mixer input portion of tubing fluidly connects to the mixer. In some examples, the first portion of tubing comprises a first segment of tubing and a second segment of tubing, wherein the first segment of tubing and the second segment of tubing are fluidly connected in parallel. In some examples, the first segment of tubing is configured to be connected to a first peristaltic pump head, and the second segment of tubing is configured to be connected to a second peristaltic pump head. In some examples, the second portion of tubing comprises a third segment of tubing and a fourth segment of tubing, wherein the third portion of tubing and the fourth portion of tubing are fluidly connected in parallel. In some examples, the third segment of tubing is configured to be connected to a third peristaltic pump head, and the fourth segment of tubing is configured to be connected to a fourth peristaltic pump head. In some examples, the mixer comprises an input fluidly connected to the first portion of tubing, an input fluidly connected to the second portion of tubing, and output fluidly connected to the mixture container. In some examples, the mixer comprises a Y-connector, a helical mixer, or a static mixer. In some examples, the tubing kit includes a first dampener connector that fluidly connects the first portion of tubing to the dampener and to the mixer and a second dampener connector that fluidly connects the second portion of the tubing to the dampener and to the mixer. In some examples, the mixture container is a bag, vessel, or bottle.

[0009] In one aspect, the present disclosure refers to a system for forming a pharmaceutical composition or mixture of pharmaceutical compositions, the system comprising: a first container containing a first pharmaceutical composition; a second container containing a second pharmaceutical composition; a first portion of tubing fluidly connected to the first container; a second portion of tubing fluidly connected to the second container; a dampener fluidly connected to the first portion of tubing and fluidly connected to the second portion of tubing; a mixer for mixing the first pharmaceutical composition from the first portion of tubing and the second pharmaceutical composition from the second portion of tubing; a first dampener connector that fluidly connects the first portion of tubing to the dampener and to the mixer; a second dampener connector that fluidly connects the second portion of tubing to the dampener and to the mixer; a mixture container for collecting the mixed first pharmaceutical composition and second pharmaceutical composition from the mixer; a first peristaltic pump head connected to the first portion of tubing for pumping the first pharmaceutical composition from the first container to the mixture container; and a second peristaltic pump head connected to the second portion of tubing for pumping the second pharmaceutical composition from the second container to the mixture container. In some examples, a system for forming a pharmaceutical composition or mixture of pharmaceutical compositions, the system includes: a first container containing a first pharmaceutical composition; a second container containing a second pharmaceutical composition; a first portion of tubing fluidly connected to the first container; a second portion of tubing fluidly connected to the second container; a dampener fluidly connected to the first

UAACCCCAGGGUUGGUCAAUUUCGUGCCAGCCACACCG (SEQ ID NO:17). In some examples, the 3' UTR comprises the sequence CUCGAGCUGGUACUGCAUGCACGCAAUGCUAGCUGCCCCUUUCCCGUCCUGGG UACCCCGAGUCUCCCCCGACCUCGGGUCCCAGGUAUGCUCCCACCUCCACCUGC CCCACUCACCACCUCUGCUAGUUCCAGACACCUCCCAAGCACGCAGCAAUGCA GCUCAAAACGCUUAGCCUAGCCACACCCCCACGGGAAACAGCAGUGAUUAACC UUUAGCAAUAAACGAAAGUUUAACUAAGCUAUACUAACCCCAGGGUUGGUCA AUUUCGUGCCAGCCACACCGAGACCUGGUCCAGAGUCGCUAGCCGCGUCGCU (SEQ ID NO:13). In some examples, the poly(A) sequence comprises 120 adenine nucleotides. In some examples, the RNA comprises an RNA molecule comprising, in the 5'→3' direction: the polynucleotide sequence GGCGAACUAGUAUUCUUCUGGUCCCCACAGACUCAGAGAGAACCCGCCACCAU GAGAGUGAUGGCCCCCAGAACCCUGAUCCUGCUGCUGUCUGGCGCCCUGGCCC UGACAGAGACAUGGGCCGGAAGC (SEQ ID NO:1); a polynucleotide sequence encoding the one or more neoepitopes resulting from cancer-specific somatic mutations present in the tumor specimen; and the polynucleotide sequence AUCGUGGGAAUUGUGGCAGGACUGGCAGUGCUGGCCGUGGUGGUGAUCGGAG CCGUGGUGGCUACCGUGAUGUGCAGACGGAAGUCCAGCGGAGGCAAGGGCGGC AGCUACAGCCAGGCCGCCAGCUCUGAUAGCGCCCAGGGCAGCGACGUGUCACU GACAGCCUAGUAACUCGAGCUGGUACUGCAUGCACGCAAUGCUAGCUGCCCCU UUCCCGUCCUGGGUACCCCGAGUCUCCCCCGACCUCGGGUCCCAGGUAUGCUC CCACCUCCACCUGCCCCACUCACCACCUCUGCUAGUUCCAGACACCUCCCAAGC ACGCAGCAAUGCAGCUCAAAACGCUUAGCCUAGCCACACCCCCACGGGAAACA GCAGUGAUUAACCUUUAGCAAUAAACGAAAGUUUAACUAAGCUAUACUAACC CCAGGGUUGGUCAAUUUCGUGCCAGCCACACCGAGACCUGGUCCAGAGUCGCU AGCCGCGUCGCU (SEQ ID NO:2).

In one aspect, the present disclosure refers to a method for transferring pharmaceutical compositions using peristaltic pumps comprising: pumping a first composition from a first container through a first portion of tubing using a first peristaltic pump; pumping a second composition from a second container through a second portion of tubing using a second peristaltic pump; dampening pulse in a fluid flow of the first composition in the first portion of tubing and dampening pulses in a fluid flow of the second composition in the second portion of tubing using a dampener fluidly connected to the first portion of tubing and fluidly connected to the second portion of tubing; and mixing the first composition from the first portion of tubing and the second composition from the second portion of tubing in a mixer fluidly connected to the first portion of tubing and the second portion of tubing, wherein a first dampener connector fluidly connects the first portion of tubing to the dampener and to the mixer and a second dampener connector fluidly connects the second portion of tubing to the dampener and to the mixer. In some examples, a method for transferring pharmaceutical composition using peristaltic pumps includes: pumping a first composition from a first container through a first portion of tubing using at least one peristaltic pump; pumping a second composition from a second container through a second portion of tubing using at least one peristaltic pump; and dampening pulse in a fluid flow of the first composition in the first portion of tubing and dampening pulses in a fluid flow of the second composition in the second portion of tubing using a dampener fluid connected to the first portion of tubing and fluidly connected to the