**Bioproduction** 

# How do I support increased volumes of media to be prepared when scaling to larger bioreactors?

According to a 2014 study<sup>1</sup> of manufacturing and market trends, dry media hydration was the most common method of media preparation, with dry-format media accounting for 90% of the media purchased by large-scale bioprocessing manufacturers due to their lower costs and smaller storage footprints. Preparing dry media quickly and consistently can be critical to enabling a smooth transition to larger bioreactors.

Gibco<sup>™</sup> Advanced Granulation Technology<sup>™</sup> (AGT<sup>™</sup>) products are a well-established and scalable dry media format for Gibco<sup>™</sup> cell culture products. AGT products are designed to overcome common challenges associated with dry media preparation, such as multiple hydration steps, pH adjustments, long hydration times, inconsistent batches, and clumping and floating of powders on the surface of the medium. The AGT format was introduced in 2001 as a media format that offers increased stability, scalability, ease of use, and consistency.





#### References

1. Deets Beat, Inc. (2014) Advanced Granulation Technology (AGT dry media format) Culture Media - Benefits and Case Studies. http://assets.thermofisher.com/TFS-Assets/LSG/brochures/AGT\_CaseStudy\_White\_Paper\_FINAL. pdf?ICID=bpd\_cc\_white\_paper\_agt\_benefits\_case\_studies\_agt

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#### Stability

Test data from stability studies demonstrate a shelf life of 24 months at 2–8°C for most AGT media. To be established, a wide study was conducted choosing worst-case components because of their sensitive nature and low concentrations in the media. Analytical consistency of components during the shelf-life study were within the specification of  $\pm$ 20% of the theoretical concentration. Aside from storage, shipment conditions were also tested using a matrix approach where the most complex chemically defined formulations were tested to support international shipment. It demonstrated that shipment at either of two temperature ranges (2 to 8°C and –10 to –20°C) does not affect the form, fit, or function of the product.

#### Scalability

The process for manufacturing AGT dry media is fully scalable, producing consistent media regardless of lot and batch sizes, which were tested at 50 and 250 kg. These scales represent the minimum and maximum levels of the granulation bowls used to produce different batch sizes in the granulator. High-performance liquid chromatography (HPLC) and other analyses of lots and batches show that biochemical constituents are homogeneously distributed throughout the granules, nutrient levels are comparable to those of conventional formats, and cell culture performance is equivalent to that of relevant reference media. In addition, multiple packaging options are available for the media themselves, all leveraging single-use containers, including bags, drums, and kegs with capacities up to 150 kg.

#### Ease of use

The AGT dry media format refers to the unique process used to manufacture highly dissolvable powder granules. As the water dries during granulation through surface fusion of partially dissolved powders, larger particles form into porous, free-flowing, highly water-soluble granules that are ready for rapid hydration and use. Upon mixing, even at large scale, no adjustment of pH or osmolality is required, simplifying the media preparation process and reducing risk of human error.

#### Consistency

The AGT dry media granules are so readily soluble that using separate mixing protocols does not result in inconsistencies in prepared liquid media. Testing was conducted to evaluate the hydration of an AGT medium in a mixing study using a variety of Thermo Scientific<sup>™</sup> HyPerforma<sup>™</sup> and imPULSE<sup>™</sup> single-use mixers (S.U.M.s). The results of the study helped demonstrate the scalability of hydrating AGT media from 50 to 200 L, outlined mixer efficiencies, and compared differences in mixing attributes between mixer types. This study supports the fact that hydration time for AGT medium preparation can be shortened even more when optimized operating settings for S.U.M. equipment are utilized.

#### Summary

All products chosen for the studies summarized here were representative of the AGT media product, demonstrating that AGT media offer the benefits of liquid or standard dry media at large scale without the common challenges encountered when increasing the volume of media procured or prepared.



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