using telemedicine and to reach patients in rural areas by telephone and other remote technology solutions. In further support of this, ACPE released a recommendation that programs encourage student development of remote interaction skills, as provision of remote care will likely continue to some degree in the future.[3] These newly developed skill sets will be invaluable as pharmacy practice continues to evolve and telemedicine is further adopted, encouraged, and reimbursed.

In response to Anderson et al,[1] our collective experiences living and precepting ambulatory care APPEs have demonstrated that ambulatory care learning opportunities conducted in remote settings are feasible and successful in cultivating student pharmacists who are practice ready upon graduation. We predict that remote rotation experiences will continue to expand, a shift that parallels the expansion of telemedicine services that emerged under the catalyst of the COVID-19 pandemic. Reliance on remote learning platforms developed out of necessity during the COVID-19 pandemic, but implementation of these strategies ultimately created new and meaningful APPEs for students who would not have otherwise been able to experience patient care outside of their home state or health education region. Further curation of remote experiences could create coast-to-coast learning opportunities without requiring the burden of travel and its associated costs. Maintenance of hybrid learning environments that combine in-person and remote patient care responsibilities beyond the COVID-19 pandemic may better serve and prepare student pharmacists as they become practitioners of the future.

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Claiming therapeutic protein stability in a clinical setting based on limited analytical data is misleading and dangerous

Protein pharmaceuticals are sensitive to various stress factors to which they can potentially be exposed during daily use and processing in a clinical setting.[1] In a recent paper published in this journal, Leja et al[2] concluded that pneumatic tube transportation (PTT) of Myxredlin (100 IU/mL human insulin in 0.9% sodium chloride in a ready-to-use intravenous infusion bag; Baxter Healthcare) can be considered in daily practice. This conclusion was based on their observation that PTT of Myxredlin did not result in foaming or loss of potency as measured by enzyme-linked immunosorbent assay (ELISA). In our opinion, the authors' conclusion is at least premature and could potentially be false. The effect of PTT on other critical quality attributes (CQAs) besides potency, such as chemical degradants, conformational variants, and especially subvisible and visible aggregates (or other particles), was not addressed, but such effects must be investigated before drawing any conclusions about product quality as a function of storage or transportation conditions. Particulate matter might contribute to serious adverse effects, such as pulmonary embolism and vascular obstruction. Moreover, protein aggregates are potentially immunogenic, which may lead to severe immunological reactions, such as formation of neutralizing antibodies, cytokine release syndrome,

and anaphylaxis.[3] Importantly, even minute amounts of such degradants may cause severe adverse effects, but are very likely to remain undetected in a potency assay.

Unfortunately, there are several other published examples of claims about storage conditions for protein pharmaceuticals that are based solely on ELISA data. For instance, Bakri et al[4] reported minimal content reduction of 8.8% and 15.9% for bevacizumab repackaged in syringes after storage at 4 °C for 3 and 6 months, respectively. In our opinion, the term "minimal" is arguable and the reason for this content loss, which might well have been due to protein aggregation, should have been elucidated. Nevertheless, based on ELISA data alone, the authors concluded that bevacizumab can be drawn into a syringe and then stored for up to 6 months. In another example, Kongmalai et al[5] studied the effect of storage temperature on the binding capacity for PCSK9 (proprotein convertase subtilisin/kexin type 9 serine protease) of 2 PCSK9 inhibitors in human plasma. Safe storage conditions were proposed based on PCSK9 binding capacity data; however, other CQAs were not investigated.

To justify stability claims for protein pharmaceuticals, in stark contrast to the examples above, it is necessary to employ suitable complementary analytical methods to assess all relevant CQAs that may compromise safety. For instance, peptide mapping by reverse-phase liquid chromatography, preferably combined with mass spectrometry detection, can be used to analyze chemical degradants; size-exclusion chromatography and dynamic light scattering can be used to detect relatively small aggregates; and flow imaging microscopy can be used to detect larger aggregates and other particles.

Altogether, claiming stability of protein drugs under storage and in use conditions based solely on protein content and potency is misleading and potentially dangerous. First, clinically relevant degradation products may have been overlooked. Second, pharmacists who are not familiar with protein stability issues may be inclined to follow the recommendations made in the flawed papers. Instead, stability assessment of protein pharmaceuticals under clinically relevant conditions requires a comprehensive analysis of CQAs. The results of such an assessment should be the basis for proper recommendations for the implementation of handling procedures in clinical practice. Only then can we safeguard product quality and improve patient safety.

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Leja et al reply

We appreciate the level of detail and consideration from van den Berg and colleagues in response to our recent publication "Transportation of a Commercial Premixed Intravenous Insulin Product Through a Pneumatic Tube System."[1]

van den Berg et al state that it would have been beneficial to perform additional analytical assessments to evaluate other critical quality attributes (CQAs) of Myxredlin (regular insulin in sodium chloride injection; Baxter Healthcare) before drawing any