

## **BYLAWS of the Registry of Adenomas of the Pituitary and related Disorders (RAPID)**

### **I. BACKGROUND**

#### **1. Rationale for a pituitary surgery patient outcomes registry (RAPID)**

Establishing a national/international pituitary surgical outcomes registry is central to improving patient care by facilitating quality improvement, research, and dissemination of best practices. In addition, it enables multi-center studies and fosters collaboration between programs for the benefit of patients. Patient registries have been essential to improving outcomes in other surgical fields, such as transplant medicine and cystic fibrosis. Previous experience suggests that initial resistance to participating in national registries by physicians and hospital administrators has been overcome as the standard of care and healthcare value have improved as a result of participating in these registries. If successful for pituitary surgery, the collaboration could be extended to other skull base pathologies such as chordoma, acoustic neuroma, esthesioneuroblastoma, etc. To our knowledge, there is no other existing comprehensive pituitary surgery multi-center outcomes registry. Therefore, the Registry of Adenomas of the Pituitary and related Disorders (**RAPID**) addresses an unmet need.

#### **2. Overview of the RAPID registry**

RAPID was developed by Dignity Health/CommonSpirit (the health system that includes the Barrow Neurological Institute (**BNI**) as part of the Barrow Clinical Outcomes Center (**BCOC**) of BNI in the spirit of collaboration to improve patient care. RAPID contains data elements important to studying pituitary surgery patient outcomes. (For example, in the pilot module designed to study acromegaly, RAPID aggregates information on patient medical history, symptoms, surgery technique, prior treatment, complications, pathology, follow-up, cost, and remission status.) RAPID also includes patient reported outcome measures (**PROMs**).

RAPID is administered by the Barrow Clinical Outcomes Center (BCOC) at the Barrow Neurological Institute (BNI) utilizing VisionTree's cloud-based, HIPAA compliant, patient outcomes platform. VisionTree has served as the database tool for numerous other multi-center studies and outcome registries. Dignity Health/CommonSpirit contracts with VisionTree to host RAPID.

Much like other outcomes registries, (e.g., American Spine Registry, Quality Outcomes Database [QOD]), each participating center will enter and have access to its own data. BCOC will conduct regular data audits and coordinate database maintenance with VisionTree. RAPID, while centered at BCOC, intends to grant all Participants equal say in the direction of RAPID and related studies.

### **3. Data Set**

RAPID will contain information on patient medical history, symptoms, surgery technique, prior treatment, complications, pathology type, follow-up, remission status, and cost. The dataset also includes patient PROMs (e.g., ACRO-QOL, SNOT-22, etc.). One of the goals of RAPID is to track long-term outcomes. Therefore, the data set includes fields for annual follow-up visits.

Like other multicenter surgical registries (e.g., American Spine Registry, QOD), each Participant enters its own data. BCOC will maintain the database environment, trouble shoot, update the registry as needed, aggregate the data, and provide routine data audits to ensure data integrity. Data entry will be a combination of manual entry, automated entry, and patient entry for quality-of-life measures. If a Participant wishes to pursue automated data entry for certain data elements, it will need to establish an interface between its medical record and VisionTree at the Participant's own expense.

### **4. Bylaws**

These Bylaws were initially adopted by the BCOC to provide structure and governance for the administration of RAPID. Each Participant will be required to abide by these Bylaws under a Participation Agreement that incorporates these Bylaws by reference. No Participation Agreement will include terms and conditions inconsistent with these Bylaws.

## **II. ADMINISTRATION OF RAPID**

### **1. Steering Committee**

#### **A. Overview**

A Steering Committee (**SC**) will be established by BCOC to coordinate overall activities of RAPID including reviewing research proposals, providing guidance on grant submissions, furthering development of the scope of RAPID as necessary, and administration of these Bylaws.

