OVERCOME THE OBSTACLES OF **YOUR DRUG DEVELOPMENT COURSE**

At PhinC Development, we help you identify, mitigate and overcome all the challenges you may face during your drug development process

PhinC Development

SUMMARY

MODELING & SIMULATION TOOLS
ESSENTIAL FOR EVERY CLINICAL DEVELOPMENT

PhinC Development is at your side to speed up your preclinical and clinical development. A specialized team is at your disposal to guide you through all the stages of your project.

It has been a long but exciting way we went through since the creation of PhinC Development. Since the 2000s, disruptive changes in the pharma industry and the emergence of applied Modeling & Simulation techniques have markedly transformed R&D organization. More than ever, we remain a preferred and reliable partner for Biotech companies to bring appropriate use of Pharmacometrics and Modeling to their drug development. Regulations are adapting continuously and agencies recommend more and more their extensive use.

PhinC Development was created in 2008 by experienced founders, upon one main purpose - providing advice and support to pharmaceutical and biotech companies. We are also proud to be at the forefront to promote the appropriate use of Modeling & Simulation. That's why we make a point of ensuring a continuous scientific exchange with the health agencies, the academic centers, the algorithm developers and the learned societies.

Being close to our partners and clients is a top priority, that's why we launched PhinC Modeling. Based in Montreal, Canada, our subsidiary is an important window on the North American market. Indeed this is a great opportunity to strengthen our implementation in the region and get in contact with all the relevant companies. Setting up partnerships with local specialized companies is also among our priorities.

Bernard Orlandini

CEO of PhinC Development.

ABOUT PHINC DEVELOPMENT

PhinC Development is the expert partner for small to medium sized pharmaceutical or biotech companies, who need to move forward in early drug research.

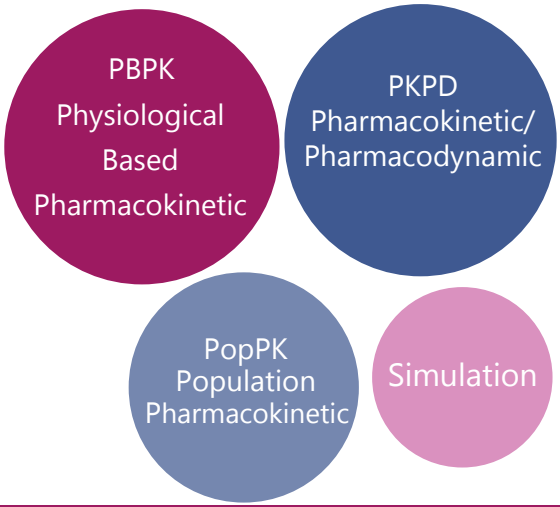
Thanks to a multidisciplinary team with thorough field experience, PhinC Development helps to take the best decisions concerning drug development using all existing pharmacology and pharmacometrics modeling & simulation tools.

PhinC Development offers more rapid and efficient solutions than one-time consulting or CROs.

We design and guide all clinical operations (files, protocols, global development strategy) and coordinate all clinical research actors to optimize your drug development from the drug candidate selection to phase IIb (or later). The application of the MIDD concept «Model Informed Drug Development» will significantly optimize the development of your drug candidate at different levels by:

- Providing essential data on the product under study from the earliest stages of development
- Strengthening scientific justifications during regulatory submissions
- Optimizing time and means to implement

PhinC Development brings you the best MIDD tool at each step to go on to the next step efficiently.



MANAGEMENT

4 founders with over 20 years of experience in the pharmaceutical industry

Bernard Orlandini
President &
Co-founder
--
Early Drug Development Expert

Virginie Gualano
Vice President &
Co-founder
--
PBPK & Pharmacokinetic Expert

Mathieu Felices
Vice President &
Co-founder
--
PopPK/PD & Biostatistics Expert

Eric Evène
Associate Director &
Co-founder
--
Pharmacometrician & Clinical Development Expert

- Pharmacology,
- Biometry,
- Pharmacokinetics,
- Pharmacometry,
- Cardiac safety
- Biostatistics,
- Modeling,
- Bioanalysis,
- FDA, ICH compliance,

At PhinC Development, we aim to place modeling at the heart of drug development.

In our experience, the greatest successes in terms of developing new therapeutic entities have been achieved through programs that have:

- **Developed reciprocal relationships between fundamental and clinical research**
- **Bridged the gap between quantitative pharmacology and clinicians**

Thus, when designing development programs, we seek to strike the right balance between the implementation of clinical trials and the use of Modeling & Simulation approaches. Indeed, on the basis of early data, essential information can be provided earlier in the development process and thus avoid or better anticipate certain clinical investigations.

