HBV Forum 3: Evaluation Report

October 24, 2017

Marriott Marquis Hotel

Washington D.C.

Facilitating Collaborative Research in Drug Development and Health Policy
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TABLE OF CONTENTS

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HBV FORUM MEETING AGENDA

12:30	**Light Lunch Reception**	
1:30	Welcoming and Introductory Remarks	Veronica Miller, Forum for Collaborative Research Pedro Goicochea, Forum for Collaborative Research
1:45	Current FDA Perspective on HBV Drug Development	**Presenter:** Poonam Mishra
2:00	FDA Perspective on HBV Diagnostic Devices	**Presenter:** Kathleen Whitaker
2:15	Quantitative Serum HBsAg Assay Validation for U.S. Patient Testing	**Presenter:** Robert Gish
2:30	Implications of HBsAg from Integrated DNA for Clinical Trial Design	**Presenter:** Bruce Given
2:45	HBV Next Generation Sequencing	**Presenter:** Leen-Jan van Doorn
3:00	Panel Discussion	Timothy Block Carol Brosgart Anuj Gaggar Edward Gane Maureen Kamischke
3:40	**Break**	
4:00	Working Group Updates: Diagnostics and Biomarkers	**Presenter:** Ed Marins, Roche Molecular Systems Gavin Cloherty
4:10	Discussion	All
4:20	Working Group Updates: Surrogate Endpoints -Achievements -Updates on Collaboration with Other Stakeholders -Next Steps	**Presenter:** Oliver Lenz, Janssen Pharmaceuticals ID&V
4:40	Discussion	All
4:50	Working Group Updates: Treatment Combination	Presenter: Oliver Lenz, Janssen Pharmaceuticals ID&V
5:10	Discussion	All
5:20	General Discussion and Wrap-up	Veronica Miller, Forum for Collaborative Research William Symonds, Arbutus Biopharma
5:30	Discussion	All
5:40	International Coalition to Eliminate HBV	Peter Revill
6:10	Discussion	All
6:20	Wrap up	Veronica Miller
6:30	**Networking Reception**	
7:30	**Adjourn**	

This is not an official function/event of the American Association for the Study of the Liver Diseases (AASLD)

BACKGROUND

The HBV Novel Therapeutic Interventions (The HBV Forum), launched in January of 2016, aims at advancing the regulatory science for HBV and its associated morbidities in real-time by providing an independent and neutral environment for ongoing multi-stakeholder dialogue.

The HBV Forum is currently comprised of 161 members representing different stakeholder groups, including members of academia, researchers, representatives of pharmaceutical and diagnostic companies, regulators from the US and Europe, and patient advocates/representatives.

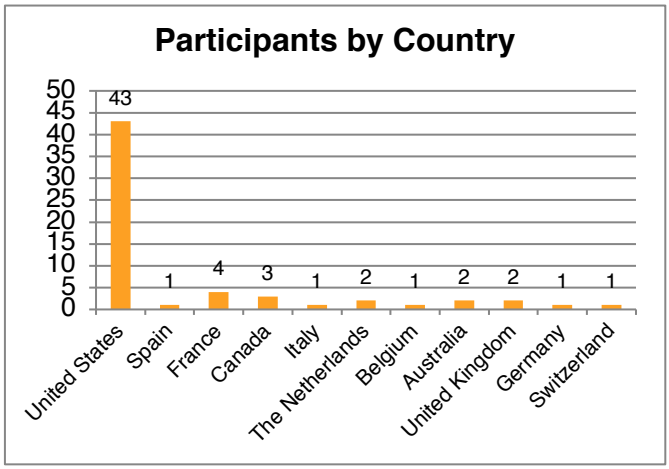
The HBV Forum has a Steering Committee (SC) consisting of 22 members that provide overall scientific leadership, suggest topics for consideration, and prioritize the research questions to be addressed in the project. In June of 2016, the Steering Committee prioritized the following topics of interest for the Forum, and organized three working groups:

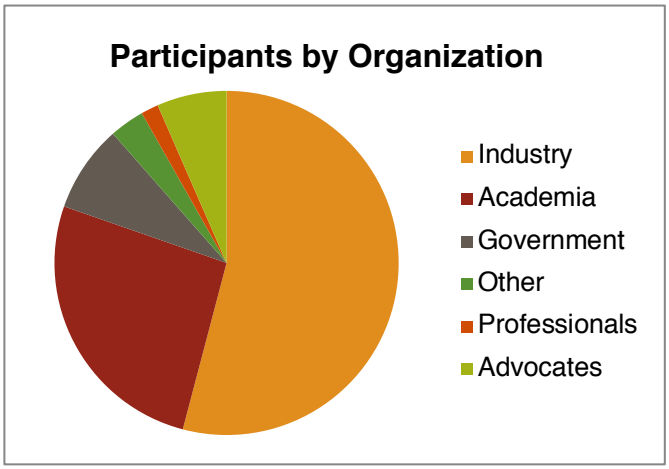
- **Diagnostics/Biomarkers Working Group**
  Co-chairs: Ed Marins, MD and Gavin Cloherty, PhD.
  Aim: Develop clarity on what is needed for biomarker acceptance and validation for HBV drug/diagnostic development
- **Surrogate Endpoints Working Group**
  Co-chairs: Marion Peters, MD and Oliver Lenz, PhD.
  Aim: Strengthen the link of surrogate markers (endpoint in clinical studies) with long term clinical outcomes (e.g., liver disease progression/HCC)
- **Treatment Combination Working Group**
  Co-chairs: Prof. Lim Seng Gee, MD and Bruce Given, MD.
  Aims: I.) Provide clarity on the requirements of novel agents in clinical development, and II.) identify mechanisms to speed up the development of combinations of different promising agents across companies

HBV Forum 3 took place on October 24, 2017, at the Marriott Marquis Hotel, in Washington D.C. following the AASLD Liver Meeting. This is the evaluation report of the HBV Forum 3.

PARTICIPATION IN THE HBV FORUM 3

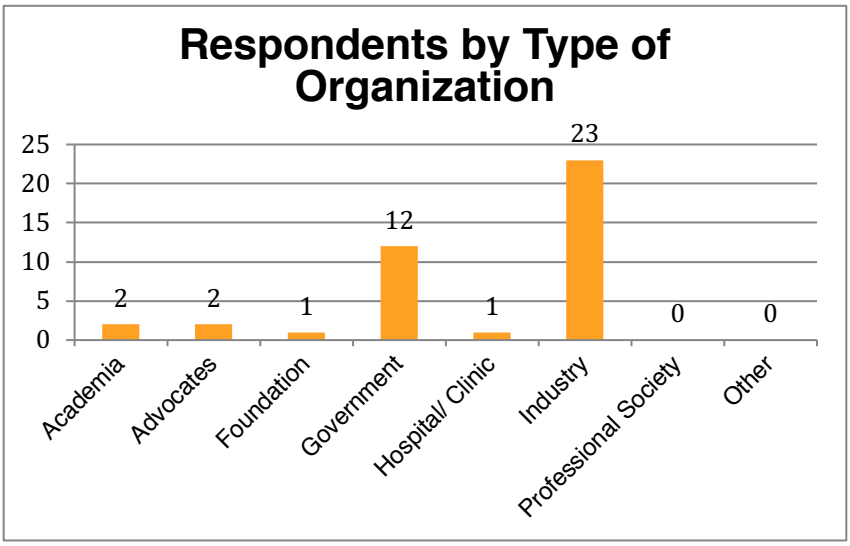
The HBV Forum 3 was attended by 61 people; 55 participated in-person, and 6 remotely. Almost half of the attendees represented industry and diagnostic companies (54.1%), and close to a quarter represented academia (26.2%). Other stakeholders included representatives from the government (8.2%), other (3.3%), professionals (1.6%), and community advocates (6.6%). A majority of participants were previous participants in HBV 2 which was held in Amsterdam, Netherlands in April of 2017.





HBV Forum 3 Evaluation

The HBV Forum 3 Evaluation was distributed on October 26th, 2017 using SurveyMonkey, and responses were collected until November 22nd, 2017. We received 41 responses, resulting in a 97.6% completion rate. Of all respondents, 34.15% reported that the HBV Forum 3 was the first event organized by the Forum for Collaborative Research that they had attended.



A little more than half of the respondents (56.1%) represented pharmaceutical companies and 17.4% reported working in academia. Other respondents represented, foundations, clinics, government organizations, patient advocates, and others.

