



**Academy of Managed Care Pharmacy
(AMCP)**

**Biologics and Biosimilars Collective
Intelligence Consortium, LLC (BBCIC, LLC)**

GOVERNANCE

Approved by the BBCIC

Board of Managing Directors October 23, 2015

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1 AMCP BBCIC CHARTER

1.1 Charter Scope

The AMCP Biologics and Biosimilars Collective Intelligence Consortium, LLC (AMCP BBCIC) Charter details the principles and policies governing consortium organization, operations, and research. The Charter documents the roles, rights and responsibilities of the various BBCIC governing bodies and BBCIC Participants, and includes individuals and institutions that receive payment through BBCIC contracts, subcontracts or grants. It is expected that all Participants and contractors will abide by all policies and procedures expressed herein and approved by the BBCIC Board of Managing Directors.

1.2 Purpose and Mission Statements

The BBCIC will provide a range of research services that support the following value propositions:

1. Address important questions about the use, impact, safety, and clinical effectiveness of biologics and biosimilars on human health.
2. Increase the rigor and credibility of real world evidence
3. Provide access to a large population for epidemiologic studies and health services research
4. Improve the efficiency and cost-effectiveness of post-marketed observational studies
5. Develop standard approaches to common data needs and address gaps in tools and methods.

1.3 BBCIC Scope Definition

(Est. Aug 2015)

AMCP established the BBCIC to address anticipated needs for post-marketed evidence generation for novel biologics, their corresponding biosimilars and other related products. Currently there is no proactive post-approval evidence generation system in the US for purposes of monitoring biologics and biosimilars. This is an important public health need. The BBCIC meets this need with its science-driven approach which leverages existing distributed research network resources. The BBCIC is the neutral convener to provide investigators, biopharmaceutical companies, managed care organizations (MCOs), integrated delivery networks (IDNs), pharmacy benefit managers (PBMs), physicians and patient advocates with an organized process to characterize patient populations and generate evidence for biologics and biosimilars in a manner that promotes robust and

relevant scientific research and exchange and with the goal of making meaningful contributions to the scientific record.

The BBCIC will conduct a range of analyses from population characterization, epidemiologic studies, and active observational sequential analysis of biologics/biosimilars using a distributed network of healthcare organizations.

Specific observational research activities may include, but are not limited to:

- Population characterization and natural history, for example:
 - Disease prevalence
 - Product exposure
 - Product utilization, switching and adherence
 - Characterization of subpopulations or cohorts
- Safety (with and without the comparative dimension), for example:
 - Detecting frequency of events
 - Assessing clinical loss of efficacy over time
 - Comparing among products' acute reactions such as anaphylaxis, injection site reactions and flu-like symptoms
- Effectiveness (with and without the comparative dimension), for example:
 - Focusing on clinical endpoints/measurable efficacy
 - Assessing real-world dosing
 - Assessing compliance and gaps in therapy

The BBCIC focus is its science-driven approach. The BBCIC scope does not include advocacy or political functions, including taking a position or commenting on legislative or regulatory proposals.

1.4 AMCP BBCIC, LLC Legal Entity

(Est. Aug 2015)

The BBCIC will be operated as a subsidiary of AMCP that is housed under a separate legal entity. The AMCP BBCIC, LLC is a single-member LLC of which the Academy of Managed Care Pharmacy is the sole member.

1.5 Participant Types and Fees

(Est. Aug 2015)

The AMCP BBCIC is organized as a consortium, composed of participating biopharmaceutical and pharmaceutical companies, managed care organizations, pharmacy benefit management organizations, patient and provider advocacy

organizations, non-profit research organizations and other organizations relevant to the mission. These organizations will be referred to as Participants.

Each Participant will be assessed a fee based on Participant type. The fees will be determined and set by the AMCP BBCIC Board of Managing Directors.

1.5.1 Participant Types

1.5.1.1 Participant Organization

--An organization providing funding and/or substantial in-kind resources of reasonable equivalent value to the cash contribution of those organizations providing funding of equal scale. The Participant Organization is allowed to appoint one (1) representative each to the AMCP BBCIC Planning Board, the Science Committee, and the Communications Committee. This is a full-fee category and includes pharmaceutical companies MCOs and IDNs and can also include other types of organizations such as PBMs, specialty pharmaceutical distribution companies, trade associations, government organizations, foundations, self-insured employers, and other nonprofit organizations.

1.5.1.2 Associate Participant Organization

--An organization that does not plan to market in the U.S. a biologic (with a biosimilar in the pipeline) or a biosimilar and having no innovator biologics with biosimilars in the pipeline for at least two years from the time of joining the consortium. This is a discounted fee category.

1.5.1.3 Public Representative Organization

--A nonprofit organization that is determined to fill the multi-stakeholder goal of AMCP BBCIC. This is a no fee category.

1.5.2 Participant Fees

Participant fees will be tiered based on revenue and type of organization.

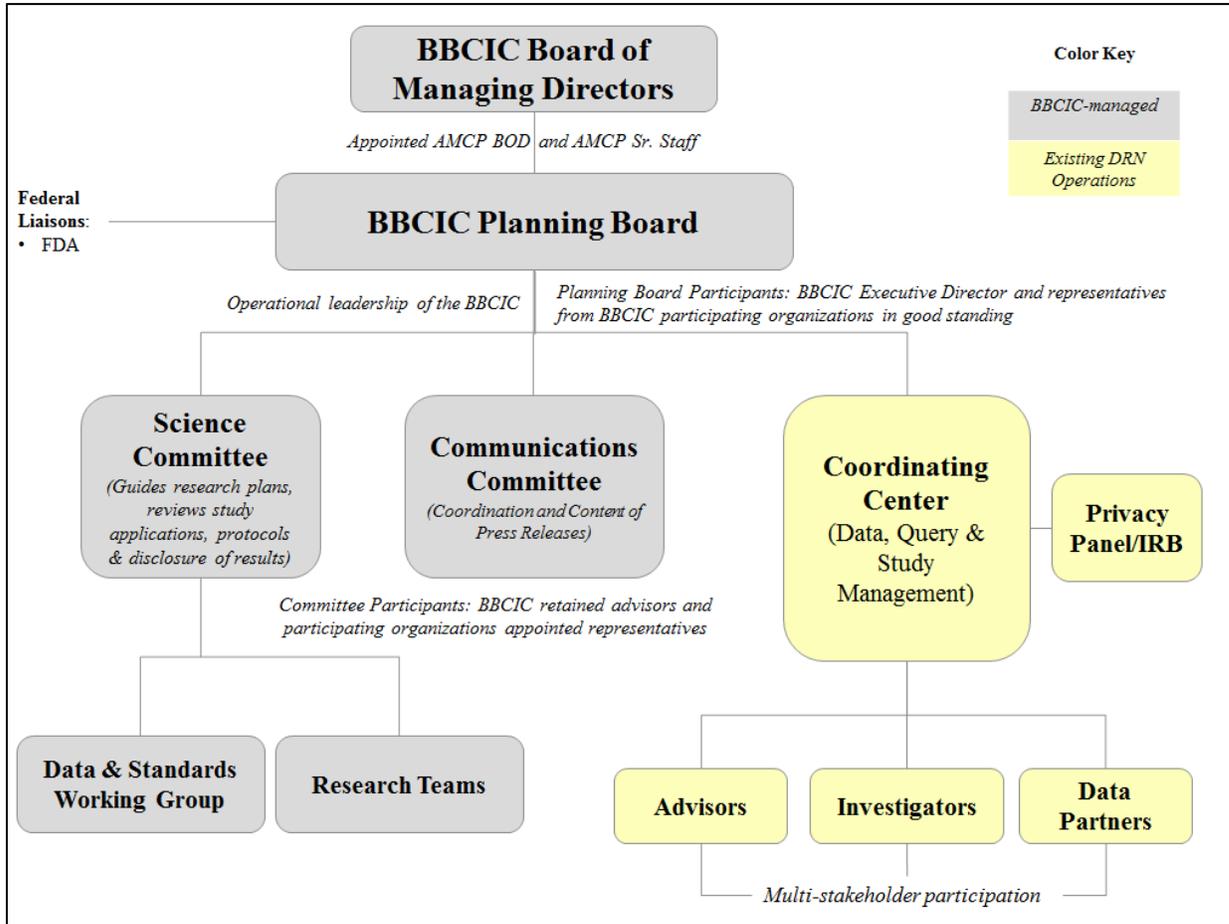
The BBCIC will determine fees annually, requiring BBCIC Board of Managing Directors final approval. The Planning Board is responsible for recommending participant fees based on the requirements of the annual research plan that is developed by the AMCP BBCIC Science Committee. The Planning Boards advances its fee recommendations to the BBCIC Board of Managing Directors for approval.

Participant fees will be made public to the BBCIC Participants in advance of Participant renewal.

1.6 Governance and Organizational Structure

The structure outlined in Figure 1 illustrates the organizational approach governing the interaction between the BBCIC Program Office and the BBCIC governing bodies overseeing all BBCIC Research and Operations. The roles and responsibilities of the BBCIC staff, the AMCP General Management Services and the BBCIC governing bodies will be described within this document.

Figure 1 BBCIC Governance and Organizational



Structure

1.6.1 BBCIC Board of Managing Directors

(Est. Aug 2015)

Composition

The AMCP BBCIC Board of Managing Directors is the governing body composed of not less than three (3) voting members, as appointed by the sole member of the LLC, AMCP. It is anticipated that there will be five (5) voting members of the AMCP BBCIC Board of Managing Directors, including: AMCP President* (serving as Chair), AMCP Treasurer, AMCP CEO, and two (2) at-large Directors. In addition, it is anticipated that the BBCIC Consortium Director and Chief Science Officer will participate in all BBCIC Board of Managing Directors meetings without a vote.

(*Note: The AMCP President may designate a current member of the AMCP Board of Directors to serve in his/her place. This is solely at the AMCP President's discretion.)

Term of Appointment

The BBCIC Board of Managing Directors is appointed by the AMCP Board of Directors. The AMCP CEO, President, and Treasurer will serve for the length of their term in that office. It is anticipated that At-Large Directors will serve two one-year terms, with rotations staggered.

Selection and Qualifications

The AMCP President, AMCP Treasurer, and AMCP CEO are selected ex officio. The At-Large Directors are selected by the BBCIC Board of Managing Directors with input from the BBCIC Planning Board. The At-Large Directors should have research experience and not be employed by the pharmaceutical industry, a managed care organization, or a PBM.

Responsibilities

The BBCIC Board of Managing Directors' role is to govern AMCP BBCIC and oversee its operations. The AMCP BBCIC Board of Managing Directors is responsible for oversight of the AMCP BBCIC including:

- Approving the Charter and Operational Policies & Procedures;
- Approving the Research Plan from a fiduciary and mission perspective, after consideration of BBCIC Planning Board recommendations;
- Approving the Operating Budget;
- Providing oversight to ensure that the Charter and all policies and procedures are followed
- Assisting the AMCP CEO in the selection of the BBCIC Consortium Director. Maintaining ongoing participation in and alignment with the BBCIC Planning Board by identifying a Board of Managers appointee to the BBCIC Planning Board

1.6.2 BBCIC Planning Board

(Est. Aug 2015)

Composition

The AMCP BBCIC Planning Board is composed of:

- BBCIC Consortium Director, ex officio, voting
- BBCIC Chief Science Officer, ex officio, voting
- One (1) representative from each of the BBCIC Participant Organizations, voting
- One (1) representative from each of the BBCIC Associate Participant Organizations, non-voting
- Up to three (3) public representatives recruited from patient/consumer/physician advocacy organizations, voting
- One (1) representative from the BBCIC Coordinating Center, ex officio, non-voting
- BBCIC Board of Managing Directors Liaison, ex officio, non-voting
- BBCIC Science Committee Chair, ex officio, non-voting

The AMCP BBCIC Planning Board will elect a Chair from within its roster annually.

Term of Appointment

The representatives of the Participant organizations serve at least a one-year term. Each representative's appointment is contingent upon remaining in the employment of the Participant organization and the Participant organization remaining in good standing on the BBCIC Planning Board.

