



CROSS-BORDER DATA TRANSFERS & BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT

Biopharmaceuticals are increasingly developed, tested, and analyzed for safety and efficacy in different countries. To perform this research and development (R&D), scientists, regulators, and others depend on the capability to transfer data securely across international IT networks.

CROSS-BORDER DATA TRANSFERS ACCELERATE PHARMACEUTICAL CANDIDATE IDENTIFICATION

Cross-border data transfers can accelerate early-stage biopharmaceutical R&D, as researchers search for the best drug candidates.

Artificial Intelligence (AI) and Target-Based Drug Discovery

As health-related data grows rapidly (increasing nearly 900 percent from 2016–2018),¹ cross-border data analytics can help speed the early identification of potentially useful drug candidates, shortening pharmaceutical discovery timelines from years to months.² This analysis depends upon data transferred from across the world containing information on “chemical properties [and] genetic information... to improve target-based discovery.”³

Data analytics applied to data sets consolidated across borders is fast-tracking target discovery. As compared with traditional methods, this includes savings of up to:

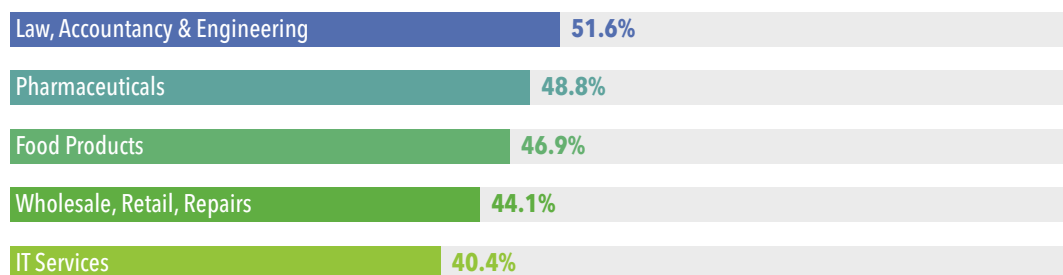
- 40-50 percent of the time required, and
- \$26 billion in costs.

Pharmiweb, *How Can Artificial Intelligence Facilitate New Drug Research and Development* (2020), <https://www.pharmiweb.com/article/how-can-artificial-intelligence-facilitate-new-drug-research-and-development>.

Cross-Border R&D Collaboration

Even before the launch of preclinical studies and clinical trials, the global R&D ecosystem depends on cross-border access to medical journals and scientific collaboration, reflected in a high proportion of relevant publications having international co-authors.⁴ Cross-border R&D collaboration has also increased in response to the COVID-19 crisis, with the World Health Organization (WHO),⁵ public-private research consortia,⁶ and national governments establishing new platforms and methods of sharing research⁷ and resources⁸ across borders. The US-Canada Cascadia Data Discovery Initiative (CCD) is another model for cross-border R&D collaboration.⁹

Top Five Sectors of Scientific Publications With International Co-authorship



Source: H. Dernis, P. Gkotsis, N. Grassano, S. Nakazato, M. Squicciarini, B. van Beuzekom, A. Vezzani, *World Corporate Top R&D Investors: Shaping the Future of Technologies and of AI*, A joint JRC and OECD Report (2019), <http://www.oecd.org/sti/world-corporate-top-rd-investors-shaping-future-of-technology-and-of-ai.pdf>.

Stages of Biopharmaceutical R&D

Stage	Purpose	Data Involved
General Research	Drug discovery, lab drug screening, drug target identification	Databases containing medical journals and studies; historical clinical trial data/results (if publicly available); libraries of chemical compounds and molecules, and their biological and pharmacological characteristics.*
Preclinical Studies	Determine safety of broader clinical trials	Same as above; <i>in vitro</i> or <i>in vivo</i> studies, and toxicity data. May also assess dosing and route of administration for the clinical trial context.
Clinical Trials	Determine whether a product is safe and effective for use in humans	<ul style="list-style-type: none"> Phase 1 data often relates to pharmacokinetic parameters—e.g., absorption, distribution, metabolization rates, and excretion in healthy participants. Phase 2 data often relates to efficacy in those affected by the underlying condition, producing a dose response relationship. Phase 3 data often relates to large numbers of participants across demographics and populations.
Regulatory Review	Review evidence, issue marketing approval, and any changes/updates post-approval	Entire dossier of evidence developed through earlier stages of biopharmaceutical R&D. Multiple regulators review the same and/or related data sets, thus requiring cross-border exchange and collaboration. Real-world evidence datasets from different markets can also sometimes complement the traditional data package.
Post-Marketing Surveillance	Ensure product is safe and effective after marketing	Data collection through reporting of adverse events, and facility inspections to ensure that good manufacturing practices are being followed, etc.