PhinC Development is an active player regarding the promotion of practices and the use of Modeling and Simulation through the organization of conferences, animation within learned associations, and the training of young Pharmacometricians or the supervision of trainees / PhD students.

WHY CHOOSE PHINC DEVELOPMENT

PHARMACOKINETICS, AN ESSENTIAL BRICK IN YOUR DRUG DEVELOPMENT

Thanks to our clinical vision we guarantee a coherent PK & PD assessment throughout your development.

We bring our PK and EDD expertise to assess project potential and design development strategies

We set-up the PK clinical studies and supervise their good execution

We develop comprehensive analysis for a thorough understanding of the drug PK properties

We deliver state-of-the-art reporting and CDISC compliant PK data

PHARMACOMETRICS, OUR SECRET WEAPON

Pharmacometrics is an emerging science that quantifies drugs, disease, and trial information. Our group of experts integrate clinical pharmacology, pharmacokinetics, and modeling to follow the drug during its development and respond to your challenges.

Modeling ADME

Absorbed by a person eyes, mouth, derm or by injection

ABSORPTION

Distributed in the body through the bloodstream and acts on its target organ

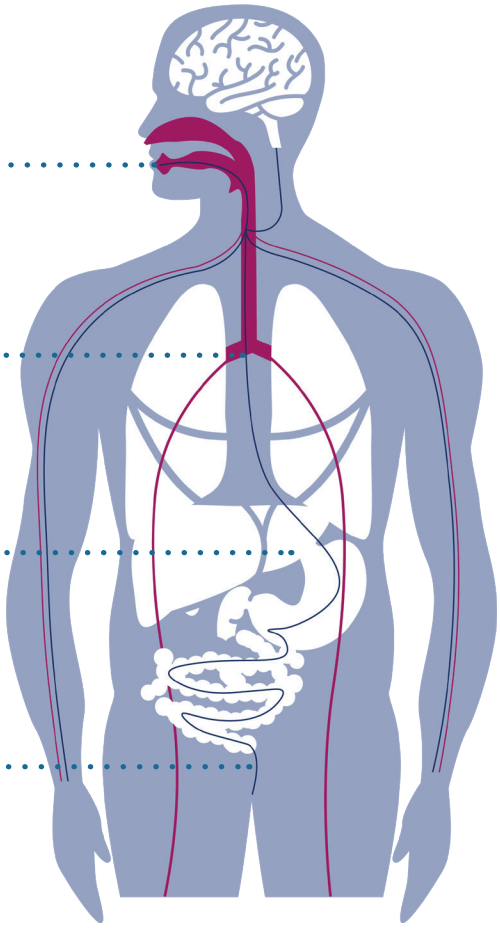
DISTRIBUTION

Transformed (Metabolized)

METABOLIZATION

then eliminated from the body (Excretion)