The Public representatives serve a two (2) year term (staggered). The ex officio members of the Planning Board serve for so long as they hold the applicable position.

Selection and Qualifications

Representatives from the Participant organizations are selected by each applicable Participant.

Representatives from the public are recommended by the BBCIC Planning Board and appointed by the AMCP BBCIC Board of Managing Directors. The public members should have a keen interest in improving the dissemination of unbiased scientific evidence for biosimilars and their corresponding biologics.

Responsibilities

The AMCP BBCIC Planning Board is responsible for:

- Developing recommendations for revisions to the AMCP BBCIC Charter, Operational Policies & Procedures and the Research Framework and research plans for submission to the BBCIC Board of Managing Directors for approval.

- Reviewing and approving the Annual Research Plan and associated budgets that are developed by the AMCP BBCIC Science Committee and advancing to the BBCIC Board of Managing Directors for approval.
- Reviewing and approving refinements to the AMCP BBCIC research plans or related activities developed and/or recommended by the BBCIC Science Committee, including quarterly updates to the Annual Research Plan (see Policy 2.13.1 Annual Research Plan)
- Forming subcommittees or ad-hoc advisory groups to oversee or develop plans for specific issues.
- Advising the Consortium Director on mix of disciplines and experience needed within Science Committee
- Overseeing public communications regarding AMCP BBCIC activities and findings

Commitment

The AMCP BBCIC Planning Board is expected to meet at least six (6) times per year either in person or via teleconference. Participant representatives may be asked to serve on subcommittees for specific projects.

1.6.3 BBCIC Committees

1.6.3.1 Science Committee

(Est. Aug 2015)

Composition

The BBCIC Science Committee is composed of:

- BBCIC Consortium Director, ex officio, voting
- BBCIC Chief Science Officer, ex officio, voting
- One (1) representative from each of the BBCIC Participant Organizations, voting
- One (1) representative from each of the BBCIC Associate Participant Organizations, non-voting
- One (1) representative from the BBCIC Coordinating Center, ex officio, non-voting
- BBCIC Planning Board Liaison, ex officio, non-voting
- AMCP BBCIC Planning Board Chair, ex officio, non-voting
- Independent contracted experts (budget permitting), up to 3, non-voting

The BBCIC Science Committee will elect a Chair from within its roster annually.

Term of Appointment

The representatives of the Participant organizations serve at least a one-year term. Each representative's appointment is contingent upon remaining in the employment of the Participant organization and the Participant organization remaining in good standing on the BBCIC Planning Board.

The elected Chair will serve in that capacity for one year. The Chairmanship may be held by the same Participant for no more than three (3) years.

Selection and Qualifications

The representatives from the Participant organizations are selected by the Participant. In addition, the AMCP BBCIC Consortium Director will consider appointing additional members to ensure that a mix of disciplines and expertise is achieved on the Science Committee.

Responsibilities

The BBCIC Science Committee:

- Will be accountable to the AMCP BBCIC Planning Board
- Will be accountable for the development and conduct of the overall research plan including prioritization of research topics and their quarterly updates, Research Protocols, and selection of Research Teams needed to execute the plan.
- Will be responsible for creating consensus in the event of a research related disagreement among the participants.
- Forming subcommittees or ad-hoc advisory groups to oversee or develop plans for research-related issues.
- Will recommend publication plans and other dissemination methods to the AMCP BBCIC Planning Board for final approval by the AMCP BBCIC Board of Managing Directors.
- Will be responsible for identifying data gaps and recommending methods to help address these gaps.
- May recommend data solutions that could be implemented by stakeholders. Note: See Policy 2.13 AMCP BBCIC Policy on Research Activities and Approvals for additional information

Role of Chair:

- Define the BBCIC Science Committee agenda and act as facilitator at its meetings
- Call for special BBCIC Science Committee meetings in compliance with the Operating Agreement.

- Report to BBCIC Planning Board on the status of the activities and research projects

1.6.3.1.1 Protocol Research Teams

(Est. Aug 2015)

The Protocol Research Teams will develop protocols that are used for the specific AMCP BBCIC research questions for the identified biosimilars. The composition of the Protocol Research Team will include a Principal Investigator or Co-Principal Investigators – one as a Data Lead and one as a Science Lead, who are appointed by the AMCP BBCIC Science Committee. The Science Lead will be an individual with experience in conducting studies around the compound or class of compounds in question. The Data Lead will be an individual with experience using the Mini-Sentinel Common Data Model for distributive research. The Science Committee will issue a call for nominations to BBCIC Participants for each Protocol Research Team. The Research Teams will be reflect the various Participant stakeholders and include data, clinical, epidemiology, statistics and HEOR expertise.

The BBCIC Science Committee may also appoint subject matter experts where the expertise does not already exist on the Science Committee. BBCIC Participants may volunteer additional in-organization observational research experts to assist the Protocol Research Team.

Responsibilities

The Protocol Research Teams:

- Will write formal Research Protocols to be approved by the Science Committee.
- Conduct approved Research Protocols working with the Coordinating Center who will run the data and apply analytic methods defined by the Research Team.
- Develop and submit to the Science Committee any protocol changes needed, including changes needed to investigate any potential safety-related findings of interest (see Policy 2.14.2 Process for Informing the Science Committee of a Safety-Related Finding of Interest).
- Provide quarterly updates on Research Protocols to the Science Committee.

1.6.3.2 Communications Committee

Composition

The AMCP BBCIC Communications Committee is comprised of one (1) representative from each Participant organization if the Participant organization so chooses.

Term

The representatives of the Participant organizations serve at least a one year term. The representative's appointment is contingent upon remaining in the employment of the Participant organization and the Participant organization remaining in good standing on the BBCIC Planning Board.

Selection and Qualifications

The representatives to this Committee are selected by the Participant organization.

Responsibilities

The AMCP BBCIC Communications Committee responsible for coordinating the review and feedback from their respective organizations on proposed BBCIC press releases.

1.6.4 BBCIC Ad-Hoc Work Groups

(Est. Aug 2015)

The BBCIC Planning Board may from time to time establish ad-hoc working groups to support Planning Board and Committee activities. These may include (but not be limited to) a Data and Standards Working Group addressing data gaps and developing and recommending standards in support of the research plan.

1.6.5 BBCIC Staff

1.6.5.1 BBCIC Consortium Director

(Est. Aug 2015)

The BBCIC Consortium Director will provide overall and day-to-day management of the BBCIC. The Consortium Director will be an employee of the Academy of Managed Care Pharmacy serving in the capacity of the BBCIC Consortium Director through a Service Agreement between AMCP and the BBCIC. The Consortium Director will report to the AMCP CEO.

The BBCIC Consortium Director's roles and responsibilities include the following:

- Fiscal management
- Manages the staff of the BBCIC and external consultants including the Coordinating Center

- Serves as the staff liaison to the BBCIC Board of Managing Directors to keep the AMCP Board of Managing Directors informed about key activities, program status and issues including
- Recruiting of BBCIC Participants
- Fundraising
- Contract management
- Support the Planning Board and Sub-Committee Chairs in the management of meetings.
- Ensure compliance among BBCIC Participants with adopted policies and strategies
- Ensure ongoing communication, consultation and collaboration among the Committees and ad-hoc working groups
- Develop and monitor compliance with agreements between the BBCIC and its partners and vendors
- Work with the financial services provided by AMCP to oversee financial management, budget preparations and presentation of budget to the Planning Board and ultimately to the Board of Managing Directors for approval
- Serve as the primary point of contact for the BBCIC including serving as the official spokesperson and coordinating external communications.

1.6.5.2 Chief Science Officer

(Est. Aug 2015)

The Chief Science Officer (CSO) is responsible for the scientific objectives of the program. The CSO will work closely with the Planning Board and the Committees to maintain the research framework and ensure that research plans are defined and executed successfully. The CSO will also ensure that data requirements are prioritized, standard analysis approaches are agreed upon and solutions to data gaps are addressed to ensure the rigor and integrity of research.

1.6.6 BBCIC Distributed Research Network Coordinating Center

(Est. Aug 2015)

The research network coordinating center function will be contracted to an existing coordinating center, which will be recommended by the Planning Board and approved by the AMCP Board of Managing Directors. The Coordinating Center will:

- Serve as interim Chief Science Officer for the BBCIC
- Work with BBCIC staff to provide input on policies and the Research Plan
- Develop the Research Synopsis on behalf of the Science Committee
- Work with Research Teams to determine the approach to fulfill the program evidence generation priorities

- Coordinate Data Partner and Investigator activities
- Arrange for a multi-site IRB approval process
- Manage Data, query and analytic methods as directed by Protocol Research Teams and their approved Research Protocols
- Manage policies on security of data.
- Manages studies, including compliance with applicable regulatory and protocol requirements
- Coordinate Institutional Review Board (IRB) approvals (see Policy 2.2.1 Institutional Review Board Approval of Research Protocols).
- IT infrastructure management
- Hold contracts with all data partners
- Hold contracts with investigators (where investigator funding is required)
- Hold liability insurance for breach of data

1.6.7 Data Partners

(Est. Aug 2015)

The BBCIC will enlist data partners who currently work with the Coordinating Center. . Data partners will have demonstrated one or more of the following abilities before selection:

- Manage data in the selected common data model format
- Access to administrative and lab test results
- Perform source record validation (chart pulls)
- Access to electronic medical records
- Ability to link new patient level data sources as they become available
- Cost-effective data management and query operations

New data partners will be considered (e.g., registries), budget permitting, if they are able to substantially address protocol gaps (See Policy 2.4.3 Expansion of the Common Data Model).

1.6.8 Advisors

(Est. Aug 2015)

The BBCIC Consortium Director may from time-to-time hire paid advisors to support Planning Board and Committee work.

1.6.9 Federal Agency Liaisons

(Est. Aug 2015)

The BBCIC Consortium Director may, with approval from the Board of Managing Directors and Planning Board, seek to establish liaisons with U.S. Health and Human Services (HHS) federal agencies such as the Food and Drug Administration (FDA). Consideration of other liaisons should be based on advancement of active surveillance results and methods.

1.6.10 Organizational Liaisons

(Est. Aug 2015)

The BBCIC Consortium Director may, with approval from the Board of Managing Directors and Planning Board, seek to establish liaisons with health and health-related organizations to share information about biologics/biosimilars research questions/results and collaboration opportunities.

2 AMCP BBCIC POLICY AND PROCEDURES

2.1 BBCIC Antitrust Policy & Meeting Guidelines

2.1.1 Quorum and Voting

Roberts Rules of Order, as amended from time to time, shall be the BBCIC's parliamentary guide, and shall govern the conduct of meetings of the Board of Managers, the Planning Board, and BBCIC Committees.

A quorum is established when there is a majority of the Voting Members present. The action of a simple majority of Voting Members present at a meeting at which a quorum is present shall constitute the action of the Board or Committee, with the exception that a super-majority (60%) will be required for the following approvals:

- Annual Research Plan
- Safety and Effectiveness Research Protocols
- Descriptive Analysis Protocols

No proxy voting is allowed.

2.1.2 Antitrust Policy

(Est. Aug 2015)

All BBCIC staff member and Participants shall be presented with a copy and an orientation by the BBCIC Consortium Director or designee to the following:

1. It shall be the duty of every individual to monitor for matters having antitrust implications, and to intervene and cause to cease and desist any prohibited course of action or discussion no matter how trivial and inadvertent.
2. All meetings associated with BBCIC will follow a published agenda and conclude with appropriate comments. There will be no secret meetings.
3. When discussing any issue, pros and cons must be presented in a fair and balanced way in order that listeners may make their own judgments. All officers, committee persons, and Participants will avoid leading any person away from, or to, any product or service.
4. Individual Board of Managing Directors, Planning Board Participants, Committee Participants or any other BBCIC volunteer, contractor or vendor will not represent themselves as speaking on behalf of BBCIC unless cleared to do so by the BBCIC or the BBCIC Board of Managing Directors.

