SPEAKER SPOTLIGHT:
STEVE HOFFMANN

STEVE HOFFMANN, Director, Inflammation & Immunity, Research Partnerships
Foundation for the National Institutes of Health

Steve Hoffmann is the Director, Inflammation and Immunity in Research Partnerships at the Foundation for the National Institutes of Health (FNIH). In this role, he provides strategic planning, programmatic management and research administration of a broad portfolio of established and emerging projects in inflammation, toxicity, infectious disease and other autoimmune diseases.

Steve has worked for over 20 years in the field of translational biomarkers, molecular immunology and precision medicine with a focus on multi-stakeholder partnerships and project development. Prior to FNIH, Steve worked as both a project and product manager at Meso Scale Discovery and Transplantation and Autoimmunity Branch at NIH/NIDDK leading efforts in molecular profiling of surrogate biomarkers of rejection, tolerance and drug toxicity in human renal and islet cell transplant trials. Steve holds a MS in Pathology and Laboratory Medicine from UNC-CH and a BS Biochemistry and Biophysics from Pittsburgh University.

What is the Biomarkers Consortium and what is your main role within it?

The Foundation for the National Institutes of Health (FNIH) Biomarkers Consortium (BC) is a public–private partnership that aims to facilitate drug development with biomarkers across a range of therapeutic areas. The BC is organized to address specific precompetitive biomarker projects, giving participating stakeholders a role in the design and conduct of projects and making the results freely public. Ultimately, the goals of the BC are to accelerate the development of new medicines, inform regulatory decision making, and improve patient care. I am the Director of the Inflammation and Immunity portfolio of projects at FNIH and this also covers the multiple projects in the Inflammation and Immunity Steering Committee – one of the 4 committees (by disease area; incl – Cancer, Metabolic Disorders, Neuroscience) that provide critical development and overall management of BC projects.

What are some of the key accomplishments of the Biomarkers Consortium within the past few years?

As a general overview, the BC has launched over 30 launched projects. These projects have generated over 50 project team publications and have been cited in publications over 800 times. Importantly, these projects have generated nine tools that are being used by the pharmaceutical industry in drug development to make clinical trial decisions. Finally, the work of BC projects has contributed to 5 FDA Guidance documents, 1 FDA Biomarker Qualification, and the advancement of 12 therapies toward FDA approval. The therapies have been in cancer and bacterial infections. Some specific, recent (2018) highlights are presented here.

Therapeutics Advanced Using Tools Generated by Biomarkers Consortium Projects:

- Community-Acquired Bacterial Pneumonia and Acute Bacterial Skin and Skin Structure Infections (CABP/ABSSSI) Project –Tigecycline (expanded label)
- Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia (HABP/VABP) Project – Ceftazidime/Avibactam (AVYCAZ)

FDA Biomarker Qualification Milestones:

Letter of Intent (LOI) Approval (1st Step in Biomarker Qualification Process):

- Clinical Evaluation and Qualification of Osteoarthritis Biomarkers (PROGRESS OA) Project − Legacy OA Imaging LOI approved to move forward to a qualification plan (May 7, 2019) to qualify MRI composite measure

New Tool Qualified (Final Step in Biomarker Qualification Process):

- Clinical Evaluation and Qualification of Translational Kidney Safety Biomarkers (Kidney Safety) Project. First ever qualification by the FDA of a clinical safety biomarker and the first qualification for the Biomarkers Consortium on July 25, 2018. Composite measure biomarker can be used to detect acute kidney injury for drugs being tested in normal volunteers in Phase 1 clinical trials.

Consensus Statements and Documents Generated (Consensus decisions are to develop and release "FDA Guidance to Industry." that ensure understanding and consistency across the therapeutic development industry.)

Contributions to FDA Guidance:

- FNIH/FDA Evidentiary Criteria Workshop – A whitepaper generated through the workshop contributed to the contents of the new "Biomarker Qualification: Evidentiary Framework Guidance for Industry and FDA Staff" released in December 2018
- HABP/VABP Project – Recommendations submitted to the FDA will be incorporated into updated 2019 Guidance
- OA Biomarkers Project – Contributed to the release of the "Osteoarthritis: Structural Endpoints for the Development of Drugs, Devices, and Biological Products for Treatment, Guidance for Industry" in August 2018

23 Scientific Publications (I&I representative selections below)

- 7 manuscripts from FNIH OA Biomarkers Project
- 2 manuscripts from Antibacterial Projects CABP/ABSSSI and HABP/VABP

What role does the Biomarkers Consortium play in engaging the wider biomarker community to implement new frameworks and initiatives?

