

# Adjuvants

Immunotherapy & Vaccine Development  
From Avanti Research™

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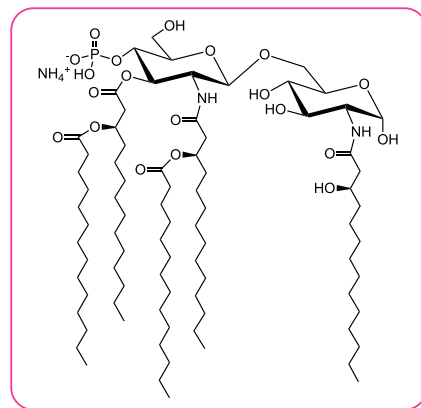
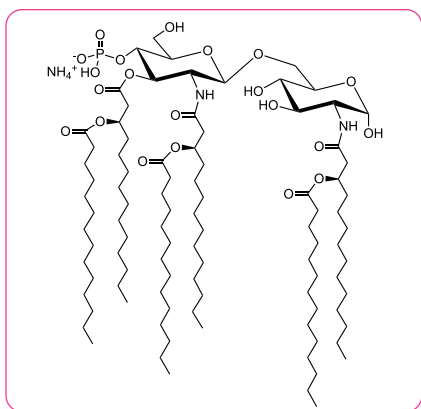
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of Avanti Research™ to customers  
outside the United States.



# Monophosphoryl Lipid A (MPLA) Adjuvants

## MPLA 3D-PHAD™

The highly pure MPLA analog, 3D-PHAD™, provides a homogeneous synthetic equivalent for the deacylated MPLA derived from bacterial LPS. While comparable to bacterial MPLA and other synthetic MPLA analogs at eliciting an immune response in a liposomal adjuvant system, 3D-PHAD™ is less pyrogenic than its bacterial-derived mimic. Extensive preclinical testing with 3D-PHAD™ demonstrated equivalency to PHAD™, and human trials have been scheduled for launch. 3D-PHAD™ is protected under Pat No. 9,241,988. Licensing opportunities are available for vaccine or immunotherapy commercialization.

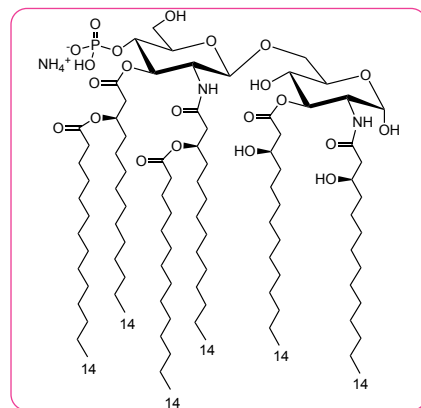
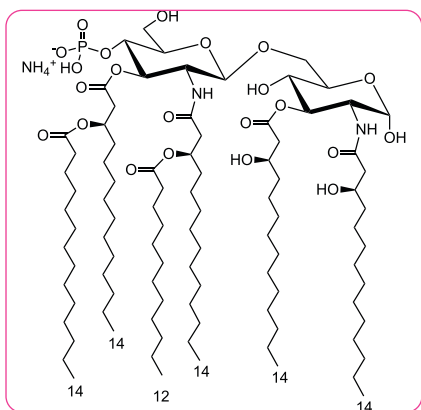


## MPLA PHAD™

PHAD™ is a synthetic structural analog of monophosphoryl Lipid A (MPLA) that has been shown to boost the immune system through activation of the toll-like receptor 4 (TLR4) resulting in production of proinflammatory cytokines and antigen-specific effector CD4+ and memory CD8+ T cells. Also referred to as GLA, this adjuvant has been administered to well over 1000 human subjects without serious adverse events. PHAD™ is available in bulk quantities for vaccine development and commercial manufacturing.

## MPLA 3D(6-acyl)-PHAD™

The MPLA structural analog, 3D(6-acyl)-PHAD™, is the synthetic MPLA most closely related to the reported structure of MPL® Adjuvant used in GSK's Adjuvant Systems AS01, AS02, and AS04. As with other synthetic MPLA analogs manufactured by Avanti™, it is structurally homogeneous and highly purified, and mimics the TLR4 agonist activity of bacterial MPLA.