2.1.3 Antitrust Guidelines for ALL BBCIC Meetings

(Est. Aug 2015)

BBCIC meetings must be conducted in a manner that avoids the fact or appearance of conduct that may violate the antitrust laws. The BBCIC must assure that certain subject areas (noted below) are not discussed at BBCIC meetings and that no illegal agreements are reached or carried out through the organization. The below summarize the standards of conduct and legal restraints which must be observed at BBCIC meetings to protect against violations of the antitrust laws.

PROHIBITED SUBJECT AREAS: AVOIDING POTENTIAL ANTITRUST LIABILITY

Each BBCIC Participant has the responsibility to avoid raising improper subjects for discussion. BBCIC Participants are encouraged to familiarize themselves with their own company's or organization's guidelines and to abide by them.

Discussion of or activities and programs relating to the subjects set forth below are improper and should not be permitted. To discuss or engage in conduct on these topics at BBCIC meetings could lead to an understanding or agreement expressly made or implied which may subject the BBCIC and individual Participants to legal liability under the antitrust laws:

- Industry-wide or individual company prices (current or projected) or matters related to pricing such as costs, profits, contractual terms and conditions (e.g., discounts, credit terms), wages/salaries, market allocation, market shares/sales, clients/customers
- Encouraging boycotts, exclusions of products/services or "refusals to deal" with individuals, companies or governmental entities
- Subjects that could be viewed as fostering unfair practices involving advertising, standardization, certification or accreditation
- Limitations on individuals or organizations that would result in restricting their ability to engage in a business or business practice or inappropriately exclude them from participation in BBCIC activities
- An individual company's product or service offerings including design, characteristics or pricing information; specific sales, distribution, marketing and/or R & D plans; confidential or non-public product/service information or product/service development or commercialization strategies

Note: Do not discuss or exchange information on the subject areas described above at social gatherings or "rump" meetings incidental to BBCIC meetings, even in jest.

PERMISSIBLE SUBJECT AREAS

In general, discussion of or activities and programs relating to the following subjects are proper and permitted.

- BBCIC Research Protocols, data requirements, statistical and epidemiological methods, and analysis of results
- Reporting and exchanging information on general industry or professional developments, concerns and economic trends
- Describing advances/problems in relevant research and technology
- "Best practices" discussions: Providing general information to assist and identifying methods by which an individual or company can improve performance (efficiencies, profitability, management, etc.); however no agreements should be reached as to the use of a particular practice or to exclude a competitor from using a different practice

Note: A subject appropriate for discussion can be rendered inappropriate by an improper approach to it (e.g., a cover up to harass competitors or to reach an agreement through the use of a governmental process that would otherwise be unlawful).

2.2 Policy on the BBCIC Commitment to Protecting the Privacy of Patients

BBCIC Participants and Collaborators must observe all applicable federal and state patient privacy- and security-related laws and regulations.

If a potential for harm is discovered via the process of scientific discovery, clear standards and directives must exist to communicate information in a timely and effective manner that minimizes risk to all concerned. This communication, to be reviewed and approved by the Planning Board, can be to patients, stakeholders and most importantly regulatory bodies (e.g., the FDA). (See Policy 2.9.1 Confidentiality Policy.)

2.2.1 Institutional Review Board Approval of Research Protocols

(Est. Aug 2015)

The HHS Office of Human Research Protections (OHRP) 45 CFR Part 46, “Common Rule” applies to the activities that are included in the BBCIC. It is therefore necessary for the Coordinating Center to obtain approval from its centralized Institutional Review Board (IRB) or Collaborating Institutions to obtain approval from IRBs or Privacy Boards, or to obtain waivers of authorization under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), to participate in BBCIC activities (45 CFR §164.512(b)).

2.2.2 Individual Health Information

(Est. Aug 2015)

2.2.2 Individual Health Information

(Est. Aug 2015)

The BBCIC will follow the approach established for the FDA Sentinel Initiative that protects the privacy and security of individual health information. Data Partners will maintain physical and operational control over the data in their possession and execute analysis programs distributed by the BBCIC Coordinating Center behind their own firewalls. The output of these programs will be provided to the Coordinating Center in summary format. The Coordinating Center will aggregate Data Partner responses to queries and send results from the individual Data Partner level and aggregated across all Data Partners to the Research Team.

The BBCIC does not receive or possess personally identifiable information (PII), as defined by the Privacy Act of 1974 or Protected Health Information as defined by HIPAA in the conduct of its activities. The BBCIC will follow the approach established for the

FDA Sentinel Initiative that protects the privacy and security of individual health information. This approach is summarized below:

- Data Partners will maintain physical and operational control over the data in their possession. Data partners execute analysis programs behind their own firewalls. These programs are distributed to them by the BBCIC Coordinating Center. The output of these programs will be provided to the Coordinating Center in summary format, no patient level data is sent to the Coordinating Center. The Coordinating Center will aggregate all individual Data Partner query results for the research teams.
- To run analysis programs, data partners maintain Limited Data Sets that contain no direct personal identifiers. The Limited Data set does contain a Data Partner generated Patient ID that can be used by the Data Partner to link back to source records, when authorized for specific projects, in order to enhance the dataset available for research by adding additional data or to check source records to investigate a Finding of Interest.
- Direct patient identifiers may be used by Data Partners when necessary to gather additional clinical and demographic information or to link their data to data from other sources, as required by specific projects. Prior to sharing additional information with the Coordinating Center, direct patient identifiers must be stripped in accordance with HIPAA requirements and any subject authorizations, if any.
- Data Partners must not have actual knowledge that any information sent to the Coordinating Center could be used alone or in combination with other information to identify an individual who is the subject of the information.
- If the Coordinating Center inadvertently receives direct patient identifiers, it will return or destroy the data immediately.
- Individual health information may be shared by Data Partners with other data holders, such as hospitals and registries, as necessary (for example, to validate health exposures and outcomes of interest or report adverse events) in accordance with these policies and all applicable state and federal regulations (e.g., HIPAA).

2.2.3 Minimum Necessary Standard

(Est. Aug 2015)

Only the minimum amount of data necessary to respond to specific queries, as determined by the BBCIC Science Committee, or by the Coordinating Center or specific project workgroups on behalf of the BBCIC, will be requested by Collaborators.

2.2.4 Security

(Est. Aug 2015)

BBCIC data are managed in accordance with the national standards established by the HIPAA Security Rule. Data in the possession of the Coordinating Center are also

managed in accordance with the Federal Information Security Management Act of 2002 (FISMA). Administrative, physical, and technical safeguards are employed to ensure the confidentiality, integrity, and security of electronic health information (45 CFR Part 160 and Subparts A and C of Part 164; 44 U.S.C. § 3541, et seq).

2.3 Specially Protected Health Information

2.3.1 State Laws and Regulations

(Est. Aug 2015)

It is the responsibility of BBCIC Data Partners to determine whether state laws regulate the use and disclosure of health information for BBCIC purposes and to comply with any such laws. The Coordinating Center, with input from the BBCIC attorney, Science Committee and in consultation with Data Partners, may provide additional guidance to assist Data Partners in assessing whether state law applies to a particular BBCIC query and in determining how to comply. However, it is ultimately the responsibility of each Data Partner to assess and maintain compliance with relevant state laws and regulations.

2.3.2 Federal Laws and Regulations –Alcohol and Drug Abuse Treatment Data

(Est. Aug 2015)

Federal regulations contained in 42 CFR Part 2 address information held by federally-assisted alcohol or drug abuse treatment programs. These regulations protect information that identifies an individual as someone who has applied for or received substance abuse treatment. The Part 2 regulations do not apply to information that does not identify an individual. If Data Partners request medical record information from a federally-assisted substance abuse treatment program to confirm a drug safety finding of interest, the program will be required to obtain individual patient authorization to provide that information if it reveals that the patient received substance abuse treatment. The Data Partner must provide an affidavit to the Coordinating Center that this policy was followed.

2.4 Data Management and Access

(Est. Aug 2015)

The BBCIC Coordinating Center, Data Partners, and BBCIC Research Teams are each responsible for the stewardship of data in their possession.

2.4.1 Distributed Data Approach and Common Data Model

(Est. Aug 2015)

The BBCIC will utilize an existing distributed research network, that leverages FDA’s Mini-Sentinel distributed data approach in which BBCIC Data Partners maintain physical and operational control over their electronic health data in their existing environments (i.e., behind their respective firewalls). BBCIC Data Partners execute standardized data queries distributed by the Coordinating Center and then share the output of these queries, typically in summary form, with the Coordinating Center.

2.4.2 Common Data Model

(Est. Aug 2015)

The Common Data Model is a data structure that standardizes administrative and clinical information across Data Partners. Data Partners maintain or provide access to data in common data model format. The Common Data Model makes it possible to execute standardized programs developed by the Coordinating Center in collaboration with the Data Partners. The Common Data Model relies on existing standardized coding schema (e.g., ICD-9-CM, HCPCS/CPT, NDC and batch if available) to minimize the need for ontologic mapping and enable interoperability with appropriate evolving healthcare coding standards and is compatible with other common data models using the same data types. The Coordinating Center will facilitate active participation by the BBCIC Data Partners in the use of the Common Data Model. The Coordinating Center works closely with the Research Teams to ensure that participants of those Teams fully understand the characteristics of the data and that the Common Data Model is designed to meet their needs. Data Partners provide knowledge and expertise to ensure appropriate use and interpretation of data in the Common Data Model format.

2.4.3 Expansion of the Common Data Model

(Est. Aug 2015)

The Coordinating Center, in collaboration with BBCIC Science Committee, may work with Data Partners to incorporate other data sources into the Common Data Model. These additional data sources may represent “original source data” or “external source data”, as necessary.

New data partners will be considered (e.g., registries), budget permitting, if they are able to substantially address Protocol gaps. Access to other new data centers unaffiliated with the Coordinating Center that substantially address Protocol gaps could be achieved in 3

ways: adding the data to the DRN, linking to the data, or commissioning a Protocol directly through the new data center.

2.5 Data Repositories

2.5.1 Original Source Data

(Est. Aug 2015)

Data Partners possess several types of data acquired through their normal activities (referred to herein as “original source data”), including administrative claims data, outpatient and inpatient electronic health records (EHRs), demographic information, outpatient pharmacy dispensings, and registry data. Data Partners retain stewardship and possession of both original source data and data transformed into Common Data Model format. Data Partners manage and store the data in accordance with their own institutional policies.

2.5.2 Use of External Source Data

(Est. Aug 2015)

Data Partners may be asked to collect information from sources other than their own institution (referred to as “external source data”) for purposes such as identifying or confirming exposures or outcomes of interest. Data Partners must clearly differentiate external source data from the Data Partner’s original source data and Common Data Model- formatted data. Data Partners must limit access to external source data collected for BBCIC purposes to authorized individuals engaged in related BBCIC activities. Data transfer from external sources to Data Partners is done in keeping with customary standards of secure file sharing (e.g., encrypted Secure File Transfer Protocol).

2.5.3 Coordinating Center Data

(Est. Aug 2015)

Data Partners are not to share direct patient identifiers with the Coordinating Center and must adhere to the HIPAA minimum necessary standard (see Policy 2.2.2 Individual Health Information). Data are provided by Data Partners in summary (i.e., aggregate) form, unless there is a specific need for person-level information. Example: person-level information might include information (stripped of direct patient identifiers) regarding individuals who received specific vaccines on specific dates when such information is required to respond to a particular BBCIC query.

The Coordinating Center shares de-identified summary results with the BBCIC at the individual Data Partner level and aggregated across all Data Partners. Under most circumstances, Data Partners are not identified when information is provided to the BBCIC or project workgroups. Access to the non-summarized data (identifying a Data Partner and/or individual patient) is limited to authorized individuals within the Coordinating Center or others authorized by the Coordinating Center to act on its behalf, such as outside individuals participating in workgroups related to task orders.

2.5.4 Data Transfer

(Est. Aug 2015)

Data transfer between Data Partners and the Coordinating Center and between the Coordinating Center and the BBCIC is done by means of a secure web-based file sharing system. The Coordinating Center complies with standards established by the HIPAA and FISMA.

2.6 Data Use Limitations

Data Partners may use their own original source data transformed into Common Data Model format for other purposes, such as research, as long as they comply with applicable state and federal laws and regulations, including HIPAA and the Common Rule.

