What could be the cause of the anaphylactic reactions being reported in some recipients of the mRNA vaccines?

The Pfizer/BioNTech COVID-19 vaccine contains polyethylene glycol (PEG). As stated in Pfizer/BioNTech’s own “Information for UK recipients”: “This vaccine contains polyethylene glycol/macrool (PEG) as part of ALC-0159”. The MHRA’s own Public Assessment report states that the PEG used in the Pfizer vaccine, ALC-0159 (2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide), is considered novel in that it has “not been used in an authorised medicinal product in the UK” PEG has never been used before in an approved vaccine. The Moderna vaccine also contains PEG in the form of 1,2-dimyristoyl-rac-glycerol3-methoxypolyethylene glycol-2000 [PEG2000-DMG].

There is increasing speculation that PEG may be triggering the anaphylaxis. Polyethylene glycols are known to cause IgE-mediated allergic reactions. These hypersensitivity reactions may not be rare; Yang et al (2015) found anti-PEG antibodies in around 42% of healthy adult individuals.

A recent 2020 article suggests the prudence of advance testing, of potential recipients of PEG-containing pharmaceuticals, for anti-PEG antibodies. In this paper the authors state, “A main message is that correct measurement of anti-PEG antibodies and individual proneness for C activation might predict the rise of adverse immune reactions to PEGylated drugs and thereby increase their efficacy and safety.” It needs to be considered whether this recommendation should be given before administration of the Pfizer/BioNTech or Moderna vaccines, to reduce the risk of allergic and anaphylactic reactions.

It is notable that in 2017, an article, about the lipid nanoparticle (LNP) encapsulation being used for delivery of mRNA vaccines, was published by 14 authors, all of whom gave a Moderna venture or Moderna Therapeutics as their contact address. The LNP, termed “platform” in the article, contains PEG. The biodistribution of an experimental mRNA vaccine, after intramuscular injection in mice, was analysed. This study found evidence of the mRNA vaccine, beyond the muscle, in plasma and tissue in 17 different body sites including brain, heart, testes, and bone marrow, within a few hours of injection. This would suggest that the mRNA does not break down as fast as expected. A recent video shows a neurologist, Dr Chris Shaw, postulating that it is plausible that vaccine LNPs containing mRNA can be carried to distant sites in the body, and may even be crossing the blood brain barrier, where they could set up inflammatory reactions, leading to adverse effects and symptoms post-vaccination.