#### **B. Steering Committee Membership**

- i. Members of the initial SC will be investigators affiliated with BNI. These initial members may continue to serve on the Steering Committee as long as they are conducting related research.
- ii. Each Participant will be eligible to appoint one individual to the SC who is an Investigator on an approved Project to serve as a member of the SC. Membership of the SC Member will continue as long as an institution is a Participant. Participants will follow their own process for selecting their SC Member. Participants may change their SC Member on a yearly basis at their discretion upon written notice to the chairperson of the SC.
- iii. In addition to the SC Members appointed by a Participant, the SC may appoint individuals to serve as SC Members At-Large for one- year terms by a majority vote of the then serving SC Members. The number of SC Members At-Large will not constitute a majority of the SC Members.

iv. Individuals appointed to the SC under subsections ii. or iii, above, will be referred to as “SC Members” and will have voting rights on the SC.

v. As part of its oversight of RAPID, the SC will approve the annual budget, approve, and monitor expenditures of funds (or cause them to be approved and monitored), and cause to be conducted an annual audit of RAPID, including Participant fees, external contracts, grants, gifts, and other sources of income, and will audit and monitor RAPID to ensure data integrity, security and compliance with Participation Agreements, contracts, and applicable law.

vi. The SC may solicit suggestions regarding the direction of RAPID activities and related research proposals from individuals who are not part of the SC. However, these individuals will not be SC Members and will not be allowed to vote on actions of the SC including project approvals and amendments.

vii. SC members are required to attend at least 2/3 of the meetings of the SC in person, virtually, or by proxy approved by the SC chairperson.

viii. Motions by the Steering Committee will require majority voting. The Steering Committee chairperson will abstain from voting except in the event of a tie.

### **C. SC Officers**

i. Chairperson. The SC will elect a chairperson (**Chairperson.**) The Chairperson will oversee the general direction of RAPID and the operation of the SC including organization of SC meetings, strategic planning, leading SC members, and guiding the structure of RAPID.

ii. Secretary. A secretary will be elected by the SC (**Secretary.**) The Secretary will work with the administrative staff to maintain the RAPID Bylaws, develop policies and procedures, review and maintain meeting minutes, as well as any other work as determined by the SC.

iii. Treasurer. A treasurer will be elected by the SC (**Treasurer.**) The Treasurer will work with the administrative staff to review the RAPID budget, seek sources of funding, aid in grant submission, and review any contracts annually (e.g., VisionTree).

iv. Scientific Lead. A scientific lead will be elected by the SC to guide the current and planned scientific progress of RAPID objectives (**Scientific Lead.**) This will include organizing scientific meetings, following up with Study sites, acquiring resources as needed to facilitate group research, and guiding SC members on the Study submission and Publication processes described below. The Scientific Lead will be rotated among Participants to improve participation by all SC members.

v. Terms. The terms of the Chairperson, Secretary, and Treasurer will be two (2) years. The Scientific Lead will serve a one-year term.

## **D. Meetings**

SC Meetings will take place at least monthly to review the direction of RAPID, data submission, and other issues. Meetings can take place by phone, teleconference, or in person as determined by the Chairperson.

## **2. Bylaws - Amendment**

Updates and changes to RAPID bylaws may be made annually and will require a majority vote of the SC to implement.

## **III. PARTICIPANTS**

### **1. Becoming a Participant**

Investigators conducting or proposing to conduct research related to pituitary surgical outcomes that would benefit from access to RAPID (**Investigator**) may submit a proposal to the SC as provided below. When a proposal is approved by the SC each institution participating in a research project (**Study**) will become a Participant upon signature of a Participation Agreement and payment of applicable fees (**Participant.**)

Individuals interested in RAPID should contact Ildiko Torok, MD from the **Project Management Team** or the SC Chairperson (currently Andrew Little, MD) to indicate their interest in becoming a Participant. A start-up packet including a Participation Agreement and IRB templates will be provided.