2.6.1 Authorization to Use External Source Data

(Est. Aug 2015)

In the conduct of BBCIC activities for BBCIC research, the Coordinating Center, including all its components, for data obtained outside their own institution, the Coordinating Center may use such data only as authorized by the external source and in keeping with all applicable data privacy regulations. Such data may not be reused, re-disclosed, altered, or sold for any purposes other than those defined in the base contracts and subsequent task order contracts without specific authorization from the external data source and the BBCIC.

Unauthorized use will be reported by the external data source, BBCIC staff or BBCIC Research Teams to the BBCIC, the BBCIC Science Committee and the Coordinating Center. The user will be allowed an opportunity to remedy the situation on terms that are satisfactory to the BBCIC Board of Managing Directors and those institutions whose data was used for the unauthorized purpose. State or Federal reporting requirements for data breach will also need to be met by the user. Failure to follow these policies and

procedures will result in exclusion of the user from future participation in BBCIC activities.

2.6.2 BBCIC Access to Data

(Est. Aug 2015)

The BBCIC obtains unlimited rights to access and to use all BBCIC data in the possession of the Coordinating Center and first generated in performance of the contract for BBCIC's research. In keeping with the Confidentiality sections of the Coordinating Center contract and Policy 2.9 (Confidentiality & Statement of Confidentiality), confidential proprietary data and information submitted by or pertaining to specific institutions or organizations will not be publicly disclosed without the written consent of the respective institutions, except to the extent required by law. Access to this data is governed by relevant laws and regulations.

2.7 Data Retention

2.7.1 Data Partners

(Est. Aug 2015)

Data Partners will retain original source data in Sentinel Common Data Model format used for BBCIC research for at least four years from the time that the project is deemed complete by the BBCIC unless instructed otherwise by the Coordinating Center at the direction of the BBCIC. The Coordinating Center will provide instruction to the Data Partners regarding retention requirements for all data activities, including exactly what data must be retained.

Data Partners will retain data obtained from external sources to meet the needs of specific projects, and data derived from these external sources, for no longer than four years after the project is deemed complete by the BBCIC unless instructed otherwise by the Coordinating Center at the direction of the BBCIC. External source data will be subsequently destroyed in accordance with standards set by the [National Institute of Standards \(NIST\)](#) in place at that time. The BBCIC, the Coordinating Center, and the Collaborating Institutions may review and revise this provision if it is determined that these data retention requirements do not adequately meet the scientific needs of BBCIC activities.

2.7.2 Coordinating Center Data

(Est. Aug 2015)

The Coordinating Center will keep data resulting from BBCIC Research, at both the individual Data Partner and aggregate levels, for at least four years from the time the project is deemed complete by the BBCIC unless instructed otherwise by the BBCIC.

The Coordinating Center will retain data obtained from external sources to meet the needs of specific projects, and data derived from these external sources, for no longer than seven years after the project is deemed complete by the BBCIC, unless instructed otherwise by the BBCIC.

2.8 BBCIC Commitment to Transparency

The AMCP BBCIC is committed to transparency in all aspects of its research and operations. The BBCIC will communicate in a variety of ways with the external scientific and medical community and with the public. The BBCIC will observe standard academic practices and regulatory requirements regarding its obligation to report research activities and findings.

2.8.1 Report of Research Findings

(Est. Aug 2015)

The BBCIC Research Team's Principal Investigator(s) and the Science Committee will oversee BBCIC Research Communications to ensure timely disclosure of results in peer-reviewed scientific or technical publications or presented at scientific conferences. The BBCIC will establish processes to ensure that BBCIC Research Protocol includes reporting (publication) and dissemination plans.

2.8.2 BBCIC Research Reports Transparency

(Est. Aug 2015)

All external communications regarding the BBCIC will be undertaken consistent with the BBCIC Policies covering Confidentiality, Antitrust, Intellectual Property and Conflict of Interest (see Policy 2.9, 2.1, 2.11, and 2.10, respectively). The BBCIC requires all BBCIC Research Reports to be communicated promptly in an appropriate scientific forum.

In addition, the conduct of these Research Reports will be governed by specific additional policies and procedures, as follows:

- The Research Team will register all BBCIC Research Protocols in ClinicalTrials.gov prior to initiating the study. Methodological and other projects will be registered at HSRProj

(http://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm). The Planning Board will consider future need for registrations in other registries such as the EMA Post Authorization Efficacy and Safety Studies (PAES and PASS).

- The PI is responsible for completing a Research Report within 3 months after the completion of research. Extensions may be requested of the Science Committee. A copy of the draft Research Report is to be provided to the BBCIC Science Committee at least 60 days prior to submission for publication or research symposia or media presentation for comment and suggestions. This review process is required for all BBCIC Research Reports, whether draft or final. The Consortium Director has discretionary authority to reduce the duration of the pre-submission notification period on a case-by-case basis.
- The BBCIC Science Committee may submit comments back to the authors within 20 days, but the authors are not obligated to accept or respond to these comments. BBCIC Participants, including the BBCIC Planning Board and Committees, may not prevent or restrict the release of BBCIC Research Reports. The Final Research Report will be submitted to the Science Committee by the PI at least 5 days before submitting for publication.
- No less than 30 days prior to the publication submission, meeting or media presentation, the PI will post to clinicaltrials.gov a standalone results table to support presentation of key findings. (Journal editors generally accept this as not constituting prior publication.)
- The BBCIC requires that BBCIC Research Reports be submitted for publication within 6 months after the completion of the Research Report. When published, the publication will be posted on the BBCIC.org site. If six months have elapsed after the publication submission and the publication does not give a publication date or a release, the BBCIC Science Committee may release such results at its discretion on the BBCIC.org site.
- The PI of a BBCIC Research Report must notify the Consortium Director and the BBCIC Science Committee when the approved manuscript or abstract is submitted, which journal or conference was selected and whether the manuscript or abstract/proposal was approved or rejected by the journal or conference organizers (e.g. a copy of paper and cover letter will suffice). Notice must also be given of proposed publication date, at least 30 days before the proposed date. Once published, a reprint or copy of the manuscript or abstract should be sent to the Consortium Director or other contact to whom s(he) delegates authority
- Where appropriate, the Research Team will report verified findings of interest to regulatory authorities (see Policy 2.14 [Safety-related Findings of Interest](#))
- All BBCIC Research Reports will appropriately reference the BBCIC and describe the use of any BBCIC resources in the creation of manuscripts. However, in recognition of the fact that the BBCIC does not exercise editorial control over scientific communications, all BBCIC Research Reports will also include a disclaimer stating that the communication represents only the opinions of the author(s) and not necessarily those of BBCIC or any BBCIC Participants.

- The BBCIC represents a collaboration of many different stakeholders in providing financial support and intellectual capital, and will represent personal intellectual contributions from many sources. BBCIC Research Reports will appropriately recognize the collaborative nature of the BBCIC in general and the relative contribution of ideas and discoveries from all relevant individuals. BBCIC Research Reports will therefore reflect the International Committee of Medical Journal Editors (ICMJE) practices and requirements pertaining to group authorship except in circumstances where there is broad agreement that a specific individual or individuals are entirely responsible for relevant intellectual contribution to and composition of the BBCIC Research Report.
- Where group authorship is appropriate, the initiator of a manuscript proposal generally assumes first authorship. If an order of authorship is appropriate, s(he) should first attempt to determine such order of authorship in collaboration with others in the writing or research group. The relevant BBCIC Committee will assist in resolving any conflicts or questions that occur with respect to appropriate identification of authorship. The lead author should elicit specific commitment for involvement in the manuscript from the co-authors, circulate drafts for co-author input and coordinate revisions. Selection of the journal for initial submission is the responsibility of the writing group.
- Disclosure of Payments to Healthcare Professionals. The BBCIC Consortium Director, will ensure that BBCIC Research Reports properly disclose payments to healthcare professionals and financial reporting requirements (see Policy 2.10 Conflict of Interest Policy & Compliance).
- The BBCIC Consortium Director and Chairperson of the BBCIC Planning Board must review and approve all BBCIC press releases pertaining to BBCIC Research Reports.

2.8.3 Press Releases and other Communication (not including Research Reports)

(Est. Aug 2015)

Aside from the BBCIC Consortium Director, BBCIC Chief Science Officer, and the Chairperson of the BBCIC Planning Board, no BBCIC Participant or Supplier, will be authorized to speak publicly on behalf of the BBCIC without the prior approval of the Consortium Director. FDA and other governmental authorities will not be authorized to speak on behalf of BBCIC. BBCIC will have no control over external communications such authorities may make about BBCIC or its activities, except with regard to information protected from public disclosure under applicable law, such as information submitted to FDA in an Investigational New Drug (IND) filing.

2.9 Confidentiality & Statement of Confidentiality

2.9.1 Confidentiality Policy

(Est. Aug 2015)

All Confidential Information (defined below) is privileged and strictly confidential. It is the policy of the BBCIC that all BBCIC Board of Managing Directors, BBCIC staff, all Participant Organizations on the BBCIC Planning Board, BBCIC Committees, BBCIC Working Groups, and all others serving in connection with the BBCIC (collectively, "Individuals") must maintain the confidentiality of all Confidential Information and only use such Confidential Information in connection with the BBCIC. As this policy refers to Participant Organizations, it is understood that to develop strong research, sharing of BBCIC information within the Participant Organization will occur. This Confidentiality Policy is not intended to prevent disclosure where disclosure is required by law.

Individuals must exercise good judgment and care at all times to avoid unauthorized or improper disclosures of Confidential Information. Conversations in public places should be limited to matters that do not pertain to Confidential Information or to other information of a sensitive or confidential nature. In addition, Individuals should be sensitive to the risk of inadvertent disclosure and should, for example, refrain from leaving Confidential Information on desks or otherwise in plain view where it could be seen by unauthorized persons.

The communication of confidential information to FDA or other government authorities, and to their employees and representatives, may result in the information becoming publicly disclosable by those authorities. Confidential information cannot be shared with such authorities or their employees or representatives without the approval of the Planning Board.

Each Individual must certify, in writing, that he or she will not disclose to or discuss Confidential Information with anyone, including any governmental organization who has not been officially designated to participate in the BBCIC, unless such disclosure is specifically authorized by the BBCIC Consortium Director in writing in advance (see Policy 2.9 Statement of Confidentiality). Where specific Confidential Information includes data or information provided by or relating to any Participant Organization or its business or product(s), such Participant Organization's written authorization must also be obtained before disclosure of any such information to any governmental agency or authority [or any other party who is not an Individual].

In the event that any individually identifiable health information is collected by Individuals, Individuals must comply with all applicable federal requirements governing the use of such information, including but not limited to the HIPAA.

For purposes of this Confidentiality Policy and the accompanying Statement of Confidentiality, “Confidential Information” means documents, associated materials and information provided by /to Individuals in connection with the BBCIC, materials prepared by reviewers in connection with the peer review process, and discussions and communications (whether written or oral) associated with the BBCIC; provided, however, that any of the foregoing that (i) can be demonstrated to have been in the public domain or publicly known at the time of disclosure to the Individual; (ii) can be demonstrated to have been in the possession of or that can be demonstrated to have been readily available to the Individual from another source prior to disclosure thereto in connection with his or her association with BBCIC; (iii) becomes part of the public domain or publicly known by publication or otherwise, not due to any unauthorized act by the Individual; (iv) can be demonstrated to have been independently developed or acquired by the Individual without reference to or reliance upon such Confidential Information; or (v) is required to be disclosed by law, shall not be deemed to be Confidential Information. When distributing information among Individuals, it is the responsibility of the Individual distributing the information to determine whether such information is its Confidential Information and to clearly label all Confidential Information as such. Failure to label should not neutralize rights nor excuse disclosure and misuse.

For purposes of this Confidentiality Policy and the accompanying Statement of Confidentiality, “Confidential Information” does not include published and final BBCIC Research Reports, published and final BBCIC Research Protocols, published and final BBCIC Research Symposia and published and final Media Presentations (see Policy 2.8.2 BBCIC Research Reports Transparency).