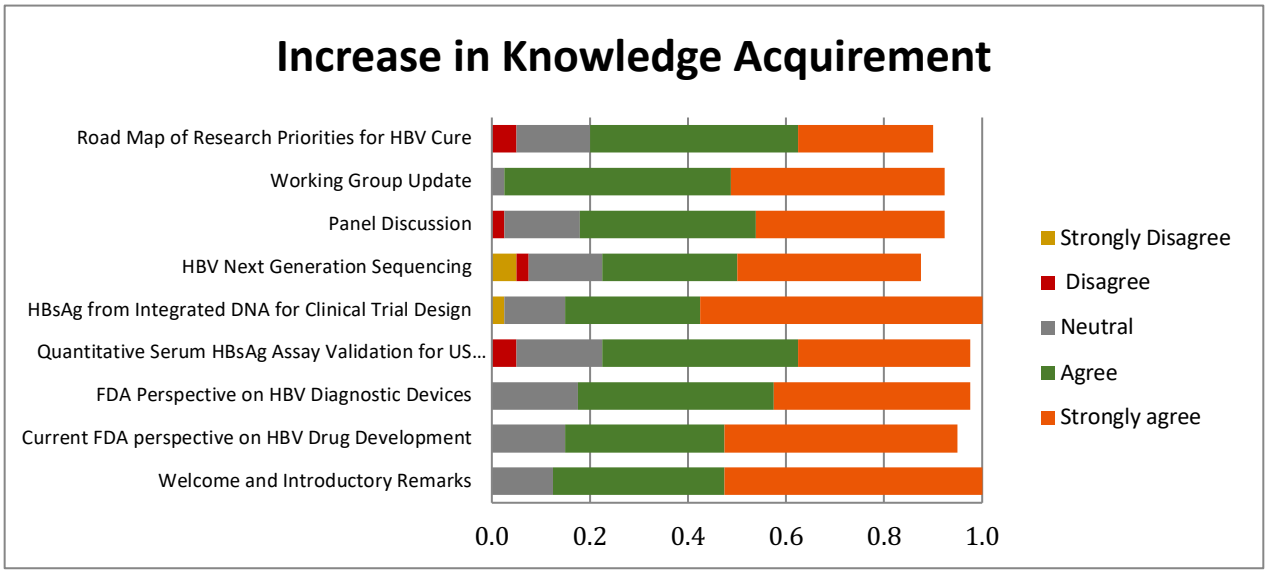
Of those from industry, 15 respondents reported their role in their organizations as either Project Lead or Director (65.22%) and 4 respondents reported their role as Chief Medical or Scientific Officer (17.39%).

Opinions about the HBV Forum

All the respondents to the evaluation agreed that the discussions at HBV Forum 3 would help guide the work of their organizations, that they are interested in attending HBV Forum 4 in Paris, France (82%), and that they would recommend other colleagues or peers to join the HBV Forum (97.5%). All respondents agreed that participating in the HBV Forum is valuable to their work.

HBV FORUM 3 SESSIONS

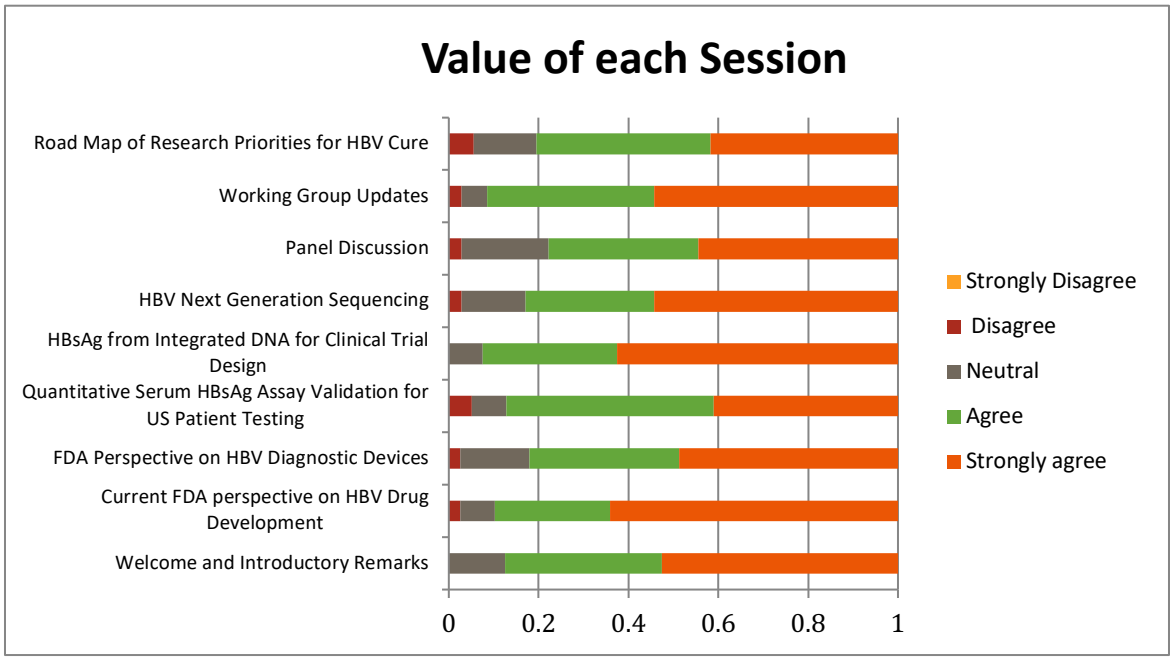
The HBV Forum 3 was organized into nine sessions, at least 72.5% of respondents (of those who attended) reported that they either “strongly agreed” or “agreed” that they learned something valuable in each session. The “Implications of HBsAg from Integrated DNA for Clinical Trial Design” session was rated as one of the most valuables. The majority of the evaluation respondents (89.74%) reported that the information presented during the Working Group Updates session was highly informative. Another session that was reported as highly informative was the Quantitative Serum HBsAg Assay Validation for US Patient Testing.



