aHUS Registry Scientific Advisory Board (SAB) Charter

Alexion Pharmaceuticals, Inc.

Protocol Number M11-001 (aHUS Registry)
AN OBSERVATIONAL, NON-INTERVENTIONAL, MULTI-CENTER, MULTI-NATIONAL STUDY OF PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME (AHUS)

Version: 4.0
Date: 18 October 2022

aHUS Registry
Scientific Advisory Board Charter

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1 Objectives

The Scientific Advisory Board (SAB) is a collaborative scientific board and advocacy group for the aHUS Registry (Alexion Protocol number M11-001), an international, observational study collecting safety, effectiveness, and quality of life data on patients with aHUS. Alexion Pharmaceuticals, Inc. ("Alexion") is the sponsor of the Registry. Management of the Registry and participating sites is the responsibility of Alexion. The aHUS Registry aims to improve the understanding of aHUS by observing patients over time and analyzing the natural history of the disease, treatments utilized and outcomes.

The purpose of the SAB is to:

- Advise the Alexion aHUS Registry Leadership Team on appropriate strategic direction,
- Identify and prioritize medical questions related to knowledge gaps in aHUS and advise on the parameters and analyses to address these questions, review collected data and provide clinical interpretation and analysis,
- Advise a decision framework for the review and approval of requests for consideration of analyses of data from the aHUS Registry,
- Help liaise with other important groups with an interest in aHUS (e.g., International Pediatric Nephrology Association [IPNA], International Society of Nephrology [ISN]).
- Participate and provide support, as appropriate, in the development of publications including congress submissions/presentations.

2 Members

Membership includes both external clinical experts and (1) Alexion medical personnel. In addition, Alexion personnel from a Registry Leadership Team (RLT) which includes medical, operations, epidemiology, data management, scientific communications and patient advocacy when required. The membership of the SAB for the aHUS Registry currently includes those listed below.

2.1 SAB Members

Name	Country	Institution
Franz Schaefer (Chair)	Germany	University Clinic Pediatric Nephrology
Gema Ariceta (Co-Chair)	Spain	Hospital Valle d'Hebron
Katerina Anokhina	Switzerland	Alexion Pharma
Gianluigi Ardissino	Italy	Fondazione IRCCS Cá Granda, Ospedale Maggiore Policlinico
David Cohen	USA	Columbia University

Margriet Eygenraam	Canada	Patient Advocate, aHUS Canada
Fadi Fakhouri	Switzerland	Centre Hospitalier Vaudius
Véronique Frémeaux-Bacchi	France	Hôpital Européen Georges Pompidou
Larry Greenbaum	USA	Emory University
Nicole Isbel	Australia	Princess Alexandra Hospital
Christoph Licht	Canada	The Hospital for Sick Children and University of Toronto
Eric Rondeau	France	Retired
Jeff Schmidt	USA	Patient Advocate, aHUS Alliance
Marie Ann Scully	UK	University College London Hospitals NHS Foundation Trust
Johan Vande Walle	Belgium	UZ Gent Dienst Nefrologie

2.2 Membership Guidelines

Each member of the SAB from the scientific community will have one or more of the following skills:

- Experience and recognized expertise in diagnosing and treating patients with aHUS.
- Peer-reviewed publications in the field of aHUS, including but not limited to diagnostics, genetics, clinical management and outcomes.
- Experience with the development or management of disease registries.

Membership will include Alexion representation and could include patient advocate(s) which is optional.

The term of membership is 2 years, and a member may serve more than one term. Prior to the end of their term, at the discretion of the Chair, Co-Chair and Registry Leadership Team, members may be invited to continue their membership for an additional term. However, members have the right to terminate their membership at any time by notifying the SAB Chair and/or Co-Chair as well as the Registry Leadership Team. It is requested that departing members commit to completion of ongoing projects where possible or agree to no longer be involved.

Membership may be terminated for failure to participate in two meetings consecutively (or for any other reason) at the discretion of the Chair and Co-Chair.

Within the terms noted membership turnover should be limited to 50% at any one time or to allow change by natural attrition.