2.9.2 Annual Attestation of Confidentiality

(Est. Aug 2015)

Each Individual (as defined in Policy 2.4.1), must complete the following Statement of Confidentiality at the start of his/her term and annual each August.

Statement of Confidentiality

I, the undersigned, have read and understand the **Confidentiality Policy for the AMCP Biologics and Biosimilars Collective Intelligence Consortium** (the “BBCIC Confidentiality Policy”) and agree to comply with and be bound by it. I agree to treat as confidential all Confidential Information to which I am exposed or which is made available to me in connection with BBCIC activities, and I will not use such Confidential Information for my own benefit or profit. In addition, I will not share such Confidential Information with others beyond my organization unless specifically instructed or authorized to do so in writing by BBCIC and as applicable by the Participant Organization(s) to whom such information relates. I agree to destroy or return all Confidential Information in written form upon request.

I further agree to comply with all federal requirements, where applicable, governing the use of any individually identifiable health information, including but not limited to the Health Insurance Portability and Accountability Act of 1996.

I further understand that any breach of the BBCIC Confidentiality Policy could result in irreparable injury and damage to individuals involved in the process or the BBCIC, for which the individual and the BBCIC may have no adequate remedy at law, and that, upon such breach, the BBCC and the relevant individual may be entitled to seek injunctive relief in addition to any other remedy to which it may be entitled at law or in equity.

Name (Please Print)

Signature

Date

2.10 Conflict of Interest Policy & Compliance

2.10.1 BBCIC Conflict of Interest and Disclosure Policy

(Est. Aug 2015)

Disclosure of Personal Involvements and Other Matters Potentially Affecting Service on and Participation in the Activities of the Board of Managing Directors, BBCIC Planning Board, BBCIC Committees (BBCIC Boards and Committees), and all others serving in connection with the BBCIC (collectively, "Individuals")

Introduction

The BBCIC LLC accords special importance to the established policies and procedures for assuring the integrity and hence the confidence in the deliberations and decisions of its appointed Board of Managing Directors as well as the activities undertaken by other BBCIC governance groups. The BBCIC Board of Managing Directors recognizes that the credibility and acceptance of decisions and actions by the BBCIC Planning Board and Committees can be undermined by allegations of lack of objectivity, conflict of interest, or misconduct on the part of its governance groups.

If decisions and activities of the BBCIC Board of Managing Directors Planning Board and Committees are to be accepted, respected and effective, they must be and must be perceived to be:

- Free of any significant conflict of interest, and
- Not compromised by bias, and
- Untainted by allegations of professional misconduct.

This policy addresses the above issues by examining the question of potential sources of bias and conflict of interest in the activities of the BBCIC Board of Managing Directors and the BBCIC Planning Board and Committees and the question of participation by persons who are subject to formal investigations of allegations of professional misconduct in the activities of the BBCIC Planning Board and Committees.

Defining "Bias" and "Conflict of Interest"

Bias - The question of potential sources of "bias" ordinarily relates to views or positions taken that are largely intellectually motivated or that arise from the close identification or association of an individual with a particular point of view or the positions or perspectives of a particular group. Such potential sources of bias are not necessarily disqualifying. Indeed, it often is necessary, in order to ensure that the BBCIC Boards and Committees are fully competent, to have the BBCIC Boards and Committees comprised in such a way as to represent a balance of potentially biasing backgrounds or professional or organizational perspectives.

Conflict of Interest - It is essential, however, that the work of BBCIC Boards and Committees not be compromised by any significant conflict of interest, or in some circumstances the appearance of a significant conflict of interest, on the part of any Participant of the BBCIC Boards and Committees or anyone associated with the work of a Committee (e.g., volunteers, consultants, staff, etc.). For this purpose, the term "conflict of interest" means any financial or other interest which conflicts with the service of an individual because it (1) could impair the individual's objectivity or (2) could create an unfair competitive advantage for any person or organization. The existence of a significant conflict of interest ordinarily disqualifies an individual from service.

Potential bias and conflict of interest are considered in the selection process for Individuals of the BBCIC Boards and Committees. They are also considered thereafter with respect to specific deliberations, activities and decisions as the BBCIC Boards and Committees engage in the performance of their respective responsibilities.

Guidelines

The diversity and complexity of the BBCIC's work make it difficult to establish complete, all-encompassing rules that will anticipate and address every possible situation involving bias or conflict of interest. The following guidelines addressing commonly occurring situations are provided as an aid to defining and identifying possible bias or conflict of interest in connection with the BBCIC staff and BBCIC Boards and Committees as well as other functions and activities of the BBCIC.

Individual Economic Impact - Actions taken by the BBCIC may sometimes result in an economic benefit or loss to particular individuals or entities. In those instances where the BBCIC Boards or Committee participants are employed by or connected with the entity that may be directly or indirectly affected economically and there is the potential of an indirect economic impact on the individual or on others with whom the individual is associated or related (including the entity), this would normally constitute a possible source of bias. In these circumstances the existence of possible bias would not ordinarily disqualify an individual from service but would be a factor to be taken into account.

But where the potential economic effect on the BBCIC Boards and Committees participants or on others with whom the individual is associated or related is substantially more direct and immediate, there may be a conflict of interest. An individual should not participate in a BBCIC deliberation, decision or activity (including policy recommendations or other similar advice) in which there is a significant possibility that such deliberation, decision or activity would have a direct and substantial impact on the individual, on others with whom the individual is closely associated (including the entity), or on any person with whom the individual has a close personal relationship, e.g. spouse, child, parent, etc. In addition, an individual should not participate in a BBCIC deliberation; decision or activity where an independent observer could reasonably conclude that the individual's objectivity could be compromised because of its potential economic impact. (There may be cases where the Boards or Committees may specifically

want this individual's input into some or all of the discussion, but would require that the individual recues himself/herself from the vote or decision.)

Proprietary Information - BBCIC Boards and Committees participants employed by or associated with a particular group should not be given access to proprietary information (e.g., trade secrets, confidential financial information, etc.) of a competitor or potential competitor unless appropriate safeguards have been established that reasonably protect the interests of all parties. Otherwise, such access may create an unfair competitive advantage, as well as possible legal liability for improper disclosure or use. In situations involving access to proprietary information, the matter should be referred to the BBCIC Board of Managing Directors and Consortium Director for guidance.

Public Statements and Positions - A BBCIC Boards and Committees participants may have become committed to a fixed position on a particular issue through public statements, through publications, through close identification with the positions or perspectives of a particular group, or through other personal or professional activities. This would ordinarily constitute a potential source of bias. In extreme situations -- e.g., where the individual is an officer of another organization that espouses the same position on the issue -- the situation may constitute a conflict of interest. In those situations, the matter should be referred to the President of the BBCIC Board of Managing Directors or Consortium Director for guidance.

Designing or Implementing Procurements - The BBCIC may from time to time make arrangement for the procurement of services or goods. To avoid possible conflicts of interest, any BBCIC Board or Committee participant who is employed in any capacity by, or who has a financial interest in or other economic relationship with, any organization that may seek an award under such a procurement -- as well as any individual who may seek such an award directly on his or her own behalf -- may participate in discussion and decision regarding such procurement only after the following requirements have been met: (1) the BBCIC Board of Managing Directors or Consortium Director must be informed of such circumstances, and (2) the individual or organization must be advised that, in order to avoid creating an unfair competitive advantage, the individual's participation may cause the procurement group to limit the participation of the individual and/or the eligibility of the individual or organization to seek an award. The individual involved should recuse himself/herself from the decision-making process.

Access to BBCIC Information - The opportunity to have access to sensitive BBCIC information during the course of volunteer activities at the BBCIC, may confer an unfair competitive advantage if abused or misused. A BBCIC Board or Committee participant should not participate in any activity involving sensitive BBCIC information if the individual intends to use, or uses, such information for their own direct and substantial economic benefit. The same rule applies if the individual intends to disclose, or discloses, such information to other individuals or to organizations in such a manner that a direct and substantial economic benefit may be conferred on such individuals or organizations.

The restrictions described above do not apply to information once it has entered the public domain. In specified situations (e.g., confidential financial, strategic and proprietary information), special limitations on access to and use of BBCIC information will be required.

Reviewing One's Own Work - Where a publication or work product of a BBCIC Board or Committee Individual is reviewed as part of the general activities of the BBCIC Board or Committee on which the Individual serves, the participation of the BBCIC Board or Committee Individual in that activity would not ordinarily constitute a source of bias or conflict of interest. However, an individual should not participate in an activity of a BBCIC Board or Committee when a critical review and evaluation of the individual's own work or that of his or her immediate employer is the central purpose of the activity, but such BBCIC Board or Committee Individual may provide relevant information to the Board or Committee.

The guidelines set forth above are intended to address common situations and to convey a sense of the manner in which situations not specifically addressed above will be handled. Any other situation involving "bias" or "conflict of interest," as those terms are generally defined above, is also subject to this policy.

Procedures for Addressing Possible Bias and Conflict of Interest

The BBCIC follows a procedure that seeks to (1) guard against conflict of interest and unreasonable bias, (2) maximize the credibility of its work, (3) identify situations where an individual's service in a particular capacity would be inappropriate, and (4) provide the BBCIC with timely information that permits it to defend it and its credibility and reputation against allegations of bias or conflict of interest.

The request for disclosure of information relating to possible bias and conflict of interest is not intended to challenge the personal integrity of any individual. It is designed to elicit only such information as is relevant and merits disclosure in light of the bias and conflict of interest policy set forth above. The responsibility for determining what information must be reported rests in the first instance with the individual; in reliance upon the individual's own sense of integrity and good judgment.

The individuals serving on the **BBCIC Board of Managing Directors and Planning Board and its Committees** are required upon their selection and then annually to complete a Statement of Disclosure Form listing relevant relationships, interests, and positions taken that may constitute a potential source of bias or conflict of interest within the meaning of this policy. The Forms are to be submitted to the BBCIC's Consortium Director and will be considered by the BBCIC as confidential, except that (1) they will be distributed for review by the BBCIC **Board of Managing Directors**. The review will take place annually at the first meeting of each fiscal year so that the BBCIC **Board of**

Managing Directors may discuss the general questions of bias and conflict of interest, and the relevant circumstances of individuals serving on that specific governance group; (2) they may be released, on a privileged basis, if an Individual of the specific Board so requests when there is a potential question of bias or conflict of interest regarding a specific matter before the BBCIC Board of Managing Directors or Planning Board and if the President of the BBCIC Board of Managing Directors and the Consortium Director concur, (3) an individual's Form may be released with the approval of that individual who completed the Form, and (4) they may be released when such release is required by law.

If in the course of the BBCIC Board of Managing Directors and Planning Board and its Committees consideration of a matter, questions arise regarding the existence on the part of an Individual of bias and/or conflict of interest, the affected Individual may recuse himself/herself from the discussion, or, the individual serving as Chair may direct that the affected Board Individual be excused from that portion of the meeting during which the issue is being addressed. If the affected Individual is the Chair, s (he) may recuse himself/herself from that portion of the meeting during which the issue is being treated, or, the Board, based upon a positive vote on the part of a majority of the Board Individuals present, excluding the individual serving as chair, may direct that the individual serving as chair be excused from that portion of the meeting.

If previously unknown relationships, interests and positions revealed by the Forms or through Board discussions raise questions, the matter should be brought President of the Board of Managing Directors or the Consortium Director who will take them up with the individual involved. If questions persist, the final decision regarding a particular individual's service with respect to a matter under consideration by the Board rests with the President of the BBCIC Board of Managing Directors or the Consortium Director.

Procedures for Committee and Working Group Individuals

Individuals appointed to Committees are required to become familiar with the BBCIC Governance Manual. Committee Participants should make known to the committee chair or the BBCIC's Consortium Director any relevant connections and interests and any relevant positions taken that may constitute potential sources of bias or conflict of interest within the meaning of this policy in light of the tasks to be undertaken by the Committee or Work Group.

Each BBCIC Committee is required at their initial meeting and annually thereafter to review the BBCIC's policy on conflict of interest, and the relevant relationships, interests and positions taken by an individual Committee member that may constitute a potential source of bias or conflict of interest; Committee members should be asked if they have any conflicts of interest to report.