EXCRETION

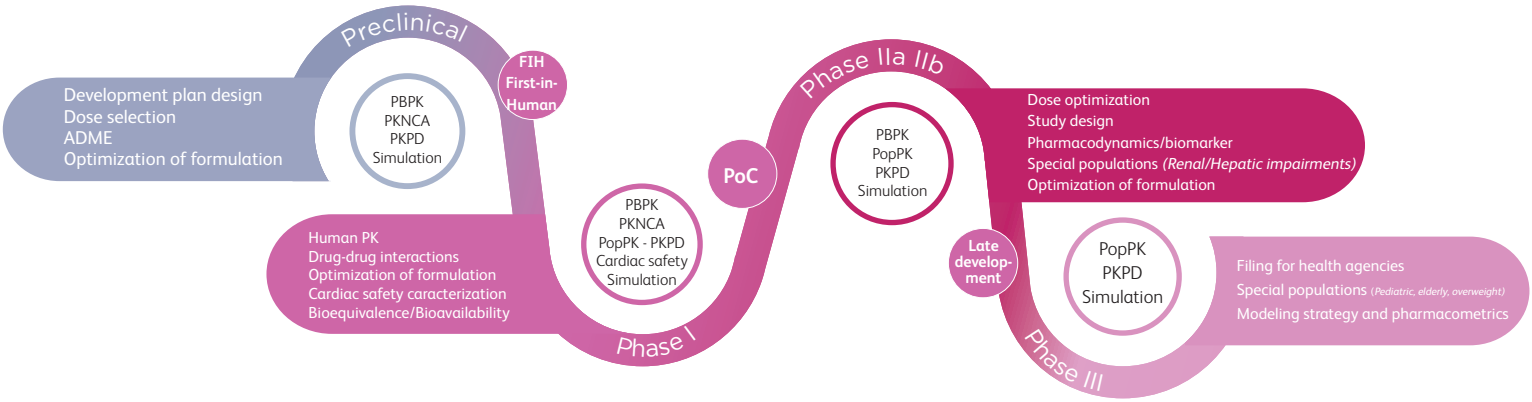


To understand pharmacometrics, think ADME

After drug intake, each step of the drug behavior within the body (ADME) must be well understood to better characterize the drug and accurately determine its optimal and safer dose.
Pharmacometrics use this knowledge in the form of Model Informed Drug Development which uses four main tools: NCA, PK/PD, PBPK and PopPK.

HOW WE DO IT

FROM DRUG CANDIDATE TO PATIENT PROOF OF CONCEPT (PoC)



zoom in (Ctrl +)

MODEL INFORMED DRUG DEVELOPMENT

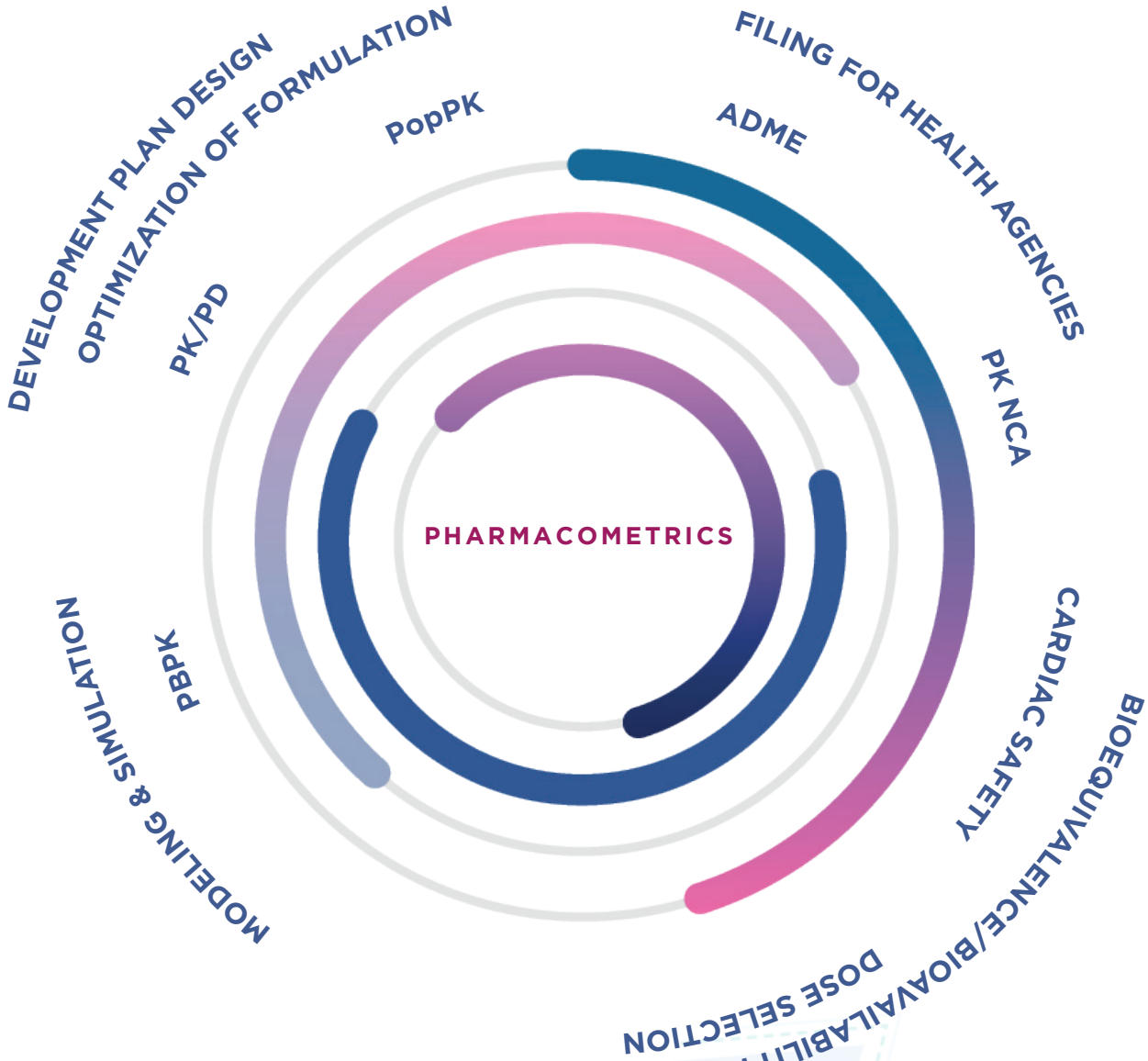
Adapted to Biotech and pharmaceutical companies

