Recently, FDA published a guidance (entitled “Design and Analysis of Shedding Studies for Virus or Bacteria-Based Gene Therapy and Oncolytic Products”) providing sponsors with recommendations on how and when to conduct shedding studies during preclinical and clinical development.

According to the guidance, the term “shedding” refers to the “release of Virus or bacteria-based gene therapy (VBGT) or oncolytic products from the patient through one or more of the following ways: excreta (feces), secreta (urine, saliva, nasopharyngeal fluids, etc.), or through the skin (pustules, sores, wounds).” The guidance also states that “shedding is distinct from biodistribution because the latter describes how a product is spread within the patient’s body from the site of administration while the former describes how it is excreted or released from the patient’s body.”

Shedding increases the risk of transmission of the VBGT or oncolytic products from treated to untreated individuals. Although these products are less infectious or virulent as the parent strains, the possibility that viruses and bacteria may be shed by a patient increases concerns regarding risk of transmission from treated to untreated individuals.

In the guidance, FDA states that the decision to require and assess shedding data is based on the biological characteristics, derivation, and genetic makeup of the VBGT or oncolytic product. It also states that shedding data may be requested if:

- “Humans have not previously been exposed to the product, as in the case of a nonhuman bacterial or viral strain;
- The product has been administered to humans, but has been modified to achieve a different in vivo tropism than the parent strain;
- The product has been previously administered to humans; however, a change in the route of administration is proposed; or
- Humans have not been previously exposed to the product, and the route of administration differs from the natural route of exposure/infection.”

FDA also outlines what is needed from shedding studies to determine the likelihood of transmission. The key aspects in designing the studies include: “the choice of clinical samples that are collected from subjects in a trial (e.g., feces, urine, nasal swabs); the
frequency of sample collection and duration of the monitoring period and the assay methodology selected to test for the presence of the shed in the clinical sample.”

The guidance offers information regarding when to collect shedding data in clinical studies, analytical assays to measure shedding, how to analyze shedding data, what to include in a clinical shedding study report, what information can be used to assess the potential for transmission, and how to monitor untreated individuals for transmission. For more information or the full details, view the full guidance [here](#).

These recommendations are nonbinding and are not legally enforceable responsibilities; however, the document does describe FDA’s current thinking on the topic and contains suggestions and recommendations. If you need assistance ensuring you are compliant with this or any other guidance document, we can help. To learn more about how we can use our [unique approach](#), which combines scientific knowledge with regulatory expertise, to help you establish and maintain compliance, please [contact us](#).