BIOMARKER DATA REPOSITORY (BmDR) Technical Frequently Asked Questions (FAQs)

Q: What is the Biomarker Data Repository (BmDR)?

A: The Biomarker Data Repository (BmDR) is a public repository for novel translational safety biomarker data from a variety of independent academic and corporate sources. This repository is funded by the United States Food and Drug Administration (FDA), as well as C-Path's Predictive Safety Testing Consortium (PSTC).

The BmDR provides stakeholders with a large, reliable repository of data on novel translational safety biomarkers from a variety of nonclinical and clinical study sources.

Masked, de-identified data from multiple sponsors are being collected and stored in a secured repository. The data will be available to Critical Path Institute (C-Path), and requestable by qualified researchers to support research that leads to the submission of documents to global regulatory agencies to qualify novel safety biomarkers for new Contexts of Use (CoUs), to modify and expand existing CoUs, and to identify appropriate exploratory safety biomarkers to advance drug development in the future.

Video Resources on BmDR:

- https://www.youtube.com/watch?v=D4QMNnPeujI
- https://www.youtube.com/watch?v=wWpssu3H8Nc

Q: Why was BmDR created?

A: BmDr started as a pilot project in 2019 at C-Path with support from the US Food and Drug Administration (FDA) (https://media.c-path.org/wp-content/uploads/20240427175713/fda-bmdr.pdf). In 2023, C-Path formally launched the effort to address the need to expand understanding and utility of emerging drug induced kidney injury (DIKI) biomarker performance by ensuring that the repository contains data sets that emphasis equal representation across US and global demographics and the spectrum of kidney diseases.

Q: How does BmDR operate?

A: BmDR works by collecting and interrogating deidentified data on emerging translational safety biomarkers studies (clinical and nonclinical) with an initial focus on kidney injury biomarkers. Research groups and pharmaceutical companies can contribute their data into the BmDR through a secure process, where it is then stored on the Data and Analytics Platform (DAP). Qualified researchers can then request access to the data to interrogate it for new applications in clinical practice and drug development to pursue novel or expanded regulatory qualifications of the biomarkers. When biomarkers are qualified, they have set ranges of values and determined contexts of use that may be used during clinical trials for drugs, and throughout the entire drug development process to monitor safety and effectiveness.

Q: What are the goals of this Data Repository?

A: This answer is twofold:

1. Short Term: Through continual importation of standard and emerging biomarker data from academic researchers, as well as pharma Early Clinical Development (ECD) and non-ECD studies under C-Path BmDR agreements, it is anticipated that qualified novel biomarker data and non-qualified biomarker data will provide opportunities to understand the performance of the biomarkers across (i) the full age spectrum (FAS), (ii) baseline Kidney Disease Improving Global Outcomes (KDIGO) chronic kidney disease (CKD) glomerular filtration rate (GFR) strata, and (iii) a broad spectrum of common and uncommon kidney diseases. Evidentiary data standards will be based upon biomarker assays quality and deidentified patient-level data (e.g., demography, medical history, biometrics [e.g. height, weight, BMI]), and other relevant factors. Data standards and quality will be maintained by the C-Path BmDR Data Analytics Platform (DAP) in accordance with Clinical Data Interchange Standards Consortium (CDISC), Study Data Tabulation Model (SDTM), and Fast Healthcare Interoperability Resources (FHIR) standards.
2. Long Term: The C-Path BmDR DAP will facilitate qualified researchers' access to high quality deidentified patient-level data, modeling expertise, Artificial Intelligence/Machine Learning capabilities, and relevant publications (BmDR-based and peer-reviewed journals-based) to contextualize and potentially expand the utility of validated tissue and body fluid biomarkers, digital histologic imaging, digital radiographic imaging, as well as incorporate non-validated novel biomarkers.

As a nexus of high-quality tissue, biofluid, and digital imaging patient-level data, the C-Path BmDR wealth of renal injury (tubular and/or glomerular) biomarker data, renal function (estimated and measured) data, and renal histologic and renal parenchymal imaging can facilitate knowledge transfer and expansion through robust analyses to expand regulatory acceptance of multifunctional safety and efficacy assessments beyond current capabilities.

Q: Who can qualify to access the data?