* See e.g., APEx Bio, *Screening Library* (2021), <https://www.apexbt.com/screening-library.html>.

CROSS-BORDER DATA TRANSFERS FACILITATE THE EVALUATION OF SAFETY AND EFFICACY ACROSS GLOBAL POPULATIONS DURING PRECLINICAL STUDIES AND CLINICAL TRIALS

Cross-border data transfers help improve preclinical studies and clinical trials by reducing development cycles, improving data quality, facilitating participant adherence, and leading to more conclusive safety and efficacy findings. Trial processes may necessitate data transfers among participants located in different countries—sponsor(s), clinical trial sites, contract research organizations (CROs), recruitment vendors, central laboratories and imaging service providers, among others. This includes:

Good Clinical Design and Practice in a Cross-Border R&D Context

Clinical trial design is often inherently cross-border in scope. Trial architects often consider relevant cross-border circumstances as they develop the protocols that set out a trial's objectives, design, and methodology. Likewise, regulators are designing more efficient approaches to cross-border trial design, as exemplified by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E6 (Good Clinical Practice) and ICH E8 (General Considerations for Clinical Studies).

- **Cross-border outcome modeling.** Multi-country planning can improve trial design and outcome modeling, thus leading to better design protocols, predictive analysis, and risk management.
- **Cross-population representativeness.** Cross-border data transfers enable global insights and the early identification of patterns in trial data. "Global studies ensure that new products are safe and effective across different demographics, and [especially for rare and neglected diseases, can help identify]... a representative sample of trial subjects."¹⁰
- **International legal compliance.** A cross-border design helps ensure compliance with different countries' drug regulatory approval requirements, sectoral data privacy rules (e.g., General Data Protection Regulations (GDPR), Health Insurance Portability and Accountability Act), and perspectives of Independent Ethics Committee (IEC), and Institutional Review Boards (IRB). Yet, cross-border collaboration, including for public sector research, remains challenging.¹¹

Enabling Both Remote and Onsite Clinical Trials

Cross-border data transfers are important to the conduct of remote and onsite clinical trials in the following ways:

- **Cross-border clinical trial operations.** An accelerated trend toward cross-border digitization of clinical trial processes is regarded by some commentators as "the biggest innovation emerging from the COVID-19 crisis."¹² Cross-border cloud- and patient-centric clinical trial technologies can also help improve patient access, diversity, speed, and representativeness, especially as more than 80 percent of clinical trials don't meet initial enrollment timelines.¹³
- **New uses for wearables.** Cloud-based digital tools can evaluate data from wearables and Internet of Things devices in real-time, allowing for early identification of anomalies and promising results alike.¹⁴ Supported by robust privacy protections, remote monitoring enabled by these technologies can also help improve clinical trial processes through higher recruitment rates, better compliance, and lower drop-out rates.

CROSS-BORDER DATA TRANSFERS HELP REGULATORS ENSURE PRODUCT SAFETY AND EFFICACY

Cross-border data transfers are also critical to regulatory review in different countries—both for applicants and regulators who may seek to workshare, collaborate, or refer to one another's reviews. This includes:

- **Cross-border regulatory collaboration.** The US Food & Drug Administration (FDA) Oncology Center of Excellence launched [Project Orbis](#), a cross-border collaborative framework to share information in regulatory reviews of oncology products across Australia, Brazil, Canada, Singapore, Switzerland, the UK, and the United States.¹⁵
- **Cross-border data sharing platforms.** Cross-border data exchange initiatives like the [Accumulus](#) platform can help facilitate coordinated global assessments of therapies in multiple countries.
- **Global regulatory structured data submissions.** Global regulators are beginning to introduce structured data submission frameworks to improve regulatory data management and regulatory review processes.¹⁶ Applicants are also investing in Regulatory Information Management Systems (RIMS) that offer cloud-enabled approaches to managing and streamlining the submission of regulatory approval dossiers.¹⁷

Project Orbis: Cross-Border Regulatory Collaboration in Oncology Product Reviews in Seven Countries

Project Orbis is an initiative of the FDA Oncology Center of Excellence, which provides a framework for concurrent submission and review of oncology products among international partners.