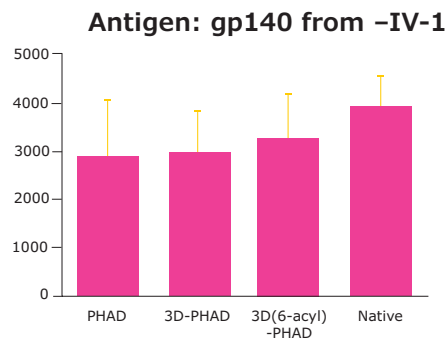


## MPLA PHAD™-504

PHAD™-504 was designed as a synthetic structural analog of detoxified MPLA derived from *E. coli* lipopolysaccharide (LPS). It is structurally similar to PHAD™, differing only in the length of a single fatty acid chain. As expected, the activity of PHAD™-504 is quite similar to that of PHAD™, making the two products interchangeable as adjuvants in vaccine or immunotherapy formulations.

## Equivalence of Synthetic MPLAs

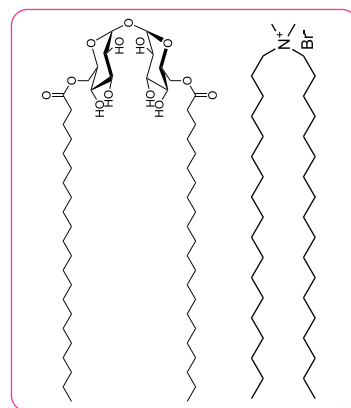
PHAD™, 3D-PHAD™, and 3D(6A)-PHAD™ have been tested extensively on animals using a variety of antigens. In all cases, these adjuvants exhibit a similar activity and safety profile to bacterially-derived MPL. The graph demonstrates the equivalency of the three synthetic adjuvants to the bacterially-derived MPL, when presented in a liposomal carrier system (DMPC/ DMPG/cholesterol).



## TB Vaccines

### Trehalose Dibehenate (TDB) and DDA

Incorporation of the glycolipid trehalose 6,6'-dibehenate (TDB) into cationic liposomes composed of the quaternary ammonium compound dimethyldioctadecylammonium (DDA) produce an adjuvant system which induces a powerful cell-mediated immune response and a strong antibody response, desirable for a high number of disease targets.



### References

1. Larrouy-Maumus G, Layre E, Clark S, Prandi J, Rayner E, Lepore M, de Libero G, Williams A, Puzo G, Gilleron M. Protective efficacy of a lipid antigen vaccine in a guinea pig model of tuberculosis. *Vaccine*. 2017 Feb 9. pii: S0264-410X(17)30159-7.
2. Derrick SC, Yabe I, Morris S, Cowley S. Induction of Unconventional T Cells by a Mutant Mycobacterium bovis BCG Strain Formulated in Cationic Liposomes Correlates with Protection against Mycobacterium tuberculosis Infections of Immunocompromised Mice. *Clin Vaccine Immunol*. 2016 Jul 5;23(7):638-47.
3. Rose F, Wern JE, Ingvarsson PT, van de Weert M, Andersen P, Follmann F, Foged C. Engineering of a novel adjuvant based on lipid-polymer hybrid nanoparticles: A quality-by-design approach. *J Control Release*. 2015 Jul 28;210:48-57.

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Cat. No.	Description
699855P	3D-(6-acyl) PHAD™ Monophosphoryl Hexa-acyl Lipid A, 3-Deacyl (Synthetic), powder
890810P	18:0 DDAB Dimethyldioctadecylammonium (Bromide Salt), powder
890810C	18:0 DDAB Dimethyldioctadecylammonium (Bromide Salt), chloroform
699500P	Kdo2-Lipid A (KLA) Di[3-deoxy-D-manno-octulosonyl]-lipid A (ammonium salt), powder
699851P	3A-MPLA Monophosphoryl Tri-acyl Lipid A (Synthetic), powder
699854P	4A-MPLA (isomer C3) Monophosphopdyl Tetra-acyl Lipid A, powder
699800P	MPLA (PHAD™) Monophosphoryl Lipid A (Synthetic) (PHAD®), powder
699852P	3D-PHAD™ Monophosphoryl 3-Deacyl Lipid A (Synthetic) Pat No. 9,241,988, powder
699810P	PHAD™-504 Monophosphoryl Lipid A-504, powder
890808P	22:0 Trehalose D-(+)-trehalose 6,6'-dibehenate, powder
890809P	Trehalose monooleate D-(+)-trehalose 6-monooleate, powder

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- Cationic Lipids (Transfection)
- Neutral Lipids
- Mini-Extruder

MilliporeSigma  
400 Summit Drive  
Burlington, MA 01803

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