A: Any institution or researcher that desires access to BmDR data can initiate a request. The request must include the requester's organizational information and must declare the specified research to be done with the data set(s). C-Path then grants access to the institution to use the data set(s) for the sole purpose of performing the analysis set forth in the prespecified research plan, subject to the terms and conditions of the Data Use Agreement. Requesters may include (but are not limited to):

- Academic researchers
- Major Pharma researchers
- Non-major Pharma or Biotech Companies researchers
- Other researchers

If interested in accessing BmDR data, please contact bmdr@c-path.org.

Q: How can I request data from the BmDR?

A: First, you will need to create an account with the host organization for the BmDR, Aridhia, by following this link: https://fair.dap.c-path.org/. Once you have an account, you can browse and request access to available data sets. You can also request a workspace on the BmDR's Data Analytics Platform by following this link: https://workspaces.westeurope.dap.c-path.org/#/workspaces/new_request

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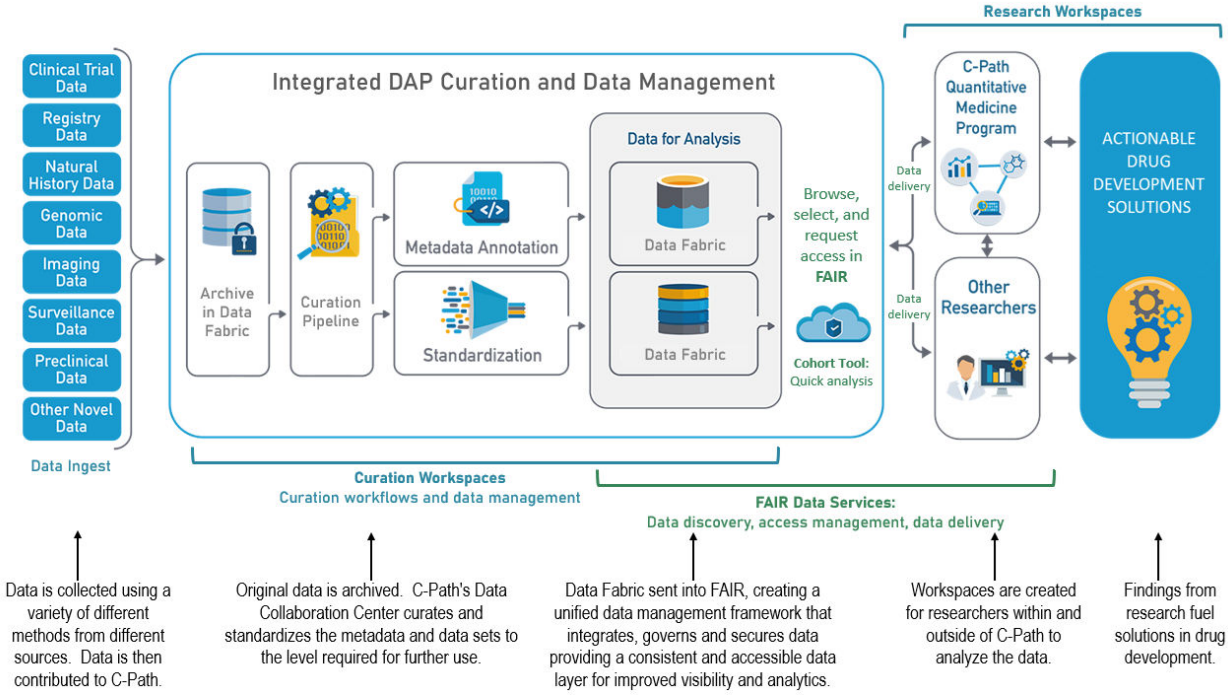
Q: Are any analytics tools available on the platform?

A: Beyond creating an account to access the repository, the BmDR DAP houses workspaces which are available to approved users. Workspaces can be requested here or during the process of requesting access to data sets. While in the Data and Analytics Platform (DAP), users have access to R Studio, Jupyter, and virtual machines within each workspace.

Q: What does the Data and Analytics Platform (DAP) process look like?