If in the course of the Committee's consideration of a matter, questions arise regarding the existence on the part of an Individual of the Committee of bias and/or conflict of

interest, the affected Committee Individual may recuse himself/herself from the discussion, or, the Committee Chair may direct that the affected Individual be excused from that portion of the meeting during which the issue is being addressed. If the affected Committee Individual is the Chair, the Chair may recuse himself/herself from that portion of the meeting during which the issue is being treated, or, the Vice Chair (or designee), acting with a positive vote on the part of a majority of the remaining Committee Individuals, may direct the Chair to be excused from that portion of the meeting.

If previously unknown relationships, interests and positions be revealed through Committee discussions that raise questions, the Committee chair will take them up with the individual involved. If questions persist, the final decision regarding a particular individual's service with respect to a matter under consideration by the Committee rests with the President of the BBCIC Board of Managing Directors.

Procedure for Addressing Allegations of Professional Misconduct

Allegations of professional misconduct may also undermine the credibility and acceptance of decisions and actions by the BBCIC Boards and Committees. In the event that an individual serving on a Board or a Committee is notified by his or her employer or by a federal or state regulatory agency that he or she is the subject of a formal investigation for professional misconduct, the individual is required to inform the BBCIC Consortium Director, or if the BBCIC is notified through other means that a formal investigation for professional misconduct is being conducted, the BBCIC Consortium Director, who, in consultation with the affected Individual and others as appropriate will determine if the allegations raise concerns about the ability of the individual to effectively perform the function of the position held within the BBCIC. Should the Consortium Director in consultation with the Board conclude that continued service would jeopardize the BBCIC, pending final resolution of the formal investigation for professional misconduct the Individual may be asked to recuse himself/herself from specific issue discussions, resign or be removed by the Board. If the individual is determined to have not engaged in professional misconduct, he or she will be asked to resume his or her position of Board or Committee service.

Information related to alleged professional misconduct will be considered by the BBCIC as confidential. Access to such information within the BBCIC will be restricted to those individuals who are required to be informed by virtue of their official responsibilities. Such information will be disclosed outside the BBCIC only with the approval of the affected individual, or as required by applicable government regulations or as otherwise required by law.

2.10.2 BBCIC Conflict of Interest Statement of Disclosure

(Est. Aug 2015)

The BBCIC requires that each participant of its Board of Managing Directors, Planning Board, and Committees submit to the Consortium Director a disclosure statement annually and upon change of employment. This process discloses a participant’s relationship with other organizations that may lead to a potential conflict of interest. A conflict of interest would exist when a Board participant has a connection to another organization such that s(he) would have a direct or indirect interest in a transaction with BBCIC, or his/her duty to remain loyal to an act at all times in the best interests of BBCIC and its Individuals would be hampered or compromised. Please list below the organization(s) with which you have a connection as that term is defined in this Statement, the nature of the connection and the number of years you have had the connection. (Attach a sheet of paper if additional listings are required.)

Statement

As a participant of the BBCIC Board of Managing Directors and the BBCIC Planning Board and its Committee, I duly disclose to the Biologics and Biosimilars Collective Intelligence Consortium, a listing of organizations that may lead to potential conflicts of interest with the interests of BBCIC and its participants. This is required of me under the *BBCIC Conflict of Interest Policy* as a means to identify potential conflicts of interest during my tenure as a participant on the:

- BBCIC Board of Managing Directors
- BBCIC Planning Board
- BBCIC Science Committee
- BBCIC Communications Committee

Organization	# of Years	Connection

I understand this document is confidential and may only be reviewed by the BBCIC's Board of Managing Directors.

Name (Signature)	Date	Participation Year
Name (Please Print Below)		

Please submit, in confidence, to Consortium Director, AMCP BBCIC, 100 North Pitt Street, Suite 400, Alexandria, VA 22314.

2.10.3 BBCIC Conflict of Interest Policy for Government Employees

(Est. Aug 2015)

The BBCIC Board of Managing Directors may determine, in its sole discretion, that the BBCIC Conflict of Interest Policy does not apply to an individual who is a government employee if (i) the individual is subject to other conflict of interest restrictions under applicable federal regulations or policies, and (ii) in the judgment of the BBCIC Board of Managing Directors, such other regulations or policies are adequate to address potential conflicts of interest that may arise in connection with the individual's role.

2.11 BBCIC Intellectual Property

(Est. Aug 2015)

Participants shall not contribute or disclose to BBCIC or any contractor (i) any proprietary trade secret or (ii) property that is covered by patents or patent applications.

Consistent with the mission of BBCIC, any end product, including reports, studies, and/or white papers, is intended to be published and shared publicly and that no individual or Participant Organization shall assert any claim, including ownership, in copyright or otherwise over or to any such work.

BBCIC Research Reports will appropriately recognize the collaborative nature of the BBCIC in general and the relative contribution of ideas and discoveries from all relevant individuals. BBCIC Research Reports will therefore reflect the International Committee of Medical Journal Editors (ICMJE) practices and requirements pertaining to group authorship except in circumstances where there is broad agreement that a specific individual or individuals are entirely responsible for relevant intellectual contribution to and composition of the BBCIC Research Report. All BBCIC Research Reports will

appropriately reference the BBCIC and describe the use of any BBCIC resources in the creation of manuscripts. However, in recognition of the fact that the BBCIC does not exercise editorial control over scientific communications, all BBCIC Research Reports will also include a disclaimer stating that the communication represents only the opinions of the author(s) and not necessarily those of BBCIC or any BBCIC Participants. In addition, The BBCIC Consortium Director and Chairperson of the BBCIC Planning Board must review and approve all BBCIC press releases pertaining to BBCIC Research Reports.

Treatment of Intellectual Property Created as a Result of the BBCIC

Certain types of intellectual property may be generated in the course of pursuing BBCIC objectives, including, but not limited to analysis methods for screening and evaluating observational data, processes for integrating and interpreting screening and evaluation results, and white papers and other materials intended for publication. Ownership of such types of intellectual property shall be governed by the Table 1 “Intellectual Property (IP) Generated by the BBCIC Project.”

Table 1. Intellectual Property (IP) Generated by the BBCIC Project

Intellectual Property	Creator	Ownership
Charter	BBCIC	BBCIC
Annual Research Plan	BBCIC	BBCIC
Research Topic Nomination	BBCIC	BBCIC
Research Synopsis	Harvard Pilgrim/ Research Team	BBCIC
Research Protocol	Research Team	BBCIC
Study Report	Research Team	BBCIC
Publications	Research Team	Authors
Software Tools	Harvard Pilgrim	Harvard Pilgrim
Common Data Model	Harvard Pilgrim	Harvard Pilgrim
Statistical Methods	Research Team	Authors
Data Partner Contracts	Harvard Pilgrim	Harvard Pilgrim
Coordinating Center Policy, Procedures and Policies	Harvard Pilgrim	Harvard Pilgrim
Distributed Databases	Data Partners	Data Partners
Distributed Research Network Processes (e.g. Data Management, Data Quality, Query Fulfillment, etc.)	Harvard Pilgrim	Harvard Pilgrim
Testing process and environment	Harvard Pilgrim	Harvard Pilgrim

To the extent any Intellectual Property not set forth in Table 1 is authorized, created, conceived, reduced to practice, or developed jointly by BBCIC and Participant, such Intellectual Property shall be owned jointly by BBCIC and its Participants. The foregoing shall only apply to the joint work (as a whole). Any rights in any contributed BBCIC information or materials shall remain solely the property of BBCIC and Participant shall have only a limited right and license to use such BBCIC information or materials only for the purposes of, in accordance with, and during the term of this

Agreement. BBCIC and Participant shall promptly disclose any such joint Intellectual Property to the other and each shall keep any information related thereto confidential in accordance with the confidentiality obligations herein:

- Each Participant may provide de-identified data and other information (“Data”) to BBCIC and/or one or more contractors as part of its participation in the BBCIC; Such Data shall not be used by BBCIC, AMCP or any individual for any purpose other than the purpose defined in this Agreement.
- During the term of this Agreement, Participants will provide to BBCIC a royalty-free, fully paid-up, non-exclusive, worldwide license to use the works, trademarks, and/or inventions which have been provided by Participant to BBCIC in the course of the Participant’s participation in the BBCIC solely to the extent reasonably necessary to accomplish the mission of BBCIC.
- During the term of this Agreement, BBCIC provides to its Participant a royalty-free, fully paid up, non-exclusive, worldwide license to use, reproduce, and display the Intellectual Property authored, created, conceived, reduced to practice or developed by the BBCIC pursuant to this Agreement for any purpose consistent with BBCIC’s mission.

Certain types of pre-existing data, know-how and intellectual property may be contributed by or acquired from a Participant in order to achieve the BBCIC’s objectives, including but not limited to:

- Methods or processes for extracting, structuring or normalizing large databases into a common framework and technical infrastructure for housing data and facilitating analyses
- Databases or other information technology assets
- Analysis methods for screening and evaluating observational data, as well as processes for integrating and interpreting screening and evaluation results

The following terms will govern the use of pre-existing data, know-how and intellectual property:

- Participants in the BBCIC will retain full ownership of pre-existing data, know-how and intellectual property they contribute to the BBCIC.
- Each Participant will grant to BBCIC and other Participants, as necessary, a limited, non-exclusive, royalty-free and remuneration-free license to use each Participant’s relevant pre-existing data and intellectual property only for research purposes and only in connection with the carrying out of the mission of the BBCIC.
- Neither the AMCP, BBCIC nor any BBCIC Participants will gain any ownership rights to pre-existing data, know-how and intellectual property of Participant or any other party solely as a result of Participant or parties’ participation in the BBCIC and those non-exclusive rights will cease at the termination of the BBCIC.

- Pre-existing data know-how and intellectual property contributed to the BBCIC may be governed by confidentiality and other specific agreement terms as necessary.
- In cases where goods and services are procured on commercial terms for the BBCIC from third-party contractors, the BBCIC will negotiate all terms governing existing intellectual property, and document these terms in the supplier contract.

To the maximum extent possible, and subject to the public health goal limitations imposed by the section below, any BBCIC invention (any subject matter and discovery patentable or otherwise protectable under Title 35 of the United States Code that is conceived or first reduced to practice in the conduct of the BBCIC) will be placed in the public domain and made freely available for use. For example, broad availability of analytical methods, tools, and best practices for screening and evaluating observational data that might arise from the BBCIC are likely to be considered useful to assure the public health and would be expected to follow this principle.

- If making a BBCIC invention freely available will not advance the public health, the BBCIC Board of Managing Directors, solely in its discretion, may agree to enable a means to ensure intellectual property protection. Such instances may include but are not limited to, the need to protect information technology know-how or other intellectual property that could be important to incentivize longer-term or larger scale information technology investments necessary to enable a nationwide observational outcome system.
- In the above circumstances, Participants agree that plans and terms will be negotiated between the inventing party(ies) and the BBCIC and will be subject to the approval of the BBCIC Board of Managing Directors to ensure that the public benefit is achieved. It is anticipated that such terms would include, at a minimum, a remuneration-free non-exclusive license to the BBCIC with the right to transfer or sublicense the license to another nonprofit entity that will further the use of observational data to strengthen the monitoring of medical product safety post-approval, if applicable, at the conclusion of BBCIC.
- In cases where goods and services are procured on commercial terms for the BBCIC from third-party suppliers, the BBCIC will negotiate all terms governing intellectual property created during the course of the contract. These terms will, at a minimum, include granting the BBCIC a remuneration-free non-exclusive license to use of the intellectual property with the right to transfer the license to another nonprofit entity that will further use of observational data to strengthen the monitoring of medical product safety post-approval, if applicable, at the conclusion of BBCIC.
- BBCIC Participants and contractees will not be forbidden by virtue of their participation in the BBCIC to challenge the validity or enforceability of patents or other intellectual property of other BBCIC Participants, grantees, and contractors, including patents or intellectual property arising from BBCIC activities.