PROCESS

Applicants submit cross-border drug approval applications in seven countries for concurrent regulatory review.

Regulators meet quarterly to improve clinical trial design, data quality, and patient outcomes.

JUNE 2019 TO JUNE 2020

60
oncology marketing
applications filed,
representing
16
unique projects.

Median time-to-approval:
4.2 months
in United States
4.4 months
in other jurisdictions.

First approval:
November 2019
simultaneous United
States, Canada, and
Australia approval
decisions for a new
treatment of advanced
endometrial carcinoma.

CROSS-BORDER DATA TRANSFERS FACILITATE POST-MARKETING SURVEILLANCE AND GOOD PHARMACOVIGILANCE PRACTICE

Cross-border data transfers are integral to good pharmacovigilance practice (GVP) in the post-market surveillance context. This often includes cross-border reporting of data on adverse reactions with global regulators, regulatory inspections of global manufacturing facilities, and submission of risk management plans and post-authorization safety studies to regulatory authorities in different countries. This includes:

- **Cross-border adverse event reporting.** Information on adverse reactions to pharmaceutical products are collected and shared with regulators around the world, although personally identifiable information is only transferred in extraordinary circumstances and subject to extensive security controls. Such information must be able to move from wherever an event occurs to government regulators.
- **Cross-border facility inspections.** The ability of regulators from different countries to travel to global manufacturing facilities was curtailed during the COVID-19 crisis, leading to an increase in virtual remote facility inspections for certain limited purposes, such as documentation review.¹⁸ Going forward, such cross-border virtual inspections could complement existing processes designed to ensure product safety and efficacy, including processes relating to pharmacovigilance and good manufacturing practice.

Privacy and Security Data Controls for Cross-Border Biopharmaceutical R&D

Stage	Data Type	Is data protected by encryption?	Do cloud security protections apply? ^a	Is data pseudonymized or anonymized? ^b	Can privacy enhancing technologies be applied? ^c
Candidate Identification	Medical journals, compound libraries, etc. (containing no personal data)	Often	Yes	N/A	N/A
Preclinical Studies	Toxicity studies in vitro or in vivo (rarely human studies)	Yes	Yes	Rarely applicable	Rarely applicable
Clinical Trials	Bodily response data	Yes	Yes	Yes	Often
Regulatory Review	Marketing approval application and dossier	Yes	Yes	Yes	Often
Post-Market Surveillance	Monitoring and adverse event reports	Yes	Yes	Yes	Often

^a Cloud-based technologies can help improve data security, allowing investigators and participants to access clinical trial software applications protected by cloud-based cybersecurity, encryption, and other privacy-protective software solutions. See generally, BSA, *Moving to the Cloud—A Primer on Cloud Computing* (2018), https://www.bsa.org/files/reports/2018BSA_MovingtotheCloud.pdf.

^b To protect subject privacy, including in a cross-border R&D context, organizations pseudonymize (or “de-identify”) trial data, biospecimens, and other information. This process often involves replacing all direct identifiers with a subject identification code that is maintained confidentially at the trial site. The coded data sets may be transferred, often across borders, to contract research organizations or laboratories for analysis. EFPIA, IPMPC, MedTechEurope, and AdvaMed, *Transatlantic Healthcare Data Flows*, p. 3. Data anonymization safeguards (i.e., permanent removal of identifiers, leaving no way to link the data back to a subject) and data minimization safeguards (i.e., removal of key identifying data from certain data summaries) are also sometimes used as an effective supplementary measure to enhance privacy in certain cross-border medical R&D contexts. See e.g., Jack Shostak, *De-Identification of Clinical Trials Data Demystified*, <https://www.lexjansen.com/pharmasug/2006/PublicHealthResearch/PR02.pdf>; ALLEA, EASAC, FEAM, *International Health Data Sharing*, p. 12, Box 1.

^c To add further layers of security in a cross-border R&D context, data analytics performed on combined data sets can also make use of privacy-enhancing technologies (PETs), including differential privacy and homomorphic encryption. See ALLEA, EASAC, FEAM, *International Health Data Sharing*, pp. 36–37, 47, Appendix 3.