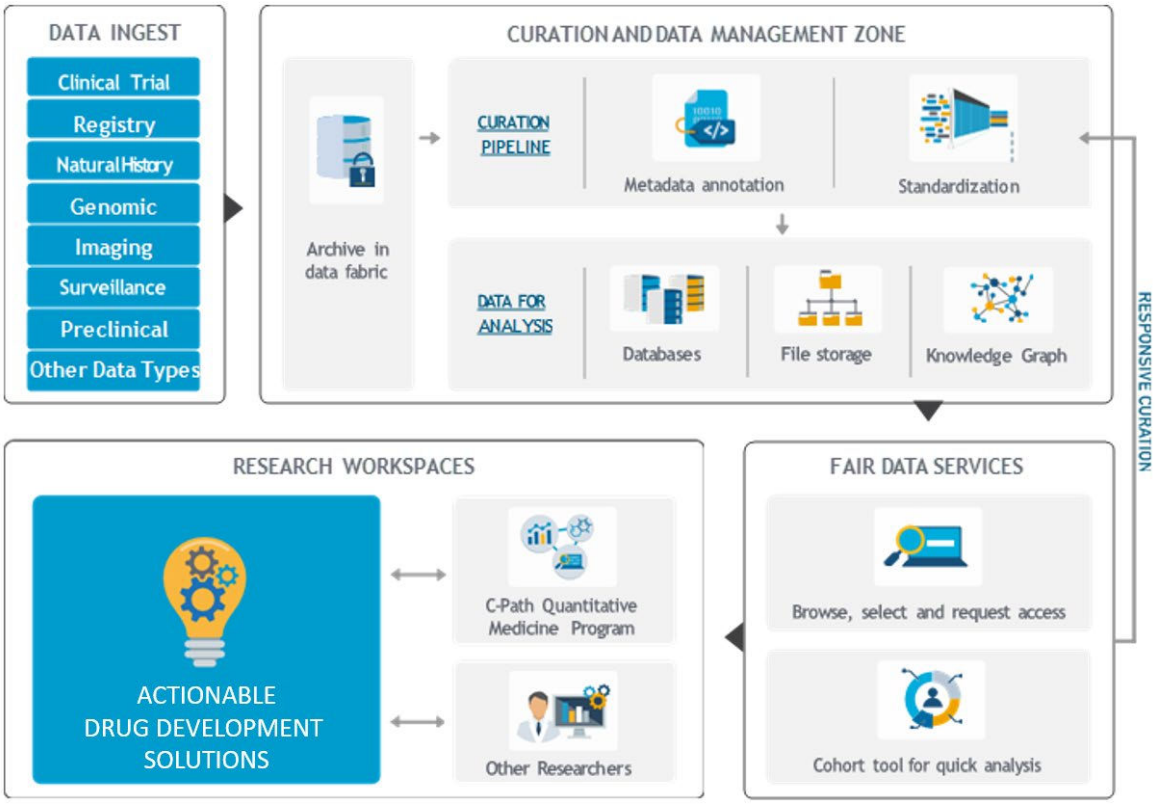
A: The data process is pictorially plotted below:



Q: What will the data flow look like?

A: Data come into the repository from a variety of sources, including clinical trial or registry data, natural history or genomic information, as well as pre-clinical data. Upon arrival at C-Path, the data goes through a curation and data management zone where the data fabric is archived. The data are then standardized into SDTM and put on the Data and Analytics Platform (DAP). On the DAP, researchers can browse through data set titles, preview information about data sets, as well as use the Cohort Builder tool for quick high-level demographics. Requests can then be made for access to the data sets. Once the request is approved and a Data Use Agreement is executed, the researcher can analyze the individual dataset in a workspace or download it for analysis. Those analyses may then be shared with

the public to inform drug development solutions. The data flow includes:



Q: Why should Pharma/Biotech/Academics participate in this Data Repository?

A: Pharma/biotech/academics should participate in this Data Repository to help expand understanding and utility of emerging DIKI biomarker performance A biomarker data repository is important because it enhances the understanding of disease trajectories and clinical outcomes. It allows researchers and clinicians to add biomarker information to real-world data sets, such as disease or drug registries, and helps qualify biomarkers for drug development.

Biomarkers can detect pathologies (or disease onset) present early in disease potentially paving the way for preventative intervention strategies, which may help patients to avoid disability, poor treatment outcome, disease sequelae and premature mortality.

Q: Who holds responsibility for managing, safeguarding, and ensuring compliance with the data collected through the repository?