As the aHUS Registry is a long-term commitment, it may be necessary to alter the membership of the SAB. A new SAB member can be proposed following either of two mechanisms at the discretion of the SAB itself:

- Replacement of a member who leaves the SAB.
- Addition to the SAB of a member from an unrepresented region/country where a significant number of patients have been enrolled in the aHUS Registry.

Any member of the SAB can recommend a potential candidate to the SAB Chair and/or Co-chair as well as the Registry Leadership Team. New members will be approved by common agreement between all members. The SAB Chair has the decisive vote if voting stands at 50:50.

All members of the SAB will elect a Chair and a Co-Chair amongst the aHUS Experts. Neither the patient advocacy nor Alexion representative can be elected as Chair and/or Co-Chair. The Chair and Co-Chair will keep their position for a term of two years, and he/she may serve up to two terms consecutively.

Elections of Chair and Co-Chair will take place via an electronic email or web-based voting mechanism. The term will start at the meeting where results are announced.

Prior to the end of the Chair or Co-Chair's term, the current Chair will make a request for nominations for any member who is eligible to be elected, ie, the Chair or Co-Chair who has served two consecutive terms is not eligible. All members will be allowed to make nominations/self-nominations by submission of name or names via email to the Alexion Registry Leadership Team.

Each nominee will be given the opportunity to accept or decline the nomination. All nominees who have accepted the nomination will be included in the balloting. A ballot will be sent to each member with the list of nominees for each position.

Each SAB member will have one vote. Elections are decided by majority vote provided a quorum of membership has participated; quorum requires two-thirds (2/3) of the entire membership. The SAB Chair has the decisive vote if voting stands at 50:50 for a position.

Topics requiring a vote will be specified in the meeting agenda. Voting can be done at a meeting or electronically.

Engagement of SAB members will be through a written agreement with Alexion containing such terms and conditions deemed appropriate by Alexion. Membership of external SAB members will only be effective upon Alexion's receipt of a fully executed agreement.

2.3 Ad hoc Advisors

Ad hoc advisors may be invited to participate in relevant SAB meetings and/or discussion to provide subject matter expertise that is necessary and may not be represented within the SAB membership (e.g., physical therapist, dentist, etc.).

In such instance, (a) all SAB members (including Alexion members) must agree if such invitation may be extended to an *ad hoc* advisor and the scope of such *ad hoc* advisor's role and (b) any applicable *ad hoc* advisor must enter into an agreement with Alexion setting forth the terms of such engagement. *Ad hoc* Advisors are not voting members.

2.4 Patient Advocacy Representative(s)

A patient advocacy representative or patient representative teams will be invited to the membership of the SAB with full membership roles and responsibilities. The invitation for membership will be the responsibility of the Chair and Co-chair of the SAB, who will closely liaise with the patient advocacy representative(s) during their membership term. The patient advocacy representative(s) will participate for a period of two years from the time they join their first meeting. The term of membership is 2 years, and a patient advocate representative(s) may serve more than one term. Prior to the end of their term, at the discretion of the Chair and Co-Chair of the SAB, patient advocacy representatives may be invited to continue their membership for an additional term. Patient advocacy representative(s) have the right to terminate their membership at any time by notifying the Chair, Co-Chair and Registry Leadership Team. It is requested that departing members commit to completion of ongoing projects where possible or agree to no longer be involved.

There will be one meeting overlap when a new patient advocacy representative(s) and the past patient advocacy representative(s) are both invited to participate.

He/she/they may participate in meetings under the following guidelines:

- Patient advocacy representatives will sign an agreement that details their roles and responsibilities, including participation in meetings, and logistical arrangements such as travel compensation.