The FDA and BC have co-sponsored and aligned on several initiatives to accelerate and define evidentiary criteria for biomarker qualification. The Developing an Evidentiary Criteria Framework for Safety Biomarkers Qualification Workshop was held on April 14 and 15, 2016. This workshop aimed at creating alignment among scientific stakeholders including the FDA, the NIH, the biopharmaceutical industry, academic researchers and patient groups regarding a proposed framework for determining the levels of evidence required to qualify biomarkers for use in drug development, with an emphasis on biomarkers used in determinations of drug safety assessments. The participants elaborated a general framework for biomarker qualification along with specific application to different contexts of use related to drug safety, including assessment of several specific case studies involving qualifying clinical markers of toxicity in different organ systems. This lead directly to both new FDA Guidance on Biomarker Qualification (https://www.fda.gov/media/119271/download) and a related joint publication (What evidence do we need for biomarker qualification, Sci. Transl. Med. 9, eaal4599, 2017).

A similar joint Workshop was done for Defining Evidentiary Criteria: Surrogate Endpoint Qualification Workshop on July 30th and 31st, 2018. This workshop aimed to elaborate the general framework for biomarker qualification along with specific application to different contexts of use (COUs), including assessment of several representative case studies involving surrogate endpoint markers of specific clinical outcome measures. Specific publications as outcomes from this Workshop are not released.

You are talking at the event on ongoing projects in Inflammation and Immunity. What are the challenges of working in this space? What do you hope to accomplish?

The success of the Biomarkers Consortium and the success of these public-private partnerships/projects in I&I are aligned with engagement of the members, recruitment of potential new partners (for both membership or support and contribution to specific projects), and adoption of the outcomes and clinical tools from these projects by the field. Similar to our reasons for attending and presenting at the Congress, is to continue outreach and awareness efforts of the FNIH and Biomarkers Consortium. The challenges of the space is certainly evident in the tremendous heterogeneity of autoimmune diseases. Often defining and stratifying disease populations or identifying multiple endotypes of each disease make both biomarker and treatment development difficult. Inflammation crosses ALL areas – neuroinflammation, Immuno-Oncology, cardiovascular and diabetes-related metabolic syndromes, etc, and requires a broad understanding and involvement of immunology, infectious disease, and multiple organ systems. Focusing project objectives and true contexts of use for specific biomarkers, with clear ROI and deliverables, is important.

Going forward, what do you think the industry will be – or should be – prioritising in the biomarkers space?

Organizations like the FNIH Biomarkers Consortium have developed strong alliances with the FDA and other regulatory agencies, key academic leaders, patient advocacy groups and industry. Successful clinical trials and drug development require well validated biomarkers and endpoints. The engagement of industry "early" in the project development process is essential to ensure project aims and outcomes align with the predominant supporting/funding stakeholders' objectives – but also these partnerships bring the cross-sector and cross-functional perspectives also needed for novel drug development and personalized medicine. There is always a push to find instant treatment response biomarkers to guide therapies or surrogates for clinical outcomes – but these often are ambitious and require specific and comprehensive validation (safety, multiple trials, multiple populations) to achieve. Industry needs to be open to sharing data, samples and expertise in partnership with other companies and sectors to share risks, costs and shorten timelines for biomarker development & drug approval – the FNIH and BC are a good neutral 3rd party, safe harbour for such partnering.

Why are you attending the 4th Annual Biomarkers & Precision Medicine USA Congress? What do you look to achieve from such meetings?

As noted above, the Congress allows the BC to highlight who we are, what we do and tout the successful project outcomes for better adoption and use by all sectors. Showing project models of success should help recruit new partner engagement for developing projects. Networking with leaders focused on biomarker development and validation, development of clinical tools for drug development and is essential for our mission and goals.

Steve Hoffmann, Speaker at the 4th Annual Biomarkers & Precision Medicine USA Congress 2019.

For further information on the Biomarkers Series, please contact: marketing@oxfordglobal.co.uk