## **IV. RESEARCH PROJECTS**

### **1. New Proposal submission**

#### **A. Content**

An Investigator or a lead Investigator on behalf of other Investigators in the case of multiple authors/contributors (**Lead Investigator**), may propose a Study to the SC for review by submitting a 2-3 page proposal to the SC describing the proposed Study including:

- Objectives (e.g., aims, hypothesis to be tested) Clearly define the Study questions (entry criteria, intervention, outcome, analysis) and research population
- Study design (inclusion/exclusion criteria, variables to be analyzed, primary outcomes, secondary outcomes, sample size and statistical plan)
- Methods (including what new analyses must be performed and what data may be needed for the Study)
- Procedures that must be followed to ensure the collection of valid and trustworthy data
- Statistical analysis plan (Plan for which variables are to be analyzed, and clinical context, a brief discussion of how different results will be interpreted and a detailed plan for the analysis and reporting of these data).
- Outline of the responsibilities of each member of the Study team
- Applicable regulatory requirements and available guidance
- Counsel from technical experts (clinical, statistical, database, developers, etc.) including those outside RAPID, when appropriate

## **B. Data and Discussion**

Lead Investigators from any Participant site may request a summary of available data and list of variables already in RAPID to evaluate potential news Study proposals. The data from RAPID will be provided for this purpose without protected health information as defined by the HIPAA Privacy Rule (**PHI**) or Participant identifiers. Study ideas can be informally discussed with other investigators or the SC members however a formal proposal and vote of the SC is required to proceed.

## **2. Application Submission Review**

### **A. Criteria**

The SC will review the proposed Study by considering the following criteria:

- Scientific merit
- Relevance to the mission of RAPID
- Feasibility both as a group and in terms of additional work for Study sites
- Originality
- Overlap with ongoing or previous projects
- Cost
- Equitable distribution of work across Study sites

### **B. Review Process**

i. SC members will concurrently review the Study proposal and provide an initial reply to the Lead Investigator within fourteen (14) business days after receipt. Proposals require approval by a simple majority of the reviewing SC members. Feedback may include constructive criticism as well as a decision to accept, revise, or reject a Study proposal. Responses from the SC that are not acceptance will include general reasons for rejection or revision. Revised proposals may be resubmitted to the SC within thirty (30) days after receipt of the initial reply from the SC.

ii. The SC may organize a Data and Safety Monitoring Board as needed for review of results from approved Studies. Quarterly review of data will be performed and discussed with the Investigators.

iii. The SC will work with Participants seeking to obtain grants on behalf of RAPID or supporting proposed Studies. Pre-submission review and approval by the SC of grants is required prior to completion or submission to a potential funder.

iv. The expectation for each Participant is to champion one specific Study at any given time, including organization of relevant variables, final data analysis, and manuscript drafting.

### **C. Study Proposal Approval**

i. If a Study is approved by the SC, the Lead Investigator is responsible for assuring that applicable IRB approval is obtained for all Participants in the Study, applying to the SC for the

required data, and making final arrangements for necessary supplies, services, equipment, or diagnostic testing.

ii. The Lead Investigator is responsible for developing a protocol to implement the Study **(Protocol)**, developing a reasonable timeline, and for the 1st draft of the manuscript describing the results, organizing revisions, and submission for publication as appropriate. The SC may assist with revision of Protocols, formalizing the Protocol, statistical analysis, data management plans, and database development.

iii. Protocols for Investigational New Drug **(IND)** and Investigational Device Exemption **(IDE)** clinical studies will be submitted by the Lead Investigator to the FDA for formal review as applicable. The Protocol may be sent informally to the FDA for preliminary review (pre-IND or pre-IDE) prior to an IND or IDE submission. The Protocol must be submitted for IRB approval after an applicable FDA review is complete. Certain Protocols must be submitted to other external and/or internal regulatory authorities, if required, for review before or concurrently with IRB submission.

iv. The Lead Investigator will distribute the final approved Protocol to all participating investigators. (It is recommended that the Lead Investigator submit the Protocol to their local IRB first, if single IRB **(sIRB)** is not being used. Once approval is obtained, the Lead Investigator's IRB, or sIRB, approval letter(s) will be forwarded to the Investigators to assist with local IRB.) The SC will maintain a copy of the IRB approval letter(s) from each Participant and place these documents in an IRB tracking system. Each Participant will maintain documentation of all their own IRB approvals and correspondence.

v. Participants will not implement a Protocol until cleared by the SC. Individual Participants will not revise the Protocol. Each Participant will retain approved Protocols and their attachments, subsequent revisions and associated correspondences with regulatory authorities, as well as any other documents required, and keep them filed in their Essential Documents binder  
([https://ichgcp.net/8-essential-documents-for-the-conduct-of-a-clinical-trial.](https://ichgcp.net/8-essential-documents-for-the-conduct-of-a-clinical-trial))

vi. Compliance with the approved Protocol is essential in ensuring that the subjects' rights and well-being are secured. Any deviation from the approved Protocol must be reported to the SC as described in the Protocol and related instructions.

vii. Approved Protocols will be assigned a protocol version number and effective date and a notification will be sent to each Investigator by the SC. Studies will be listed on the RAPID website.