A: C-Path is the data steward for contributed de-identified studies and for providing written notices, forms, and other information about your participation in the repository. All data are negotiated through an agreement between C-Path and the data contributor, with terms defined and agreed upon prior to being available on the DAP. The BmDR data are collected using a secure transfer platform and stored on the C-Path-DAP. The DAP is a centralized and standardized infrastructure to support and accelerate rare disease characterization with the goal of accelerating therapy development.

Q: What is the Data Collaboration Center (DCC)?

A: The Data Collaboration Center (DCC) was founded by C-Path to generate secure, large-scale data solutions for medical research, and provide unsurpassed expertise in curating, standardizing, analyzing and sharing medical data from around the world. We operate in a neutral space with a focus on accelerating clinical research and improved treatments by maximizing the utility of medical data. This is accomplished through robust data management and curation processes, and through the development and application of data standards and ontologies, as well as custom-built tools. The DCC possesses top-tier technical expertise and project management resources to support advanced research efforts.

The Data Collaboration Center provides the resources, services and solutions to enable multiple organizations to collaborate in a neutral setting to share data, which in turn creates new solutions and tools that accelerate drug development.

Q: Who can contribute to the data repository?

A: Masked, de-identified data from academic, government scientists, non-governmental agencies, pharmaceutical or biotech companies with clinical or nonclinical studies may be contributed to the BmDR. If you are interested in adding your data to the repository, please get in contact with Nick King (nking@c-path.org), Katrina Peron (kperon@c-path.org) or bmdr@c-path.org.

Q: What kind of data is collected?

A: All data are completely de-identified fashion so as not to trigger any patient privacy concerns and cannot be traced back to individual patients. Data for the repository can come from clinical control arms, nonclinical control arms, nonclinical active arms, basic study design elements, or from basic assay information. It can also be from regulatory submissions (that have been submitted to the FDA) including Clinical Trial Applications (CTAs), Investigation New Drugs (INDs), or New Drug Applications (NDAs).

Q: How is this data being used?

A: The BmDR data will be used for:

- Supporting submissions to regulatory agencies for novel or expanded qualifications of biomarkers, or for Phase 1, Phase 2, and Phase 3 clinical trials designs.
- Peer-reviewed journal submissions for publication.
    - Qualified researchers are required to produce publication-grade manuscript(s) of analyses performed.
- Periodic interrogation of BmDR emerging biomarkers across the full age and full disease spectra.
- New applications in clinical practice and drug development

Q: What if I change my mind about including my Pharma/biotech/academics data?

A: At any point you can choose to withdraw your data. For data to be on the platform, a Data Contribution Agreement (DCA) must be executed between the data custodian and C-Path. This agreement details the terms of data use, and typically includes language that the agreement may be terminated by the Custodian upon a material breach of any representations or covenants of the agreement by C-Path if such breach is not remedied within forty-five (45) days of the receipt by C-Path of notice of such breach from the Custodian. Either party may terminate the Agreement upon sixty (60) days written notice to the other party, provided that, if C-Path is the terminating party, C-Path agrees to use reasonable efforts to provide Custodian with at least ninety (90) advance notice of its intent to terminate so that Custodian can make other arrangements to make the data available to researchers before any data are deleted pursuant to the agreement, and C-Path agrees to use reasonable efforts to assist Custodian in transferring the Data prior to the effective date of termination

Upon termination of the DCA, C-Path will discontinue its use of the data, and will appropriately remove the data from all C-Path managed storage and repositories.

Data

Q: Why is data sharing important?

A: Data sharing is the process of making data resources available to multiple applications, users, or organizations. It involves a combination of technologies, practices, legal frameworks, and cultural elements that facilitate secure data access without compromising data integrity, which involves safeguarding an organization's data against loss, leaks and corrupting influences.
Video Resource for Data Sharing: Rick Liwski - Why is data sharing important? (youtube.com)

Q: What type of data are we looking for?

A: Deidentified data on emerging translational safety biomarker studies (clinical and nonclinical) with an initial focus on kidney injury biomarkers, including Albumin, Clusterin, Cystatic C, KIM-1, total protein, NAG, NGAL, and Osteopontin. Biomarker data from healthy volunteer populations are also of interest.

Q: Where will data be stored?

A: All contributed data will be stored in the secure C-Path Biomarker Data Repository (BmDR) Data and Analytics Platform (BmDR DAP). This is an FDA-funded initiative that provides a centralized and standardized infrastructure to support and accelerate qualification of biomarkers as tools for drug developers.