3 Roles and Responsibilities

The SAB members will be responsible for the following activities associated with the aHUS Registry:

3.1 Scientific Advisory Support

- Providing scientific and medical advice to the RLT, including for example, protocol amendment, determination of critical core variables for data collection, prioritizing medical questions to address with data from the registry, providing guidance into the analyses and interpretation of data
- Advising the framework for country/regional data analyses requests
- To assess the scientific merit, feasibility, and priority of requests for new analyses
- Providing review of country/regional publications to understand alignment with global data analyses and/or identify important country/regional differences
- For each specific data analysis or publication project, a working group will be formed to provide medical oversight for the data analysis, interpretation and

publication (in each case, this group is referred to as the "Working Group"). Each Working Group shall consist of at least one SAB member and certain Alexion employees as appropriate. Additionally, country and/or regional sub-analyses may require a National Coordinator to be part of the applicable Working Group as well.

3.2 Data Analysis and Scientific Publication

- New global analysis concepts can originate from the RLT, SAB members, or from any physician, typically National Coordinators or Investigators at Registry sites. Analysis requests should be documented on a concept sheet. Requests are reviewed by the RLT and, if endorsed, forwarded to the SAB members for review, vote, and prioritization (if approved). The Registry Medical Lead informs the SAB chair and/or SAB co-Chair about requests that have been rejected by the RLT. To be approved the analysis must receive endorsement by a majority vote of the SAB members. If the concept sheet is approved and analysis is prioritized, a SAP is generated with pre-specified table shells. Timelines for analysis are provided and agreed upon once SAP and shells are finalized.
- Country specific analysis concepts based on standard reports (i.e., those that do not require a statistical analysis plan) can originate from an investigator participating in the Registry and be submitted for consideration directly to the RLT or via the National Coordinator. These preliminary concepts must describe the medical question being asked and define the analyses. The concept may be submitted by email for review by the RLT. Any scientific publication based on these analyses requires prior review by the RLT and will be subject to any applicable publication restrictions (e.g., Confidentiality Agreements, Clinical Study Agreements, Registry Study Agreements, etc.).
- For any report required by any health authority, Alexion will be solely and entirely responsible for conducting the data analyses and writing of such report, without involving the SAB. Such report may concern data from one single region or country or overall data. All scientific publications from such analyses are subject to the same governance
- For each specific data analysis or publication project, a working group will be formed to provide medical oversight for the data analysis, interpretation and publication related to such project (in each case, this group is referred to as the "Working Group"). Each Working Group shall consist of at least one SAB member (and a National Coordinator as appropriate) and any appropriate Alexion employees.
- Working Group members must make good efforts to attend Working Group calls or face to face meetings to refine project scope, provide input on analysis approach, review and interpret data, and provide timely review of publications. Timely publication depends on a disciplined approach, including effort to limit additional requests to those within scope of the final approved concept.
- Authorship of a Registry related publication will be determined consistent with GPP3 and ICMJE guidelines and the Alexion Publication Policy and Guidance Documents. Specifically, all authors must contribute to the study design and medical oversight of the Registry, or patient enrollment and data quality, or the design of a specific analysis concept, or data analysis plan and data

interpretation, and must contribute to the discussion and development, and timely review of the publication. The Working Group should identify a plan for the development and submission of the manuscript (the "Plan").

3.3 aHUS Registry Advocacy

SAB members shall cooperate in:

- Generating awareness and interest in the Registry within the SAB member's medical community
- Advising on how best to involve professional associations, support groups, etc., to participate in and contribute data to the Registry
- Encouraging and supporting enrollment of patients in the Registry

3.4 SAB Chairperson

The SAB Chairperson will have the following roles and responsibilities, in addition to those described above, Chair can be external or internal:

- Serving as primary contact with the RLT for all topics related to the SAB
- Defining each meeting agenda together with the Registry Medical Lead
- Leading each SAB meeting together with the Registry Medical Lead

3.5 SAB Co-Chairperson

The SAB Co-Chairperson will have the following additional specific roles and responsibilities, Co-Chair can be external or internal:

- Consulting with the Chair on major SAB decisions and responsibilities as needed
- Supporting the Chair in his/her role serving as the primary contact with Alexion Pharmaceuticals for all topics related to the SAB as needed
- Assisting the Chair with defining each meeting agenda together with Alexion Pharmaceuticals as needed
- Leading SAB meetings in the Chair's absence in conjunction with Alexion Pharmaceuticals

3.6 Patient Advocacy Representative(s) (as applicable)

The patient advocacy representative(s) will have the following responsibilities:

- Provide advice on aHUS Registry-related matters from the perspective of patients and/or patient advocacy organizations.
- Advise on analyses and scientific questions of interest to the patient community.
- Generate program awareness and interest within the patient community.
- Assist with involvement of patient support groups and patients.
- Provide information on the aHUS Registry to interested patients.
- Provide advice and support to patients participating in the study.
- Liaise with other patient advocacy groups to provide a broad patient perspective from multiple countries.