PhinC Development offers consultancy and operational management services to bridge the gap between therapeutic lead identification to the clinical stage and to the patient PoC. PhinC Development optimizes your early drug development (EDD) by using an integrated 3 steps strategy:

1. Defining the drug development strategy and deployment plan
2. Implementing Model-Informed Drug Development
3. Bringing value to your Investigational Medicinal Product (IMP)

OUR SERVICES - *Overview*

Drug development is a long-term and complicated process with the involvement of multidisciplinary structures. At PhinC Development, we bring to you Modeling & Simulation tools to help you get through it with serenity.



CHOOSE THE SHORTEST & SMARTEST ROUTE
THANKS TO PHARMACOMETRICS

ADVISING AND CONSULTING

PhinC Development offers more rapid and adapted solutions than one-time consulting or CROs.

PhinC Development is not just a service provider who steps in to solve one of your problems, but rather a partner you can count on to meet your expectations. So beyond a simple intervention, we support you over time while being by your side. This allows us to better understand your needs, respond more efficiently and quickly to your requests.

Thanks to our support and advice, we provide you with essential knowledge and data about the product under study from the earliest stages of development and we allow you to:

- Make the right decisions at the right time
- Speed up your development process
- Anticipate regulatory demands
- Avoid inconsistencies in studies
- Strengthen scientific justifications during regulatory submissions
- Optimize time and means to implement

PhinC Development brings you the best Model Informed Drug Development tools at each step to go on to the next step efficiently.

PhinC Development is your partner of choice for an efficient and rapid development of your project.

PHYSIOLOGICAL BASED PHARMACOKINETIC (PBPK)

Physiologically Based PharmacoKinetic (PBPK) modeling is a mechanistic approach to predict the absorption, distribution, metabolism and excretion of drugs.

This approach is based on different elements:

- Anatomy and physiology of human or animal body
- Physicochemical properties of the drug
- In vitro data on biotransformation
- Transport of the drug

Connecting all this information in one model is possible with PBPK analysis to help you better understand the behavior of your compound and its preclinical and clinical development.

Your company already has data from preclinical studies; your drug candidate has been tested on animals; you have investigated metabolism and transporter in in vitro experimentations: these results allow to go further and start a phase I study on humans.

The PBPK study approach enables you to test in silico different dosing treatments that will be evaluated in first-in-human studies (FIH).

In addition, by avoiding unnecessary trials on healthy volunteers, PBPK can also be considered as the most adapted tool to:

- Evaluate the likely magnitude of a drug-drug interaction
- Determine PK in specific population (Pediatric, Hepatic or Renal Impairment)
- Support the clinical development of a new formulation or a food effect.

The PBPK approach helps you get over many challenges during your drug development

POPULATION PHARMACOKINETIC (PopPK)

This analysis gathers all your clinical data and uses statistical algorithms which allow you to consider all subjects and all timing points.

PopPK is a compartmental method dividing the body into well-stirred hypothetical areas (compartments) for a drug, and considering different sources of variability, using the appropriate mathematical equations.

PopPK allows accurate estimates in:

- Various subject groups, e.g. body, weight, gender, impaired organs, etc.
- Source variability, e.g. food, co-med, time of the day, etc.
- Special population analysis, e.g. elderly, obese, hepatic impairment, renal insufficiency, children, etc.

Using these tools in targeted exposure will lead to:

- Identifying relevant covariates in patients
- Simulating exposure, predicting therapeutic dose, anticipating activity for special populations
- Saving you dedicated studies in special populations
- Coverage of proper dose range
- Phases II and III dose selection rational strength for regulatory authorities

The popPK method and its use of mathematical equiations is a real saver for your clinical development course.