#### **D. Site Onboarding Process**

Each Participant will sign a Participation Agreement and will appoint a site Investigator to direct the Study at the site including timely prospective data entry. Participants will undergo an onboarding process including discussion of data entry, project goals, and review of the Protocols. Participants will certify completion of the onboarding process including

demonstration of familiarity with Study procedures and designation of staff to conduct the Study prior to enrolling subjects. (RAPID leaves compliance with site policies and specific research framework to the discretion of the individual Participant's processes and requirements.

#### **E. Responsibility for Data Entry**

- i. After a Study is approved by the SC, database and data collection forms will be finalized in discussion between the Lead Investigator, the Participants sites, and the SC. The SC will test the data entry software and hold training sessions at the Participants' sites.
- ii. Participants are responsible for entering data into RAPID using VisionTree in accordance with the approved Study.
- iii. Each Participant will identify personnel responsible for data entry. Participant will enter their relevant data in a timely manner pursuant to the workflow established in a separate data plan for the Study. The number of hours required for data entry will vary depending on factors such as number of subjects and disease conditions. As further RAPID modules are developed, the time commitments are expected to increase.
- iv. Each Participant site will undergo a periodic audit of selected subjects to assess data integrity, consistency with the Study Protocol, and timeliness of data entry. Audits will be conducted by the SC or its designee. Untimely entry of data may jeopardize the accuracy of the collected data, defeating the purpose of a registry, and may limit a Participant's future involvement with RAPID.

#### **F. Obligations of Participants**

Each Participant is responsible for obtaining any consents, authorizations, or waivers as required by applicable law to enable use and disclosure of the data as described in an approved Study and these Bylaws and for maintaining any codes or other information necessary to comply with applicable conditions of consents, authorizations, or waivers. BCOC has developed template informed consent and IRB documents to aid Participants in obtaining appropriate approvals to participate in RAPID. These documents are included in the start-up packet. The SC is available to assist Participants in completing the IRB process.

#### **G. Secondary Analysis Studies**

Investigators may use data previously gathered for a different primary Study and deposited to RAPID to answer new questions. A similar proposal to main Studies is required to be submitted to the SC for approval of secondary analysis Studies.

#### **H. Protocol Amendment Review and Approval**

- i. Protocol amendments may be required during the course of an approved Study. The Lead Investigator will initiate Protocol amendments. Protocol amendments will describe any required changes to data collection systems and will be written in the same format as the

original Protocol, and highlight the new elements. Protocol changes should be discussed with the SC and major changes require approval of the SC.

- ii. Any revision to the original Protocol or subsequent version of the Protocol that substantially affects the scientific details of the Study, safety of the subjects and/or significantly affects the scope of the research must be submitted to all Participant sites for IRB or sIRB approval as applicable. The Lead Investigator will apply for and secure FDA or other regulatory approval as required. The SC will assist the Lead Investigator in this process.
- iii. The SC will amend the version number to reflect subsequent changes to the Protocol.
- iv. Changes to the protocol may not be implemented at Participant sites without approval of the Lead Investigator, site Investigators, the IRB, and the FDA as applicable.
- v. If changes to a Protocol result in necessary changes to informed consent, the Lead Investigator will make associated changes to the informed consent form and will instruct Participant sites to submit changes to their local IRBs or the sIRB. Protocol changes made to eliminate an immediate hazard to subjects may be implemented immediately, provided that the FDA and the IRB are notified as soon as possible as provided in applicable regulations.

