PHARMACEUTICAL

New method to quantify redispersion potential of Al salts in vaccines

Introduction

Adjuvants such as aluminium salt (Alum) are commonly added to vaccines to enhance their immune responses. These adjuvants can aggregate and then settle over time due to their electrical charges. The resulting sediment can be more or less compact and difficult to redisperse depending on the strength of the bonds between particles. If such phenomena occur with storage time, the problem arises of knowing whether:

- the injected dose remains the same (Do all the active ingredients pass through the needle of the syringe despite large and compact aggregates?)
- or is the therapeutic efficacy and so the immunogenicity reduced (masked antigen in the aggregate does not get injected).

In this note, we propose a rapid evaluation method (less than 30 minutes) of the sediment redispersibility.

KEY **BENEFITS**

FAST

NO DILUTION

SENSITIVE

Reference

Investigation of the Sedimentation Behavior of Aluminum Phosphate: Influence of pH, Ionic Strength, and Model Antigens; Kevin Muthurania and al.; Pharmaceutical Research and Development; Pfizer Inc.; JOURNAL OF PHARMACEUTICAL SCIENCES 104:3770–3781, 2015).

Reminder on the technique

Turbiscan® technology, based on Static Multiple Light Scattering, consists on sending a light source (880 nm) on a sample and acquiring backscattered (BS) and transmitted (T) signal all over the height of a sample.

By repeating this measurement over time at adapted frequency, the instrument enables to monitor physical stability.

The signal is directly linked to the particle concentration (φ) and size (d) according to the Mie theory knowing refractive index of continuous (n_f) and dispersed phase (n_p): $\boldsymbol{BS = f(\varphi, d, n_p, n_f)}$

Materials & Method

To prevent the loss of immunogenicity, the solution is subjected to a controlled flocculation (by varying pH or ionic strength). This will result in weakly-bonded particles that form a loose floc and produce a low-density sediment (large amount of water entrapped) easy to redisperse.

*Conventional method: **SVR** (Sedimentation Volume Ratio)*

The conventional method to determine the flocculation amount of vaccines is to measure the height of the sediment (SVR) upon the completion of suspension settling after 24 hours. SVR is the ratio of the height of the settled sediment to that of the initial suspension. A larger value (> 0.1) of SVR should translate to better suspendability /redispersability as the sediment is less compact.

This ratio can be measured with Turbiscan from backscattering evolution as shown on the figure below.

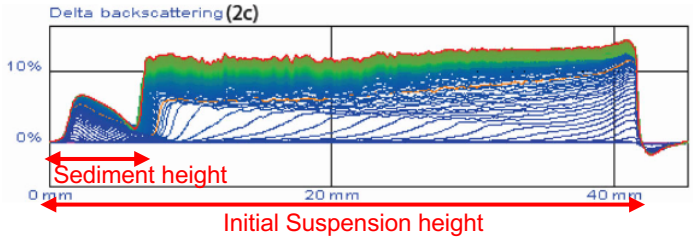

Figure 1: Delta Backscattering data for SVR measurement after 24 hours measurement