Q: Who owns the data?

A: The Data Custodian (organization that contributed the data) remain the data owner. They execute a Data Contribution Agreement (DCA) with C-Path detailing the terms of how data can be used and

shared (if applicable) from the repository, as well as termination details and what will need to happen with the data if the agreement is terminated.

Q: How can I see the information/data collected?

A: Once you create an account on the C-Path Data and Analytics Platform (DAP) using these instructions, you may view a list of available data sets and a summary of what is included in each data set. Some data sets will be available to request and download, and some will not be requestable or downloadable for analysis, depending on the agreement in place with the data custodian. In cases where a data set is not available for request or download, the BmDR team will share analyses summaries in the quarterly newsletters. All data are de-identified and unable to be traced back to any patient.

Q: How long do researchers have access to the data that they request?

A: Qualified researchers must submit a request for data, including their organizational information and a plan for their research with the data. Upon submitting the request, it goes to a review team at C-Path composed of BmDR members that review the researcher's credentials and research plan. If approved, the requester must agree to the terms in a Data Use Agreement (DUA). Upon execution of the agreement, data will be securely shared with the requester.

This agreement details the terms of data use and can be terminated by any party without cause by providing sixty days' written notice to the other party. Upon termination of the DUA, the recipient shall promptly return or destroy (at C-Path's sole election) all data sets and copies thereof provided by C-Path.

Q: How will private information be protected?

A: The security of your data is very important. C-Path's Data Collaboration Center (DCC) has a comprehensive data privacy program which encompasses all jurisdictions in which we manage subject data. This program includes policies around individual patient-level data that meet or exceed human subject research protection requirements as well as applicable regulatory policy.

Every contribution of clinical data to C-Path is governed by a Data Contribution Agreement (DCA), which specifies the scope of data sharing permitted by the contributor. Data contributors must also certify that they have met all applicable requirements to enable secondary research on contributed data. All data are encrypted in rest and in transit, accessed only for qualified research purposes governed by data use agreements.

In addition to internal controls ensuring data is secure and patient privacy is protected, the Data and Analytics Platform (DAP) that houses the data is built in the Digital Research Environment (DRE) of Aridhia Informatics. The DRE maintains ISO 27001 certification and is HITRUST certified. Additional certifications and security details about the DRE utilized by C-Path can be found on their Security and Compliance page.

The data platform meets and exceeds the physical, technical, and administrative security requirements of HIPAA and continues to improve the ability to safeguard data and measure the state of compliance.

When data is requested from the BmDR DAP, qualified researchers agree to terms and sign a Data Use Agreement (DUA) before receiving the requested data. The recipient of the data acknowledges the importance of data privacy of individuals to whom the data sets may relate to comply with all applicable national, state/provincial, and local laws and regulations regarding patient/research subject privacy, the repository, storage, processing, disclosure and use of personally identifiable information, and other uses and disclosures of the types of data contained in the data sets. The DUA includes additional details and terms to ensure data is protected.

Q: What does the DCC do with the data?

A: The Data Collaboration Center (DCC) was founded by C-Path to generate secure, large-scale data solutions for medical research, and provide ability in curating, standardizing, analyzing, and sharing medical data from around the world. The DCC operates in a neutral space with a focus on accelerating clinical research and improved treatments by maximizing the utility of medical data. This is accomplished through robust data management and curation processes, development and application of data standards and ontologies, and custom-built tools. The DCC possesses top-tier technical expertise and project management resources to support advanced research efforts.

Video Resources for the DCC:

- https://www.youtube.com/watch?v=EsxJOi2hJm0
- https://www.youtube.com/watch?v=_f4H9z3mkQg

Q: How does DCC support C-Path consortia?

A: Through the collaborative environment created by this program, the DCC provides the following:

- Customized data-sharing and analytics platforms, such as the C-Path Data and Analytics Platform (CP-DAP™)
- Secure transfer of data to and from all external sources
- Planning and execution of multisource data standardization and aggregation
- Support for FAIR (Findable, Accessible, Interoperable and Reusable) Guiding Principles of Data by utilizing unique identifiers, extensive metadata and indexed, searchable database architecture
- Sustainable curation and administration of data and its storage
- Ability for teams to work together in a secure environment to analyze and interpret data
- Security policies and frameworks which align with industry best practices
- An adherence to applicable security and privacy regulations in all jurisdictions where data are managed

Video Resource: Rick Liwski - How does DCC support C-Path consortia? (youtube.com)

Q: Will it cost me anything to be involved in BmDR?