#### **I. Trainee Involvement**

- i. Goals of trainee involvement include:
  - To complete novel, impactful Studies that will benefit the care of patients with pituitary lesions
  - To complete Studies with minimal cost, time, and resources.
  - To encourage and foster the development of promising trainees to be successful, independent clinical pituitary researchers.
- ii. Eligible trainees must meet all of the following criteria:
  - Be a resident, fellow, medical student, or graduate student
  - Have sufficient skill established or planned in advanced biostatistics to independently perform required analyses (with minimal Steering Committee supervision)
  - Have sufficient ability, knowledge, and dedicated time to learn the necessary skills quickly
  - Be directly supervised by a RAPID investigator
  - Have funding for their salary and the personal costs associated with the Study
- iii. Study proposals involving trainees will follow the Study proposal process above. In addition, the trainee and supervising RAPID Investigator must submit a trainee CV and letter of support from the supervising RAPID Investigator guaranteeing funding for the trainee & protected research time.



iv. In deciding the merits of the proposal, the SC will consider the qualifications of the trainee, with emphasis on an early track record of research productivity and independence, demonstrating great promise for developing into an independent investigator.

## **V. DATA AND PROJECT RESULTS**

### **1. Data ownership and Access**

#### **A. Generally**

- i. RAPID is owned by Dignity Health/CommonSpirit.
- ii. Participants acknowledge that the data provided to RAPID by Participant is owned by the submitting Participant. However, Participant agrees that the return of data to the submitting Participant is not feasible or required once it is integrated into RAPID or is distributed to third parties as permitted in these Bylaws and related Participation Agreement.

#### **B. Access to Participant Data**

- i. Each Participant can access their institution's RAPID data at any time with a request to the RAPID Project Management Team who will provide the requested data set. Data should be requested at least 2 weeks prior to the date that is needed.
- ii. Non-Participants may not access data from RAPID except in rare circumstances and only with SC approval.
- iii. If a non-Participant (including trainees) who is working with a Participant's Investigator would like to conduct a Study using RAPID data, permission must first be obtained via the proposal process provided above.

#### **C. Access to Other Data**

RAPID data other than that submitted by the requesting Participant can only be accessed by a Participant after approval from the SC of a Study proposal.

#### **D. Access to Data with Identifiers**

Access to RAPID data that identifies individual Participants will only be permitted with unanimous approval of the SC, ensuring that each Participant agrees to the presentation, analysis and discussion of the data as described in the applicable Study proposal and assurances that related informed consents, IRB, and other approvals allow for release and use of such data.

#### **E. Public Access**

A Public-Use Dataset (**PUD**) resulting from a Study approved by the SC will be created when required by a journal, sponsor, or granting agency. The Study proposal should specify that a PUD is intended. The Lead Investigator is responsible for providing assurances to the SC that related informed consents, IRB, and other approvals will allow for such release and use of such data.

#### **F. Multi-center Data Access**

- i. Participant Site Investigators can collaborate with the SC to analyze multi-center data at the time(s) specified in the statistical analysis plan of the Protocol. This may include phone calls, email, dedicated sessions via remote meeting software and/or site visits with the SC.
- ii. Participant sites may propose additional analyses of multi-center data after the primary analysis is complete. A proposal to the SC is required as provided above.
- iii. In general, raw, multi-center data will not be exported from the RAPID VisionTree, however, rare exceptions may be considered by the SC provided all identifiers are removed, making the dataset de-identified.

## **2. Publication**

### **A. Intent**

The SC recognizes and accepts the importance of communicating medical study and scientific data and the necessity of conveying such information in a timely manner and therefore, encourages publication in reputable scientific journals and at seminars or conferences. The SC further recognizes and accepts that Participants and their research team must have a meaningful right to publish research results without SC or other censorship, approval, or editorial control, regardless of the Study outcome.

### **B. Confidential and Identifiable Information**

Participant will not publish any confidential information provided to Participant pursuant to a confidentiality agreement, or the names or other identifiers of other Participants without express written consent (**Confidential Information.**) Confidential information does not include the Study results or descriptions of methodology. Publication of PHI will not be permitted. Published data will not enable identification of the Participant sites that contributed data.

