Carolyn Shore, PhD

Officer, Antibiotic Resistance Project The Pew Charitable Trusts 901 E Street, NW, Washington, DC 20004



School of Engineering and Science Research II

Phone: +49.421.200-3248 Fax: +49.421.200-3249 m.winterhalter@jacobsuniversity.de www.jacobs-university.de

Bremen, April 3rd, 2016

Letter of Support

Dear Carolyn,

Many thanks for sharing your confidential draft of the "Scientific Roadmap for Antibiotic Discovery" with us.

As stated clearly in the introduction of your proposal, there is an urgent need for new effective antibiotics in particular for Gram-negative bacteria. Currently we rely on a small number active molecules and for all of them natural resistance mechanisms have been detected. Facing this danger the European Union has initiated a private-public partnership with the pharmaceutical industry to set the New Drugs For Bad Bugs (www.ND4BB.eu) platform and "Translocation" is the subproject devoted to the early antibiotic development.

Pew's "Scientific Roadmap for Antibiotic Discovery" is a transformational research effort that complements Translocation's work, and fills a gap in the global research landscape for antibiotic discovery.

As an academic leader of the IMI project "Translocation" I have now more than three years of experience with a similar initiative in Europe. Our five year project started in 2013 with the goal to understand and to develop assays to quantify the mechanism of antibiotic uptake into Gram-negatives. Furthermore a second objective was to create an InfoCenter containing previous research data to allow other teams to learn from failure (and success) in the field. As we are now in year four we focus our efforts to improve the impact and we are entering data in the InfoCenter that will hopefully be useful for future projects. Based on our experience we may state the current bottlenecks:

- 1. Unlike other areas in medicinal chemistry we lack a collection of chemical compounds allowing us to escape the resistance mechanism. Partially this might be caused by the lack of appropriate screening methods.
- 2. A lot of knowledge has been acquired, however scientific publications report only successful ones. Commercial enterprises stop projects for various reasons however neither the rational nor the data is usually communicated. Improving the exchange of information on failure is an important source of information in this field and moreover might allow us to use resources more efficiently.

I fully agree with your careful analysis of the current bottlenecks in antibiotic research and I highly welcome the Pew Charitable Trusts' "Scientific Roadmap for Antibiotic Discovery." I see this initiative as complementary to Translocation and with many exciting opportunities for collaboration.

- To date, Translocation is focused on research in the European Union. The roadmap could level resources, infrastructure, and support from U.S. research facilities, academic institutions, and companies.
- Together Translocation and Pew's Roadmap initiative could move the antibacterial research community away from a "black box" mode of drug discovery and toward more rational approaches, which may enable the delivery of new agents to treat life-threatening infections.
- The roadmap lays out a specific action-oriented plan for tackling key scientific barriers to the discovery of new antibiotics and sharing that knowledge across laboratories and across borders. It complements IMI's effort to tackle the challenges posed by Gram-negative bacteria, and the dearth of raw chemical matter for development.

Throughout I found the proposal well thought and timely. On behalf of Translocation I fully support your initiative.

Mathias Winterhalter Leader of the Managing Entity Jacobs University Bremen

With my best regards,

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Mathias Winterhalter, Professor of Biophysics