A: Currently, there is no cost to contribute data nor access the data sets on the BmDR Data and Analytics Platform (DAP).

Requesting Data

Q: Is data available to international entities?

A: Yes. BmDR is a global repository containing data from all over the world. International entities that have malicious intent will not have access to any data. C-Path will not provide data to or engage with researchers from certain countries that are not in good standing with the United States (i.e. Iran, North Korea).

Miscellaneous

Q: Where can I learn more?

A: To learn more about the Biomarker Data Repository please visit: C-Path BmDR

Critical Path Institute

Q: What is the Critical Path Institute (C-Path)?

A: Critical Path Institute, or C-Path, is a global, independent, nonprofit organization dedicated to the generation of actionable solutions to transform the medical product development process. C-Path brings together regulatory agencies, biopharmaceutical firms, universities, other non-profits, and patient groups from around the world to improve public health. Together, these key players work to develop new tools and processes that can accelerate decision-making and medical product development and approval.

Q: What is a Public-private partnership (PPP)?

A: A PPP or a consortium is a collaborative group managed by a convening or coordinating organization involving multiple stakeholder organizations including at least one non-profit or 501(c)(3) organization (e.g., academia, government, or foundation) and at least one for-profit organization (e.g., pharmaceutical, biotechnology, or medical device company). A PPP may involve multiple committees and working groups. (from US FDA definition)

Q: What is C-Path's mission?

A: C-Path leads collaborations that accelerate drug development, advancing better treatments for people worldwide.

Q: How does C-Path achieve this mission?

A: C-Path achieves its mission by acting as an independent, neutral third party to form and lead public-private partnerships of regulatory agencies, biopharmaceutical firms, universities, and patient groups in a pre-competitive collaboration and sharing of scientific data.

Q: How is C-Path funded?

A: C-Path is a public-private partnership funded by government agencies such as the *FDA, grants from foundations such as the Bill & Melinda Gates Foundation, Michael J. Fox Foundation and the Polycystic Kidney Disease Foundation, as well as fees from industry participants.

*Critical Path Institute is supported by the Food and Drug Administration (FDA) of the Department of Health and Human Services (HHS) and is 56% funded by the FDA/HHS, totaling $23,740,424, and 44% funded by non-government source(s), totaling $18,881,611. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government.

Q: How can I learn more about C-Path?

A: Find out more information about C-Path at our newly updated website: Frequently Asked Questions & Answers - Critical Path Institute (c-path.org)

Predictive Safety Testing Consortium (PSTC)

Q: What is the Predicative Safety Testing Consortia (PSTC)?

A: C-Path's Predictive Safety Testing Consortium (PSTC) was founded in 2006 to serve as a pre-competitive collaboration for the independent assessment, advancement, and validation of novel drug safety tests.

PSTC was formed and officially announced by Health and Human Services (HHS) Secretary Michael Leavitt, Food and Drug Administration (FDA) Commissioner Dr. Andrew von Eschenbach, and FDA Deputy Commissioner Dr. Janet Woodcock. Upon its inception, Woodcock described the consortium as "unprecedented" and a "shining example" of the type of work the FDA would like to see conducted.

PSTC's goal is to obtain regulatory acceptance of novel drug safety tests. PSTC brings together pharmaceutical companies to share and validate innovative safety testing methods under advisement of the U.S. FDA, its European counterpart, the EMA (European Medicines Agency), and PMDA (Japanese Pharmaceutical and Medical Devices Agency). Currently, PSTC is focused on developing and obtaining regulatory qualification of improved clinical safety biomarkers for use in drug development.

Video Resource: https://www.youtube.com/watch?v=TkYokL2asO0

Miscellaneous

Q: Where can I learn more?

A: To learn more please visit: C-Path BmDR

Additional Resources:

1. **C-Path Website**
2. **BmDR Website**
3. **BmDR 1-pager**
4. **Published BmDR Newsletters**
5. **BmDR Patient-Focused FAQ**