- At the conclusion of the BBCIC, the BBCIC Board of Managing Directors will dispose of or transfer any intellectual property or data that the Coordinating Center acquires as a result of BBCIC according to Policy 2.7 Data Retention and the BBCIC Operating Agreement (see Policy 9 Winding Up and Distribution upon Dissolution).

2.12 BBCIC Participant Code of Conduct

The BBCIC Participant Code of Conduct promotes and support transparency and scientific independence throughout the research process of BBCIC studies. By applying the principles of transparency and scientific independence, the Code aims to strengthen the confidence of the general public, researchers and regulators in the integrity and value of BBCIC research.

The Code of Conduct sets out rules and principles for studies, primarily non-interventional observational studies.

The Code does not provide rules or guidance on methodological aspects or scientific standards to be used for specific studies or study types. Adherence to the principles of this Code of Conduct will increase trust of stakeholders that they have full information on which to base the assessment of the study findings.

The main principles of the Code of Conduct are scientific independence, declarations of interests, and transparency.

2.12.1 BBCIC Individuals Code of Conduct

(Est. Aug 2015)

Investigators and Individuals commit to adhere to these principles:

- The primary purpose of a study shall be to generate data of potential scientific or public health importance and not to promote or counter-promote the sale of a medicinal product;
- The design of the research shall not be aimed towards producing a pre-specified result;
- The results of a study shall always be published, preferably in a peer-reviewed journal, or made available for public scrutiny within an acceptable time frame, regardless of the (positive or negative) results and the statistical significance; the BBCIC Website should be used as a repository for all final research reports including those pending publication and those not published in a peer-reviewed

journal in the ways specified in the Research Protocol, and will reference the final publication; and

Scientific Independence

For all studies, whether (partially) financed from external sources or not, the following principles of scientific independence apply in addition to the general provisions above:

- The highest level of scientific independence is desirable from agreeing to the research plan through to protocol development, implementation of research, data analysis and publication of results;
- Remuneration for services provided shall only be granted at fair market value, as specified in the research contract and shall not depend on the study results;
- The Research Protocol must be designed to ensure scientifically valid and sound results are generated independently from any potential conflicting interest of the funder or the researcher.

Declaration of Interest

The research team members to be involved in the conduct of a study, namely the principal investigator, the data and study managers and the main statistician, as well as the future authors of the study report and any publications arising from the research shall declare existing direct and potential indirect interests of a commercial, financial or personal nature that might impact their impartiality in relation to the study.

See Policy 2.10 Conflict of Interest for additional information.

Transparency

The highest level of transparency on relevant information pertaining to the study should be ensured. This includes information on the Research Protocol and the publication of study findings. Access to this information should be provided as required in the Code to regulators, health care professionals and the scientific community, as well as patients and the general public as appropriate. As observational studies, BBCIC Safety and Effectiveness Research Protocols will be registered at Clinicaltrials.gov.

See Policy 2.8 Commitment to Transparency

2.13 BBCIC Policy on Research Activities and Approvals

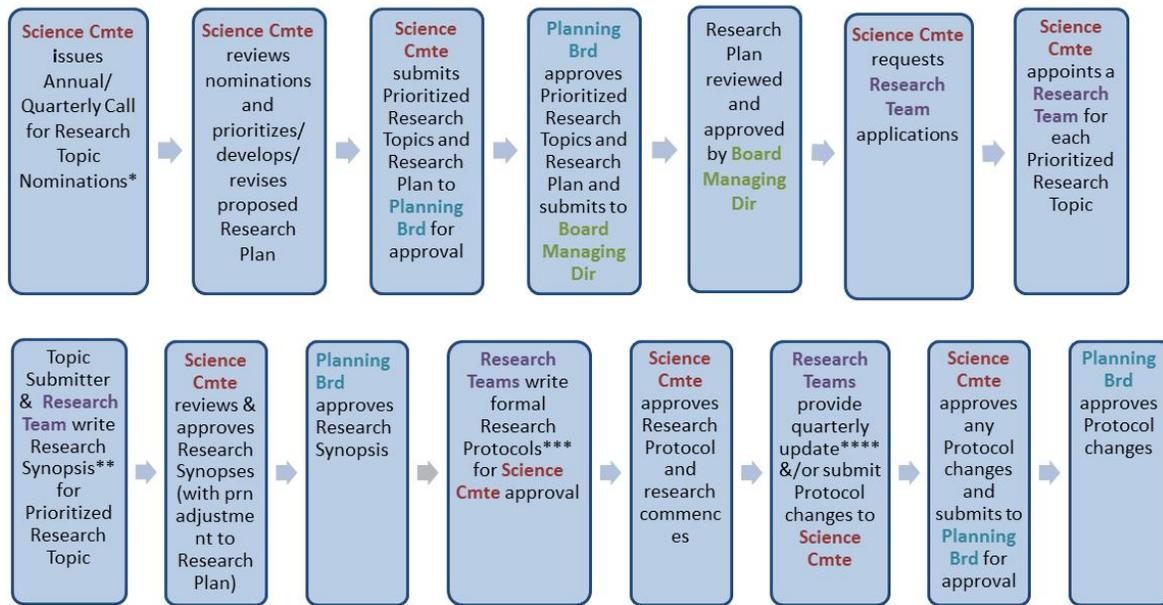
2.13.1 BBCIC Annual Research Plan

(Est. Aug 2015)

The BBCIC will establish a BBCIC Research Plan using the following process:

Figure 2. Process for Research Plan Development, Approvals and Conduct

BBCIC Policies and Procedures Research Activities and Approvals



*The Research Topic Request Form asks for a general description of the key questions to be addressed.

** For prioritized topics, the topic submitter and Coordinating Center develop a research synopsis. The synopsis provides more detail to the topic request including review of the available published literature; proposed populations, exposures and outcomes; and proposed statistical methods.

***Research Protocols define final methodology for the research project.

****Updates (and related Protocol changes) are required more frequently if Safety-Related Findings of Interest emerge (see Policy 2.14 BBCIC Policy on Safety-Related Findings of Interest)

The process will be based on the following principles:

To develop an Annual Research Plan, the Science Committee will issue an annual call for nominations to BBCIC Participants for research topics for the Annual Research Plan. Priority will be given to those topics that are related to the biosimilars most likely to be approved in the next three years. The nominations process will be repeated quarterly to allow for reconsideration of priorities. The schedule for the quarterly nominations and associated research plan adjustments shall be approved annually by the Planning Board.

The Science Committee will review and prioritize research topic nominations and develop (or revise) a proposed Research Plan. The proposed research plan (and quarterly updates) will be submitted to the Planning Board for approval. Planning Board approval of the Research Plan will be based on consistency with the list of biosimilars likely to be approved in the next 3 years, scientific import of the research question, and consistency with budget. Once approved by the Planning Board, the Research Plan and any quarterly updates will be submitted to the Board of Managing Directors for approval based on two

factors: 1) consistency with overall BBCIC goals 2) consistency with budget as outlined in the Annual Research Plan. Once approved by the Board of Managing Directors, the Annual Research Plan will be executed by the Science Committee and its Research Teams. Execution will begin by development of research project synopses. The synopses will be reviewed and approved by the Science Committee and then presented to the Planning Board for their review and approval. After approval of the synopses by the Planning Board, the Science Committee will appoint a research team that will develop the protocol for review and approval by the Science Committee. Any changes to Protocols will require the above review and approval process by the Science Committee and Planning Board. Changes to the Research Plan will require the above review and approval process by all 3 entities: Science Committee, Planning Board and Board of Managing Directors.

2.13.2 Categories of Research in the Annual Plan

(Est. Aug 2015)

BBCIC Safety and Effectiveness Research

BBCIC Research Teams will write formal Research Protocols and conduct studies to answer specific research questions. The research protocols to be included in the Annual Research Plan will be based on the biosimilars most likely to be approved in the coming year. For these biosimilars, the Science Committee will appoint Research Teams to develop Protocols with specific research questions for the identified biosimilars. A general Research Protocol template will include:

- Drug/Drug Class description
- Study Design and Analytical Tool Selection
- Cohort Identification
- Exposures
- Outcomes of Interest
- Pre-defined Covariates
- Analysis Plan
- Plan for Follow-Up of Findings of Interest
- Appendices or References

BBCIC Descriptive Analysis Protocols

The Science Committee will place priority on descriptive analyses that support the characterization of populations, including outcomes of interest, for biologics where biosimilar approval is expected within the next 2-3 years. These Protocols will provide information necessary to prepare for upcoming annual Safety and Effectiveness Research Protocols and to address data gaps.

2.14 BBCIC Policy on Safety-Related Findings of Interest

Definitions. A ‘finding of interest’ is defined as “*information that arises from an observational study, which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial.*” Any identification by the BBCIC Research Team of a potential safety-related finding of interest will be based on the Research Protocol which will explicitly pre-specify the clinical expert judgment, epidemiologic and statistical thresholds required to identify a safety-related finding.

2.14.1 Assessing the Validity of a Safety-Related Finding of Interest.

(Est. Aug 2015)

The Research Protocol will also include a plan for assessing findings of interest to ensure their validity. It will describe possible threats to validity, possible secondary analyses, and plan for quantitative bias analysis based on the threats to validity anticipated. The assessment plan follows a 3-step process:

- **Review.** Data and clinical validity, descriptive statistics, and analytic computer programs will be reviewed to ensure errors were not introduced that would affect the findings. If this does not rule out the finding of interest then:
- **Secondary Analyses.** Possible secondary analyses will be considered and run where appropriate. These may include adjusting the exposure period, consideration of additional confounders, consideration of additional comparator groups, and stratification of the cohort by disease/condition or other relevant population characteristics. If after this step, the finding of interest persists, then:
- **Tertiary Analysis.** Among other analyses, possible sources of quantitative bias will be considered in order to quantify the influence of systemic error on risk estimates.¹

2.14.2 Process for Informing the Science Committee of a Safety-Related Finding of Interest.

(Est. Aug 2015)

The Research Team will notify the BBCIC Science Committee within 3 days of its decision to begin an assessment of the potential safety-related finding of interest. The first notice will summarize the evidence supporting a potential finding of interest and the date for beginning the Review. Within 3 days of completing the Review, the Research

¹ McClure DL, Raebel MA, Yih WK et al. Mini-Sentinel methods: framework for assessment of positive results from signal refinement. *Pharmacoepidemiology and Drug Safety* 2014; 23(3–8). DOI: 10.1002/pds.3547

Team will notify the BBCIC Science Committee of its Review findings and, if applicable, notify that it is beginning Secondary Analyses. Within 3 days of completing the Secondary Analyses, the Research Team will notify the BBCIC Science Committee of its Secondary Analyses findings and, if applicable, notify that it is beginning a Tertiary Analyses. Within 10 days of completing the Tertiary Analyses, the Research Team shall interpret and report its findings to the Science Committee, along with recommendations for further study and action if needed. The Science Committee or Research Team may call a meeting of both to discuss an update and recommended best steps. The Science Committee may review and provide comments, but shall not have the authority to approve or deny the Research Team's planned next steps with the exception of instances where the protocol has been changed (i.e. introducing new data or methods.)

2.14.3 Informing licensed manufacturers of a Safety-Related Finding of Interest

(Est. Aug 2015)

The Science Committee shall, upon receipt of Tertiary Analyses reports from the Research Team of a supported finding of interest from the Research Team, contact the relevant manufacturer's pharmacovigilance team to report the BBCIC's findings. A finding of interest will be considered supported when the process of evaluating the data has suggested that the available documentation contains sufficient evidence suggesting the existence of a new potentially causal association or a new aspect of a known association. The findings will be in the form of aggregated, cohort-level summary tables, not patient-level data. The Science Committee may authorize additional work to assist the licensed manufacturer in meeting reporting obligations to the relevant regulatory authority. This may include recommending to the data partners that they assist the licensed manufacturer in obtaining patient level data.

Prior to the Tertiary Analyses report, BBCIC Participants on the Science Committee may share the notices provided by the Research Teams (see Policy 2.14.2. Process for Informing the Science Committee of a Safety-related Finding of Interest) with their pharmacovigilance teams.