Endnotes

- 1 HIT Infrastructure, *Organizations See 878% Health Data Growth Rate Since 2016* (2019), <https://hitinfrastructure.com/news/organizations-see-878-health-data-growth-rate-since-2016>.
- 2 Arash Keshavarzi Arshadi et al., "Artificial Intelligence for COVID-19 Drug Discovery and Vaccine Development," *Frontiers in Artificial Intelligence* (August 2020), <https://www.frontiersin.org/articles/10.3389/fraci.2020.00065/full>.
- 3 Joshua New, *Accelerating Data-Driven Drug Development* (2019), <https://datainnovation.org/2019/09/accelerating-data-driven-drug-development/>; see also, Duska Anastasijevic, *Mayo Clinic Completes Deidentification of Expansive Medical Dataset* (2020), <https://newsnetwork.mayoclinic.org/discussion/mayo-clinic-completes-deidentification-of-expansive-medical-dataset/>.
- 4 H. Dernis et al. *World Corporate Top R&D Investors: Shaping the Future of Technologies and of AI, A Joint JRC and OECD Report* (2019), <http://www.oecd.org/sti/world-corporate-top-rd-investors-shaping-future-of-technology-and-of-ai.pdf>.
- 5 See e.g., World Health Organization, *Global Research on Coronavirus Disease (COVID-19)*, <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov>.
- 6 Semantic Scholar, *COVID-19 Open Research Dataset*, <https://pages.semanticscholar.org/coronavirus-research>; OpenHIE, *COVID-19 Task Force* (2020), <https://wiki.ohie.org/display/SUB/COVID-19+Task+Force>.
- 7 See e.g., Pharmaceutical Research and Manufacturers of America, Biotechnology Innovation Organization, *Our Commitment to Beat Coronavirus* (2020), <https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/G-/Industry-Principles-on-Coronavirus.pdf>; IMI Innovative Medicines Initiative, *IMI Mission and Objectives* (2020), www.imi.europa.eu/about-imi/mission-objectives; *Novel Coronavirus Data Platform Data Sharing Agreement (DSA) Terms of Data Submission*, https://media.tghn.org/medialibrary/2020/01/nCoV_Data_Platform_Terms_of_Data_Submission_24Jan2020.pdf.
- 8 The public-private COVID-19 High Performance Computing Consortium offered global cross-border access to high-performance technologies with the power to "process massive numbers of calculations related to bioinformatics, epidemiology, and molecular modeling, helping scientists develop answers to complex scientific questions about COVID-19 in hours or days versus weeks or months." See *COVID-19 High Performance Computing Consortium*, www.covid19-hpc-consortium.org/; Sara Castellanos, "Supercomputers Help Researchers Speed Drug Discovery for Covid-19," *Wall Street Journal* (April 14, 2020), www.wsj.com/articles/supercomputers-help-researchers-speed-drug-discovery-for-covid-19-11586888735?mod=hp_minor_pos4; see also European Commission, *Using European Supercomputing to Treat the Coronavirus* (2020), <https://ec.europa.eu/digital-single-market/en/news/using-european-supercomputing-treat-coronavirus> (EU-based consortium of industry, research organizations, and three supercomputing centers).
- 9 Cascadia Data Alliance, *Data Science Collaborations* (2021), <https://www.fredhutch.org/en/about/about-the-hutch/institutional-partners-collaborations/cascadia-data-alliance.html>.
- 10 EFPIA, IPMPC, MedTech Europe, and AdvaMed, *Innovation without Borders: The Importance of Transatlantic Data Flows to Healthcare Innovation and Delivery*, Discussion Paper (2020) (hereinafter EFPIA, IPMPC, MedTechEurope, and AdvaMed, *Transatlantic Healthcare Data Flows*); see also, ALLEA, EASAC, FEAM, *International Health Data Sharing* (April 2019), https://easac.eu/fileadmin/PDF_s/reports_statements/Health_Data/International_Health_Data_Transfer_2021_web.pdf.
- 11 See Tania Rabesandratana, "European Data Law Is Impeding Studies on Diabetes and Alzheimer's, Researchers Warn," *Science* (November 20, 2019), <https://www.sciencemag.org/news/2019/11/european-data-law-impeding-studies-diabetes-and-alzheimer-s-researchers-warn>; see also, EFPIA, IPMPC, MedTechEurope, and AdvaMed, *Transatlantic Healthcare Data Flows*; Dara Hallian et al., *International Transfers of Health Research Data Following Schrems II: A Problem in Need of a Solution* (2021), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3688392; David Peloquin et al., "Disruptive and Avoidable: GDPR Challenges to Secondary Research Uses of Data," *European Journal of Human Genetics* (2020), <https://www.nature.com/articles/s41431-020-0596-x>; Santa Slokenberga, "EU Data Transfer Rules and African Legal Realities: Is Data Exchange for Biobank Research Realistic?" *9 International Data Privacy Law* 30 (2019), <https://academic.oup.com/idpl/article-abstract/9/1/30/5076710?redirectedFrom=fulltext>; Robert Eiss, "Confusion Over Europe's Data Protection Law Is Stalling Scientific Progress," *Nature* (2020), <https://www.nature.com/articles/d41586-020-02454-7>; PHG Foundation, *The GDPR and Genomic Data* (2021), <https://www.phgfoundation.org/report/the-gdpr-and-genomic-data>.
