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#### **PHUSE New Project Request Template**

PHUSE collaborations are organised into a number of Working Groups, each with a broad topic area. Each Working Group has specific projects designed to achieve a set of specific objectives.

Working Groups include volunteers from major stakeholders such as academia, the pharmaceutical industry, the biologics industry, the device industry, contract research organisations, core laboratory organisations, technology vendors, SDOs and interested regulatory agencies. Participation is open to anyone who wants to contribute.

The process New Project Requests follow can be found at [www.phuse.global/useful-information](https://advance.phuse.global/display/WEL/Useful+Information). They are reviewed on a monthly basis by the PHUSE Working Groups Steering Committee using the criteria described, to ensure all projects meet the needs of our community, as well as our objectives of addressing unmet computational science needs in support of health product development and regulatory review.

1. Project Title:

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| R Pilot Submission for eCTD Compliance |

1. Working Group:

Data Transparency

Data Visualisation and Open Source Technology

Emerging Trends & Technologies

Optimizing the Use of Data Standards

Nonclinical Topics

Safety Analytics

Other

Please state.

1. Problem Statement:

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| Interest in R has been growing steadily over the last few years, and several companies have their eyes set of producing a regulatory submission with significant portions of the analysis written in R. While we know that this is acceptable given the Statistical Software Clarifying Statement, there are still several challenges to overcome. Many inititiatives across industry are focused on different aspects of this challenge, including the R Validation Hub, PHUSE Clinical Statistical Reporting in a Multilingual World, R Package Validation, the R Consortium R for Regualtory submission, and the R Consortium R Tables for Regulatory Submissions. Most of these initiatives focus on topics like validation, production of expected outputs, and anticipated questions that may arise when interfacing with a regulatory agency, but one question relatively unexplored is the physical delivery of code to the agency.  The FDA has strict submission guidelines within documents like Technical Conformance Guide, and strict expectations of delivery format following the eCTD. Aspects of these requirements can make the delivery of R code non-trivial, particularly when it comes to R packages. Most R packages exist in open-source, accesible through sources like GitHub or the Comprehensive R Archive Network (CRAN), but it is inevitable that sponsors submitting to the FDA will need a method of delivering a package that cannot be generally accesible to the public. This project will address this challenge in the context of a pilot submission. |

1. Problem Impact:

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| This project has the potential to give a roadmap to submitting sponsors actively working towards R submissions. Many questions about the process of submitting R code to the FDA will be answered, and there is a large potential to identify questions that must be explored in more detail. |

1. Project Scope:

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| Fortunately there is a solid foundation already in existense on which to build this project:   * [The PHUSE Test Data Factory project upversion of the CDISC Pilot Data](https://github.com/phuse-org/TestDataFactory/tree/main/Updated) * [The Atorus replication of the CDISC Pilot Project in R](https://github.com/atorus-research/CDISC_pilot_replication) * [Merck’s open-source R package pkglite](https://merck.github.io/pkglite/)   Atorus’ replication of the CDISC pilot gives us a baseline of code to utilize as a starting place. This project replicated the original CDISC pilot’s outputs, and thus gives a solid foundation of analyis programs to submit as a test case.  Merck’s R package pkglite was specifically developed to enable the delivery of an R package through the eCTD. This package is able to package the code into a submittable format, and then unpack the code and restore its state to an installable R package, enabling the agency to utilize the delivered code as expected.  The goal of this project is to conduct a pilot submission using these available tools. The CDISC pilot replication will be submitted, and an R package will be delivered through the eCTD to evaluate if all compliance checks relevant to the programs can be met.  The scope of this project is limited to evaluating the consumability of the code. Rather than evaluate the entire submission package, we intend to verify that:   * The packaged code is compliant with the eCTD * A consumer of the eCTD on the agency side is able to unpack and install the delivered R package * A consumer of the eCTD on the agency side is able to rerun the analaysis package delivered and replicate the results   Different questions may arise during this process, but those questions will be left for further exploration in follow-ups to this project  This project is a prime candidate for additional collaboration with the R Consortium as well, as the idea was born out of discussions in the R for Regulatory Submissions project, and seen as an excellent opportunity to leverage PHUSE’s relationship with the agency. |

1. Project Deliverable(s) and Timeline(s):

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| Submission of pilot ~6 months  White paper outlining the process and lessons learned ~ 10 months |

1. Tools Required/Planned to be Developed:

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| Primary tools have been developed. Project requires a pilot submission process through the eCTD, so need collaboration with FDA. |

1. Project Lead(s):

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| Need to recruit – at least one lead should be an expert in the submission process |

1. Project Requestor(s):

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| Mike Stackhouse, Yilong Zhang |

1. Stakeholders:

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| Pharma, CRO, regulators, tech companies |

1. Email Address:

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| --- |
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