### **C. SC Review**

- i. A Participant will submit a copy of any proposed manuscript resulting from an approved Study to the SC for its review and comments thirty (30) days prior to the estimated date of submission for publication (fifteen (15) days for oral presentation).
- ii. If the SC identifies any Confidential Information in the proposed publication or presentation, Participant will delete such Confidential Information from any proposed publication or presentation during the applicable confidentiality period and the Participant and the SC will work in good faith to develop substitute language that is scientifically comparable but does not disclose Confidential Information. The above procedure for publication also applies to information obtained from prematurely discontinued or other incomplete Studies.
- iii. If the SC reasonably determines that the proposed publication contains patentable subject matter which the SC desires to protect, the SC may require the delay of publication for a period of time not to exceed sixty (60) days to allow for filing of patent applications.
- iv. SC members will:

- Review the acceptability of submitted proposals for publication based on compliance with the RAPID publication policy,
- Provide timely feedback to the Lead Investigator and primary author regarding submissions,
- Facilitate the public dissemination of results to Participants and other stakeholders through publication and presentation, and
- Be involved in revision of submitted manuscripts in coordination with the primary author as requested including critical appraisal of a manuscript, data analysis and presentation, as well as statistical insight.

v. Neutral or negative results arising from prospectively planned analyses will not constitute a reasonable justification for the SC to delay or revise a proposed publication. Comments by the SC will be given to the author(s), and a reasonable time will be given for them to consider, the comments and submit for re-review by the SC at the authors' discretion. If substantive comments of the SC are not adopted and the SC so requests, the authors will include a statement indicating that the published analysis does not reflect the views of the SC when the publication is submitted to a publisher.

vi. If no written response is received from the SC to a proposed publication is received by the primary author within the applicable review period, it may be conclusively presumed that publication or presentation may proceed without delay.

vii. Participants involved in a Study approved by the SC cannot publish site specific data which is part of a multi-center investigation unless the analysis of the primary outcome of the Study has been completed and the Lead Investigator has determined that no multi-site results will be published. However, Participant sites may submit a proposed publication or presentation of their site-specific data to the SC for review as provided above if no publication is submitted by the Lead Investigator or primary author to the SC within eighteen (18) months after Study completion.

viii. Any publication based on RAPID data must acknowledge RAPID and BNI as the data source. Publication of detailed RAPID data requires approval by the SC. Data requests for publications which are duplications of an earlier request by another Investigator may be honored at the discretion of the SC. In these cases, attempts to contact the earlier Investigators or arrange collaboration will be made by the SC.

ix. The RAPID should be cited as:

**Registry of Adenomas of the Pituitary and related Disorders (RAPID), (Month), (Year).**

#### **D. Public Presentations**

Any discussion of a Study prior to the peer reviewed presentation of the final results should be declared as "preliminary" or "research in progress". Additional restrictions or embargo on discussion of RAPID Studies (if appropriate) will be specified in the specific Study proposal and approved in advance of the Study by all Participant sites.

## **E. Authorship**

Investigators will follow the published guidelines of the International Committee of Medical Journal Editors in determining authorship for publications using data from RAPID (<http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>).

## **F. Authorship Appeals**

Participants and Investigators may appeal the inclusion or ordering of authors on publications of Studies in which they participated. Such appeals must be in writing to the SC, who will attempt to arbitrate among the individuals involved. Failure of this arbitration to resolve any aspect of the dispute will require the SC Chair to review and resolve the dispute.

## **VII PARTICIPANT FEE AND COSTS**

### **1. Participant Fee**

The annual fee per Participant is currently \$3000. This fee covers site licensing fees for VisionTree. The annual Participant fee may be changed at the discretion of the SC and will be published in the RAPID website.

### **2. BCOC Contribution**

Costs for the Project Management Team, and the initial VisionTree registration fees will be covered by the BCOC. BCOC team has developed the data entry forms, will build and test future data entry forms, provide oversight of the registry, and coordinate with VisionTree development of any additional PROMs. BCOC will onboard Participants and be available as a resource as needed.

### **3. Additional Funding**

Plans for additional funding will be sought by the SC with aims of covering Participant software licensing fees and Study personnel costs. Allocation of any obtained grants will be at the discretion of the SC.