- 12 Jerry Stewart et al., *COVID-19: A Catalyst to Accelerate Global Regulatory Transformation*, *Journal of Clinical Pharmacology and Therapeutics*, p. 2 (2020) (hereinafter "Global Regulatory Transformation").
- 13 See e.g., Kent Thoeleke, "There's a Silent Crisis in Clinical Research. And It's Not Covid-19," *STAT* (October 28, 2020), <https://www.statnews.com/2020/10/28/recruitment-retention-silent-crises-clinical-trials/>.
- 14 EFPIA, IPMPC, MedTechEurope, and AdvaMed, *Transatlantic Healthcare Data Flows*, p. 4; Global Regulatory Transformation, p. 2; McKinsey, *Digital R&D: The Next Frontier for Biopharmaceuticals* (October 31, 2018), <https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/digital-rd-the-next-frontier-for-biopharmaceuticals>.
- 15 See US Food & Drug Administration, *Project Orbis: Strengthening International Collaboration for Oncology Product Reviews, Faster Patient Access to Innovative Therapies* (2020), <https://www.fda.gov/news-events/fda-voices/project-orbis-strengthening-international-collaboration-oncology-product-reviews-faster-patient>; Clinical Cancer Research, *Project Orbis: Global Collaborative Review Program*, CCR Perspectives in Regulatory Science and Policy (2020), <https://clincancerres.aacrjournals.org/content/26/24/6412>; see also, Swissmedic, *The ACSS Consortium Welcomes the U.K. as Its Newest Member* (October 14, 2020), https://www.swissmedic.ch/swissmedic/en/home/news/mitteilungen/acss_consortium_neues_mitglied_mhra.html; ASEAN Joint Assessment Procedure for Pharmaceutical Products Public Announcement (July 2020), <https://npra.gov.my/index.php/en/directive-general/1527125-asean-joint-assessment-procedure-for-pharmaceutical-products-public-announcement.html>.
- 16 See e.g., European Medicines Agency, *Substance, Product, Organisation and Referential (SPOR) Master Data* (2021), <https://www.ema.europa.eu/en/human-regulatory/research-development/data-medicines-iso-idmp-standards/substance-product-organisation-referential-spor-master-data>; FDA, *Standardized Data for Pharmaceutical Quality/Chemistry Manufacturing and Control* (2018), <https://www.federalregister.gov/documents/2018/08/22/2018-18080/standardized-data-for-pharmaceutical-quality-chemistry-manufacturing-and-control-public-meeting>; FDA, *Regulatory Submissions Forum* (2020), <https://www.fda.gov/media/135563/download>; Health Canada, *Structured Format for Product Monographs* (2019), <https://www.canada.ca/en/health-canada/services/drugs-health-products/public-involvement-consultations/drug-products/structured-product-monograph.html>.
- 17 See generally, Gens & Associates, *2020 World Class Regulatory Information Management (RIM) Whitepaper* (2020), http://gens-associates.com/wordpress/wp-content/uploads/2020/11/GensandAssociates_Executive_WorldClassRIM_Whitepaper_Fall2020v_Release.pdf.
- 18 Global Regulatory Transformation, p. 2.

About the Global Data Alliance

The Global Data Alliance (globaldataalliance.org) is a cross-industry coalition of companies that are committed to high standards of data responsibility and that rely on the ability to transfer data around the world to innovate and create jobs. The Alliance supports policies that help instill trust in the digital economy while safeguarding the ability to transfer data across borders and refraining from imposing data localization requirements that restrict trade. Alliance members are headquartered across the globe and are active in the advanced manufacturing, aerospace, automotive, electronics, energy, financial and payment services, health, consumer goods, supply chain, and telecommunications sectors, among others. BSA | The Software Alliance administers the Global Data Alliance.