Paper SM06

R Scripts to Streamline Non-Compartmental Analysis (NCA): A Data Programmer's Dream

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ABSTRACT

Non-compartmental analysis (NCA) plays a critical role in early-stage drug development, offering streamlined pharmacokinetic (PK) parameter estimation without requiring complex assumptions. The traditional workflow, although widely accepted by regulatory agencies for bioequivalence studies, is often time-consuming and reliant on manual processes. This paper presents an automated, end-to-end solution to streamline the NCA process through the development and implementation of R scripts. The solution, named automated NCA (aNCA), seeks to significantly reduce the time and resources required for analysis while maintaining quality and compliance. By joining the Pharmaverse, an open-source collaborative network, aNCA aims to improve efficiency, reduce dependency on external vendors, and enhance data accessibility and analysis control. This paper outlines the current landscape of NCA, the proposed automated workflow, and the future outlook for widespread implementation.

INTRODUCTION

Non-compartmental analysis (NCA) is an essential tool for pharmacokinetic (PK) parameter estimation, providing valuable data such as area under the curve (AUC), maximum concentration (Cmax), half-life (t1/2), clearance (CL), and volume of distribution (Vd). The beauty of NCA lies in its simplicity, requiring minimal assumptions and allowing quick and flexible analysis suitable for early-stage drug development. Regulatory agencies, including the FDA and EMA, frequently accept NCA results, particularly in bioequivalence studies. Additionally, NCA provides foundational insights for dose-exposure relationships and complements more complex modeling approaches such as population pharmacokinetics (PopPK) and physiologically based pharmacokinetic (PBPK) models.

However, despite its simplicity, the current NCA process can be labor-intensive and time-consuming, often involving multiple teams and external vendors. This leads to inefficiencies that could be mitigated through automation, hence the motivation behind developing the automated NCA (aNCA) framework.

CURRENT LANDSCAPE

Currently, the NCA process requires approximately six weeks to complete, with varying degrees of involvement from external vendors and internal teams. External vendors typically take three to four weeks to deliver results, while internal teams, including clinical pharmacologists and data scientists, require an additional one to two weeks to finalize the analysis. The process is only 10% automated, leading to delays and increasing the risk of human error.

WORKFLOW OVERVIEW:

- External Vendor: 3-4 weeks
- Internal Teams (SPA & Pharmacology): 1 week
- Clinical Pharmacologist: 3-5 days
- Internal Teams (Finalization): 2-3 days

This current workflow is insufficient for the fast-paced demands of drug development, particularly in early clinical phases, where quick turnarounds are essential for decision-making.

FUTURE HORIZON

With the implementation of aNCA, we project a significant reduction in the time required for NCA, aiming to automate 80% of the process. This would shorten the workflow to approximately one to two weeks, drastically increasing efficiency and freeing up resources for more value-added tasks. As a result, 50-80% of the process will be handled internally, reducing the reliance on external vendors and improving overall control of the analysis.

PROJECT PURPOSE

The primary objective of the aNCA initiative is to automate and streamline the entire NCA process for both preclinical and clinical studies. In doing so, the project aims to:

- Enhance the speed and efficiency of NCAs.
- Improve data quality and analysis consistency.
- Facilitate “reverse translation” by harmonizing data structures.
- Reduce dependence on external vendors and software providers.

The project is structured around three key pillars:

1. Dataset Request and Automated Data Creation: This pillar focuses on streamlining the process of requesting and creating datasets, ensuring they are ready for NCA analysis.
2. Automated NCA Analysis: Automating the analysis process, including the calculation of key PK parameters and ensuring regulatory compliance.
3. Automated Outputs Creation: Generating comprehensive outputs such as clinical study reports (CSR) and dose-escalation results, ensuring consistency and efficiency across projects.

Through these pillars, aNCA aims to boost productivity, improve analysis control, and enable faster decision-making in drug development.

ANCA DEMO

To demonstrate the capabilities of aNCA, we have developed a video showcasing its functionality. The demo outlines the step-by-step process of automated NCA, from dataset input to final output generation. By automating these steps, the aNCA framework significantly reduces the time and effort required for each analysis, providing faster, more reliable results.

COLLABORATION WITH PHARMAVERSE

In line with our commitment to open-source development, we are in the process of integrating aNCA into the Pharmaverse, a collaborative network aimed at accelerating drug development through shared R packages. By contributing to the Pharmaverse, we aim to encourage wider adoption of aNCA, foster collaboration, and drive innovation in clinical reporting and regulatory processes.

Several organizations, including Appsilon and GSK, have expressed interest in collaborating on this project. We are currently engaged in discussions with the Pharmaverse Council to finalize the integration and ensure that aNCA meets the highest standards of quality and usability.

CONCLUSION

The aNCA project represents a significant step forward in the automation of non-compartmental analysis, offering a faster, more efficient workflow that meets the demands of modern drug development. By reducing reliance on external vendors, improving data quality, and integrating with open-source platforms like the Pharmaverse, aNCA is poised to become a critical tool for clinical pharmacologists and data scientists alike. We invite collaboration from the wider pharmaceutical community to help shape the future of aNCA and its role in accelerating drug development.

CONTACT INFORMATION

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