3.7 Registry Leadership Team

The Registry Leadership Team consists of representatives from Alexion's Global Clinical Operations, Epidemiology, Medical Affairs, GHEOR and Scientific Communications and will have the following roles and responsibilities:

- Provide medical expertise, analytical, and operational oversight of the aHUS Registry.
- Coordinate and lead SAB meetings.
- Develop SAB meeting materials including the agenda, meeting slides, and meeting summary.
- Reviewing, evaluating and prioritizing new analysis concepts for scientific merit, feasibility and tracking all analysis requests and related publications
- Reviewing publication proposals

4 Meetings

Face-to-face meetings, teleconferences, and informational sessions will be held on an as-needed basis as determined by the RLT. Up to two major meetings will take place per year with the objective of these meetings being alignment on strategy, operational improvements such as site management and data collection approaches, discussion of ongoing and planned data analyses, publications and also the need for protocol amendments. These meetings can be held face-to-face or virtually where required. SAB members agree to make every effort to attend all face-to face meetings, teleconferences, and informational sessions. Planned meetings will occur several months apart (for example in the Q1-Q2, then Q3-Q4).

If an SAB member fails to participate in 2 consecutive meetings, the SAB Chairperson and/or Co-Chairperson, or the Registry Medical Lead will contact the SAB member and discuss their future participation in the SAB.

Each meeting will be preceded by a written agenda sent to all SAB members at least 2 weeks prior to the meeting. Agendas will be prepared by the Registry Medical Lead in collaboration with the SAB Chairperson and/or Co-Chairperson. Topics for discussion identified by any member of the SAB or any participating physician should be sent to the Registry Medical Lead.

A written summary of each meeting will be sent to the SAB members within 2 weeks of the meeting.

4.1 Time and Honoraria

It is expected that SAB members' involvement will require approximately 20 to 40 hours per year (excluding travel). The SAB Chair and Co-Chair will likely expend approximately 40 hours excluding travel.

Financial conditions to compensate this will be specified in an agreement executed with each SAB member.

5 Operating Principles

SAB members agree to serve as independent contractors (to Alexion); nothing in this Charter shall be construed in any manner as an obligation or inducement for you to recommend that patients utilize Alexion's products or those of any organizations affiliated with Alexion.

6 Confidentiality and Nondisclosure

Details of Confidentiality and Nondisclosure are covered in signed Consulting Agreements.

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Charter read and acknowledged by:

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Franz Schaefer (Chair) **Date**

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Gema Ariceta (Co-Chair) **Date**

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Charter read and acknowledged by:

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Katerina Anokhina
Signer Name: Katerina Anokhina
Signing Reason: I approve this document
Signing Time: 19-Oct-2022 08:12:25 EDT
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Katerina Anokhina **Date**

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Gianluigi Ardissino
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Gianluigi Ardissino **Date**

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David Cohen **Date**

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Margriet Eygenraam
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Margriet Eygenraam **Date**

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Fadi Fakhouri
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Fadi Fakhouri **Date**

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Veronique Fremeaux-Bacchi
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Véronique Frémeaux-Bacchi **Date**

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Larry Greenbaum
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Larry Greenbaum **Date**

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Nicole Isbel
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Nicole Isbel **Date**

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Christoph Licht
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Christoph Licht **Date**

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Eric Rondeau
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Eric Rondeau **Date**

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Jeff Schmidt
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Jeff Schmidt **Date**

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DocuSigned by:
Marie Scully
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Marie Ann Scully **Date**

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DocuSigned by:
Johan Vande Walle
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Johan Vande Walle **Date**