Application Note
The drying of IgG

Background

Antibodies have a proven therapeutic modality with over 80 approved for therapeutic use and over 450 in clinical development[1]. Although similar in overall structure, antibodies are at the same time extraordinarily heterogeneous due to the presence of a variety of enzymatic and chemical modifications[2] causing many promising candidates unfit for clinical development. One way to significantly improve stability of proteins is to formulate them as dry powder, instead as solutions. However, current drying techniques are in many cases harsh to sensitive proteins, because of either excessive temperatures and/or shear forces. LaminarPace spray drying offers the possibility to gently dry either proteins or small molecules at room temperature with very little shear forces and in very high yields.

Objective

To demonstrate that the activity of antibodies, both in amount and activity, are maintained after being dried in the LaminarPace system.

Sample

Rabbit polyclonal antihuman complement factor C3c IgG[3].

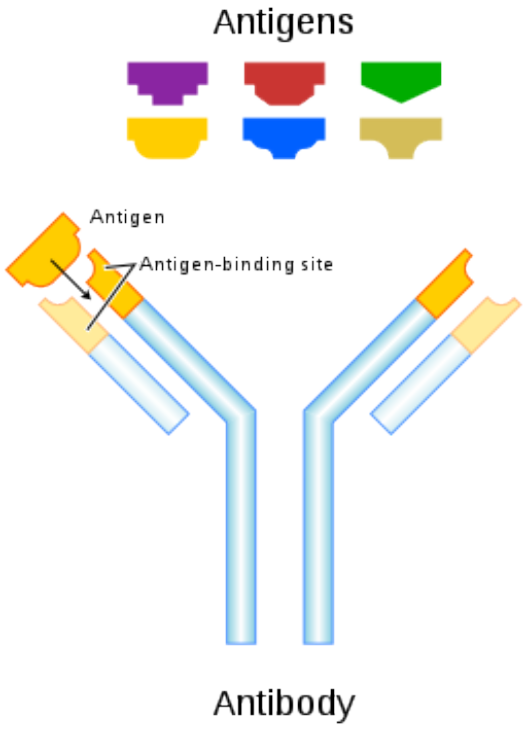
Results

The overall yield expressed as fractional recovery increases with increasing batch size loaded. The probable reason for this is that at extremely low load sizes there are certain losses in the system and sample handling not directly related to the operating principle of LaminarPace system.

Activity, before and after drying shows virtually no difference, despite the fact that polyclonal antibodies contains many different types of clones.

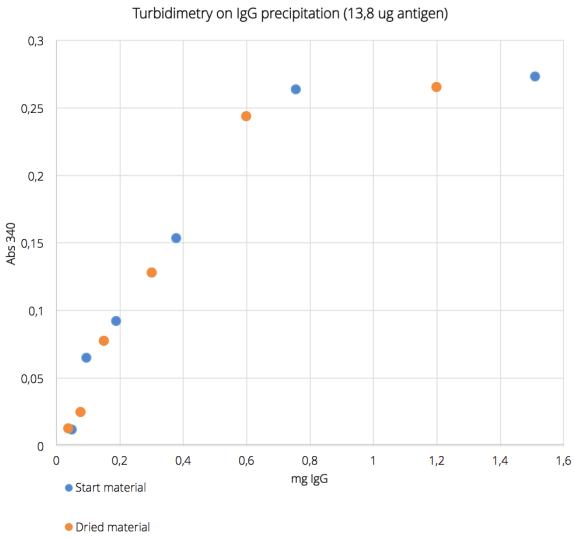
SEM pictures

The images, fig. 1 & 2, show that particles are formed in a very uniform shape with a narrow particle size distribution range.



Picture from wikipedia.org

	Sample Volume	Load	Recovered	Yield
Run 1	0,5 mL	7,5 mg	5,52 mg	73,2 %
Run 2	1,0 mL	15 mg	11,98 mg	79,4 %
Run 3	2,0 mL	30 mg	25,54 mg	84,7 %



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Solubility

The IgGs were immediately and instantly dissolved when resuspended in water, hence, indicating an amorphous state.

Spray generator

In this application the standard 5µm mesh nebulizer was used.

Excipients

No other than the solution that the IgG was delivered in.

Flow settings

In this application the following standard air flow rates were used:

Q_D: 4,2 L/min

Q_N: 2,0 L/min

Q_S: 0,5 L/min

Nebulizer setting

The sample is introduced into the drying column through a vibrating mesh nebulizer, which can be set at different reduced pulsed outputs in percent of the continuous full output. In this case 30% were set.

Filter

The micronized IgG were collected on a sub-micron membrane filter and was recovered after the production cycle was terminated.

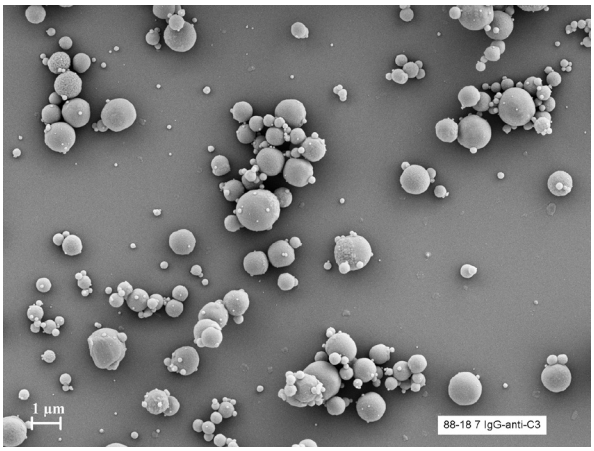

fig. 1

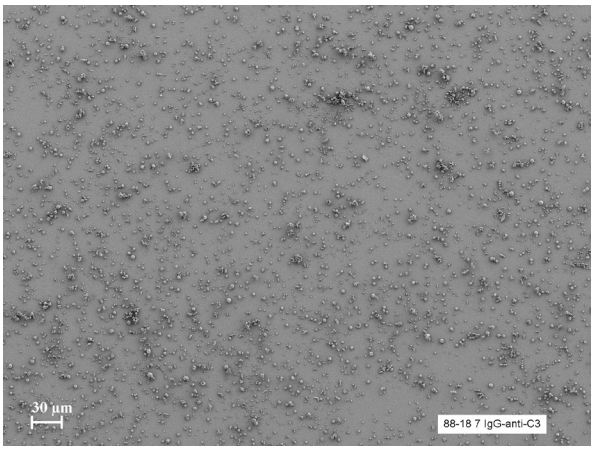

fig. 2

References

1. Antibody society
2. A new tool for monoclonal antibody analysis, Yan An et al, mAbs 6:4, 1 -15; July/aug 2014
3. Agilent Q036805-2 Complement, Rabbit Anti-Human, Polyclonal, Ig Fraction, 5 mL. Agilent X090801-2 Human Serum Protein Calibrator, Liquid form, 1 mL