2.15 Selection and Award of Grants or Contracts

2.15.1 Grantee/Contractor Selection and Award Principles

The BBCIC may acquire goods or services from a variety of partners and suppliers, including but not limited to health care data providers, systems integrators, technology providers, and consultants. These goods and services may be acquired through financial or in-kind contribution from the BBCIC Participants or other third parties, grants made or honoraria paid on behalf of the BBCIC, or commercial contracts with vendors to provide goods and services that support the BBCIC's mission. The selection and award of such

grants and/or contracts funded under the BBCIC, or the acceptance of financial or in-kind contributions on its behalf, will be conducted to ensure fairness, impartiality and inclusiveness, as well as conformity with all BBCIC policies.

2.15.2 Awarding of Contracts and Grants

(Est. Aug 2015)

- The BBCIC will solicit and award research grants and contracts by employing a structured, transparent selection process that will be available for review by the BBCIC Board of Managing Directors and the Planning Board. This process will be managed by the BBCIC Consortium Director.
- The selection process will employ objective, transparent criteria, will comply with all BBCIC conflict of interest, confidentiality, and antitrust policies, and will ensure that resulting agreements are intended to fulfil the mission and objectives of the BBCIC.
- BBCIC legal counsel will review and approve, where appropriate, all vendor or partner contracts and agreements to ensure they comply with the BBCIC conflict of interest, antitrust, and confidentiality policies and with applicable law and regulation.
- These policies do not preclude BBCIC from entering into non-competitive awards/supplements where warranted, subject to the prior review by BBCIC counsel, informing the Planning Board, and compliance otherwise with the policies and principles articulated herein.

2.15.3 Contract Authority

(Est. Aug 2015)

AMCP BBCIC Board of Managing Directors must approve all contracts and agreements with a stated contract value or fair market value in excess of \$100,000, or such other level as the Board of Managing Directors may from time to time determine.

(See related Policies 2.15.4 Contract Execution and 2.16.3 Check Signatories)

2.15.4 Contract Execution

(Est. Aug 2015)

Only the AMCP CEO, acting on behalf of the AMCP BBCIC Board of Managing Directors, is authorized to sign contracts, agreements or to engage any external firm in fee-for-service work for the AMCP BBCIC. A violation of this policy will result in AMCP BBCIC will hold at risk the individual(s) who bound AMCP BBCIC.

(See related Policy 2.16.3 Check Signatories)

2.16 Management Services

(Est. Aug 2015)

AMCP will provide management services (i.e., staffing, financial management, human resources, office space) to support the AMCP BBCIC through a Board of Managing Directors-approved service agreement.

2.16.1 AMCP and AMCP BBCIC Receipts and Disbursements Separation

(Est. Aug 2015)

AMCP and AMCP BBCIC maintain separate and distinct general ledgers; all receipts to and disbursements from AMCP and AMCP BBCIC must be clearly separated and defined by written documentation to serve as reference/backup. In the event that monies are collected by AMCP for AMCP BBCIC or vice-versa, monthly transfers will be made to the appropriate entity.

2.16.2 Budget

(Est. Aug 2015)

AMCP BBCIC's fiscal year runs from January 1 through December 31. Annually the Consortium Director, or appointed designee, shall oversee staff preparation of the operating and capital budgets so that the organization has a working budget in place by the start of the upcoming fiscal year. These fiscal and budget reports will be presented to the Planning Board and the Board of Managing Directors. The AMCP BBCIC Board of Managing Directors will review and approve the budget developed by the Planning Board.

2.16.3 Check Signatories

(Est. Aug 2015)

For disbursements up to \$5,000, one signature is sufficient – that of the AMCP CEO/AMCP BBCIC Managing Director or the Deputy to the AMCP CEO. Normally, the AMCP CEO will sign all checks with the Deputy to the AMCP CEO signing checks in the CEO's absence. For disbursements over \$5,000 up to \$100,000, the bonded amount, two signatures are required. They will be chosen from among the AMCP CEO/AMCP BBCIC Managing Director, Deputy to the CEO or the Vice President of Finance. For disbursements over the bonded amount, two (2) Officer's signatures are required which will be chosen from among the CEO, Treasurer or the President.

2.16.4 Contract Review by BBCIC Legal Counsel

BBCIC legal counsel will review and approve, where appropriate, all vendor or partner contracts and agreements to ensure they comply with the BBCIC conflict of interest, antitrust, and confidentiality policies and with applicable law and regulations.

2.16.5 Contract Authority Greater than \$100,000

(Est. Aug 2015)

AMCP BBCIC Board of Managing Directors must approve all contracts and agreements with vendors and partners with a stated contract value or fair market value in excess of \$100, 000.

2.16.6 Insurance

(Est. Aug 2015)

The AMCP CEO/AMCP BBCIC Managing Director (or designee), acting on behalf of the AMCP Board of Managing Directors will obtain sufficient insurance that will cover directors and officers (D&O) liability insurance, contractual agreements, liability and capital equipment. Insurance coverage limits are to be reviewed annually by the AMCP CEO/AMCP BBCIC Managing Director (or designee) to ensure adequate coverage.

2.16.7 Travel Reimbursement Eligibility for Non-staff

(Est. Aug 2015)

Members of the AMCP BBCIC Board of Managing Directors are reimbursed for actual reasonable allowable expenses related to travel to all Board meetings.

BBCIC Participants shall bear their own travel and accommodation expenses relating to attendance at and participation in BBCIC meetings and activities. AMCP BBCIC Board of Managing Directors, AMCP BBCIC Planning Board Participants and AMCP BBCIC Committee members will be reimbursed for travel when travelling on contractually-approved AMCP BBCIC business unrelated to Board/Committee meeting.

2.16.8 Endorsement Policy

(Est. Aug 2015)

In keeping with AMCP BBCIC's mission, the BBCIC shall not evaluate, endorse, or recommend any commercial or for-profits source of a product or service if such an activity could be construed as a marketing practice that furthers said product or service.

2.16.9 Whistleblower Policy

(Est. Aug 2015)

This Whistleblower Policy (“the Policy”) encourages employees to report to the AMCP Treasurer/AMCP BBCIC Managing Director or the AMCP BBCIC External Legal Counsel any known or suspected illegal activities or otherwise improper conduct that they believe may have been conducted by an employee, a member of the Board of Managing Directors or others associated with AMCP BBCIC in connection with regulatory compliance, finances or any other financial matters of AMCP BBCIC. This Policy prevents, by law, anyone in AMCP BBCIC from retaliating or punishing an employee for reporting to senior management, AMCP BBCIC officials, AMCP BBCIC External Legal Counsel or law enforcement conduct that the employee reasonably believes to be illegal or improper.

The Policy establishes procedures for:

- a. The receipt, retention, and treatment of complaints received by AMCP BBCIC regarding regulatory compliance, accounting, internal accounting controls, auditing or financial matters; and,
- b. The submission by employees or others, on a confidential and anonymous basis, of good faith concerns regarding questionable accounting or auditing or financial matters.

In accordance with the above, AMCP BBCIC adopts the following procedures:

1. Complaints filed with AMCP BBCIC Employees. AMCP BBCIC staff through the AMCP CEO/AMCP BBCIC Managing Director or the AMCP Vice President of Human Resources shall promptly forward to the AMCP Treasurer/AMCP BBCIC Managing Director any complaints that they have received from employees regarding regulatory compliance, financial statement disclosures, accounting, internal accounting or disclosure controls, auditing matters, disclosure violations, violations of AMCP BBCIC finance policies and procedures or other illegal or improper conduct.
2. Complaints filed with Outside Authorities (non-AMCP BBCIC employees). Any employee may choose to submit, on a confidential, anonymous basis if the employee so desires, any good faith concerns regarding any of the matters detailed in Paragraph 1 directly to the AMCP Treasurer/AMCP BBCIC Managing Director or the AMCP BBCIC External Legal Counsel. The AMCP Treasurer/AMCP BBCIC Managing Director and the AMCP BBCIC External Legal Counsel are independent individuals and are not AMCP BBCIC employees. All such concerns shall be set forth in writing and forwarded in a sealed envelope to the AMCP Treasurer/AMCP BBCIC Managing Director or the AMCP BBCIC External Legal Counsel. The envelope should be labeled with a legend such as: “To be opened by AMCP Treasurer/AMCP BBCIC Managing Director (or the AMCP BBCIC External Legal Counsel) only. This is being submitted pursuant to the AMCP BBCIC Whistleblower Policy”.

If an employee would like to discuss any matter with the AMCP Treasurer/AMCP BBCIC Managing Director or the AMCP BBCIC External Legal Counsel, the employee

should indicate this in the submission and include a telephone number (or other method of contact) at which he or she might be contacted if the AMCP Treasurer/AMCP BBCIC Managing Director or the AMCP BBCIC External Legal Counsel deems it appropriate.

Contact information for the AMCP Treasurer/AMCP BBCIC Managing Director and the AMCP BBCIC External Legal Counsel are as follows:

**AMCP Treasurer/
AMCP BBCIC Managing Director**
Treasurer - "Confidential"
AMCP BBCIC
100 North Pitt Street; Suite 400
Alexandria, VA 22314

AMCP External Legal Counsel
George E. Constantine III
Venable, LLP
575 7th Street, NW
Washington, DC 20004
202/344-8300

3. Following the receipt of any complaints submitted hereunder, the AMCP Treasurer and the AMCP External Legal Counsel shall consult with each other and thereafter the AMCP Finance Committee will investigate each matter so reported and in conjunction with appropriate staff at AMCP will take corrective and disciplinary actions, if appropriate, which may include, alone or in combination, a warning or letter of reprimand, demotion, loss of compensation, suspension without pay, or termination of employment. The investigation shall be led by the Treasurer on behalf of the AMCP Finance Committee. AMCP Officers, Directors, employees and agents who may be implicated in such investigation shall not participate in said investigation or disciplinary proceeding, except to present information directly to the AMCP Finance Committee on his or her behalf.
4. The Finance Committee may enlist, in addition to consulting with AMCP External Legal Counsel, other AMCP Board members, employees of AMCP and/or outside accounting or other advisors, as appropriate, to help conduct any investigation of complaints. In conducting any investigation, the Finance Committee shall use reasonable efforts to protect the confidentiality and anonymity of the reporting employee.
5. AMCP does not permit retaliation of any kind against employees for complaints submitted hereunder that are made in good faith. Additionally, no employee shall be adversely affected because the employee refuses to carry out a directive, which, in fact, constitutes corporate fraud, or is a violation of state or federal law, or violates any financial policies contained in the AMCP Operational Policies and Procedures Manual.
6. The Finance Committee shall retain as part of its records any such complaints or concerns for a period of no less than seven (7) years.

For additional information, please contact the AMCP BBCIC External Legal Counsel

2.16.10 Document Retention Policy and Schedule

(Est. Aug 2015)

Except as defined for research data (see Policy 2.7 Data Retention), the AMCP BBCIC adopts the AMCP Document Retention Policy and Schedule as outlined in the AMCP Operational Policies & Procedures Manual.

2.16.11 Use of AMCP BBCIC Name

(Est. Aug 2015)

Use of the AMCP BBCIC Name by external parties must be authorized by the AMCP BBCIC Consortium Director.

2.16.12 Use of AMCP BBCIC Service Mark

(Est. Aug 2015)

AMCP BBCIC's logo is a (soon-to-be registered) service mark of the AMCP BBCIC. It is registered to identify and protect programs and services of AMCP BBCIC so they can be distinguished from others. The right of AMCP BBCIC to use its service mark is incontestable and serves notice that its use is a claim of ownership over programs and services. Entities, both external and internal, that request the use of the service mark shall submit their request in writing to the AMCP BBCIC Consortium Director, or designee, for review and approval by the AMCP BBCIC Board of Managing Directors. All such requests shall be measured against existing policies, goals and governing values. Use of the service mark shall not imply any warranty.

2.16.13 AMCP BBCIC Service Mark on Publications

(Est. Aug 2015)

The AMCP BBCIC (soon to be registered) logo service mark must be printed on the front cover of all brochures, publications and printed materials distributed by AMCP BBCIC.