Respondents indicated that HBV Forum 3 facilitated new collaborations or interactions with individuals and/or organizations (90%) and that HBV Forum 3 extended existing collaborations or interactions with individuals and/or organizations (90%),

Suggestions from respondents to facilitate collaboration in future meetings included:

- Increase networking opportunities, distribute more detailed activities by the working groups
- More time for open discussions
- Request questions prior to the meetings
- Have break out session with more specific topics for discussion and less podium presentations
- Describe each working group and how participants can get involved for new participants
- Have small group interactions
- Q&A after each session
- More communication between meetings- perhaps e-newsletters or emails to give updates on progress and news



Respondents indicated that the majority agreed or strongly agreed that each individual session added value to the HBV Forum 3. Respondents indicated that "HBsAg from Integrated DNA for Clinical Trial Design" session had the highest value rating with 93% of individuals agreeing or strongly agreeing. The "Road Map of Research Priorities for HBV Cure" session had the lowest value rating with only 73% of individuals agreeing or strongly agreeing. No session received a strongly disagree response.

RECOMMENDATIONS FOR HBV FORUM 4 – April 2018, PARIS, FRANCE

Topics suggested by respondents to be considered for HBV Forum 4 included:

- What is the impact of integrated HBsAg on HBV cure?
- Discussing the language around a "cure", as it means something different among the various groups, and even to those living with the disease
- Role of capsid inhibitors in the cure or any other molecule that does not affect directly sag levels
- A review of recent clinical data and the lessons to take from this
- Pros and cons of different end points of curative strategies
- Discussion/presentations on surrogate endpoints and validating these for regulatory purposes
- Resistance testing, Presentation of Resistance data, New tools to identify resistance associated substitutions
- Update from the ALT flares WG
- Applicability of biomarkers (results follow up in clinical trials)
- More specifics on trial design according to different MOAs
- Resistance analysis of new agents including both sequencing and phenotypic assays
- A conversation between EMEA & FDA on points of their contention to help us understand where they feel there is debate
- Core antibody
- Any particular special population experience - women, incarcerated populations, children, injection drug use - how to engage in clinical trials.
- the early expression of the HBV X mRNA, which was reported at AASLD 2017 to be expressed as early as 4 hours after infection, which is prior to the formation of cccDNA
- Discuss the role of CpAMs in combination with NrtIs and the potential of this combination to lead to functional control of chronic HBV off therapy. There are still a lot of questions about how this type of combination might impact the extensive cccDNA reservoir and the amount of time that might be required to reduce it to a level that could be functionally controlled

Areas/suggestions for improvement for HBV Forum 3 included:

- Including additional members from academia, specifically clinicians such as David Spach affiliated with the University of Washington
- Scheduling:

  - Longer break time to talk with people
  - More interactive sessions, perhaps small groups by working groups
  - More time allotted for sessions
  - Earlier start time
  - If working group meetings are included in future meetings, consider making it a full day meeting to enable full participation
  - Less time devoted to naming people who are working on each project, working group, etc. Make the information available in handouts, etc. but don't devote meeting time and slides to it
- More questions & answers
- Panel could have used a bit more adrenalin and controversy
- EMA input to date seems modest, given the geography of the disease involvement of more physicians from Asia.
- Have input from APAC regulatory authorities
- Facilitate broader discussion
- Presentation of data
- More scientific input on applicable biomarkers, diagnostic tests
- Have EMA representatives in attendance
- Less time devoted to announcing each person on each working group; simply make the information available in handouts