PHARMACOKINETIC PHARMACODYNAMIC (PK/PD)

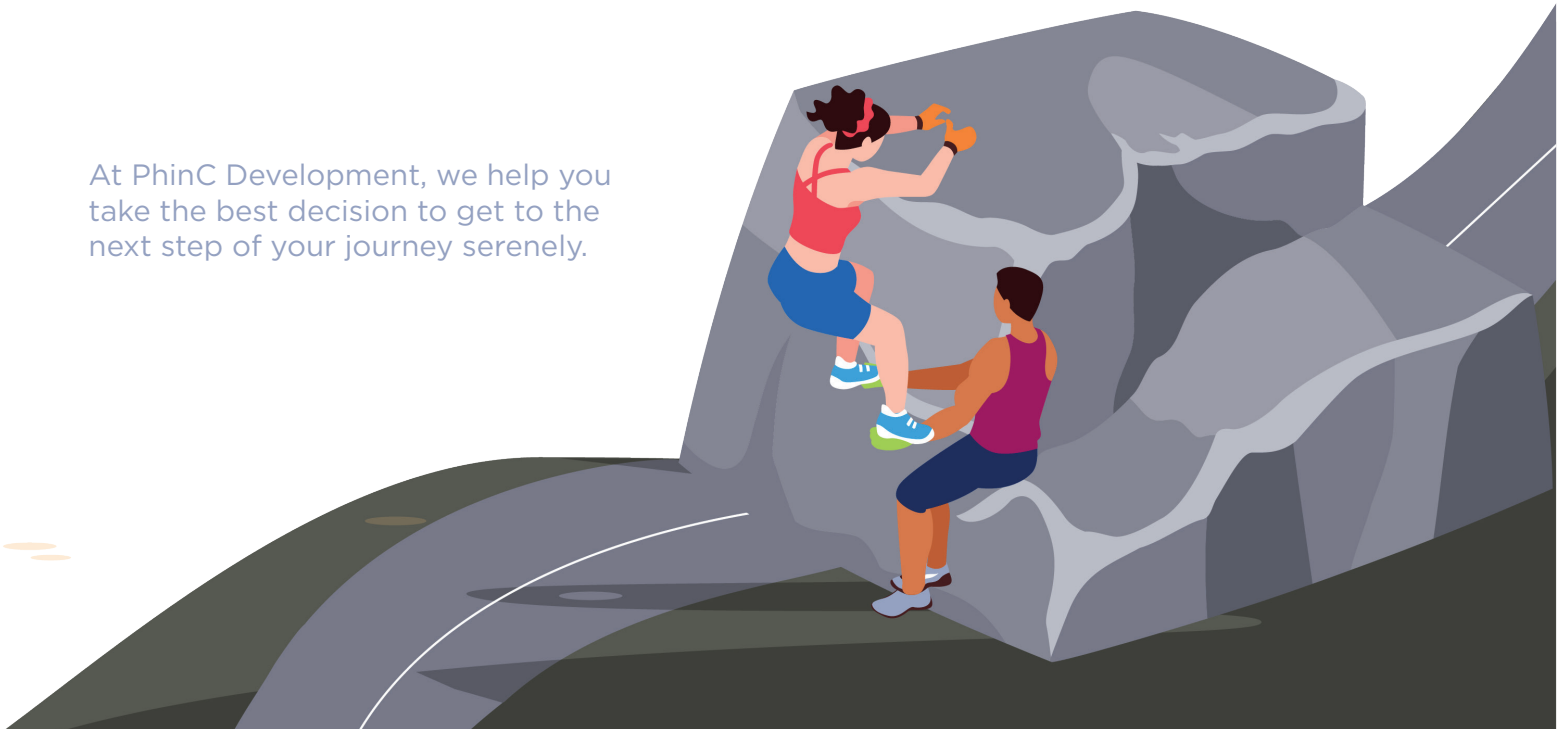
Knowing the relation between exposure and response allows a better dose selection. This helps you to be more efficient by using optimized drug concentrations.

Pharmacokinetic/pharmacodynamic (PK/PD)-modeling links dose-concentration relationships (PK) and concentration-effect relationships (PD), thereby facilitating the description and prediction of the time course of drug effects resulting from a certain dosing regimen. Pharmacokinetic/pharmacodynamic (PK/PD)-modeling is a part of the drug development process, and is a mathematical technique that predicts changes in drug efficacy over time and dose.

Using PK/PD will quantify targeted exposure, which will lead to:

- Phases I and II cohorts number reduction (money, time and patient exposure savings)
- Coverage of proper dose range
- Phases II and III dose selection rational strength for regulatory authorities.

At PhinC Development, we help you take the best decision to get to the next step of your journey serenely.



TQT ANALYSIS FOR CARDIAC SAFETY

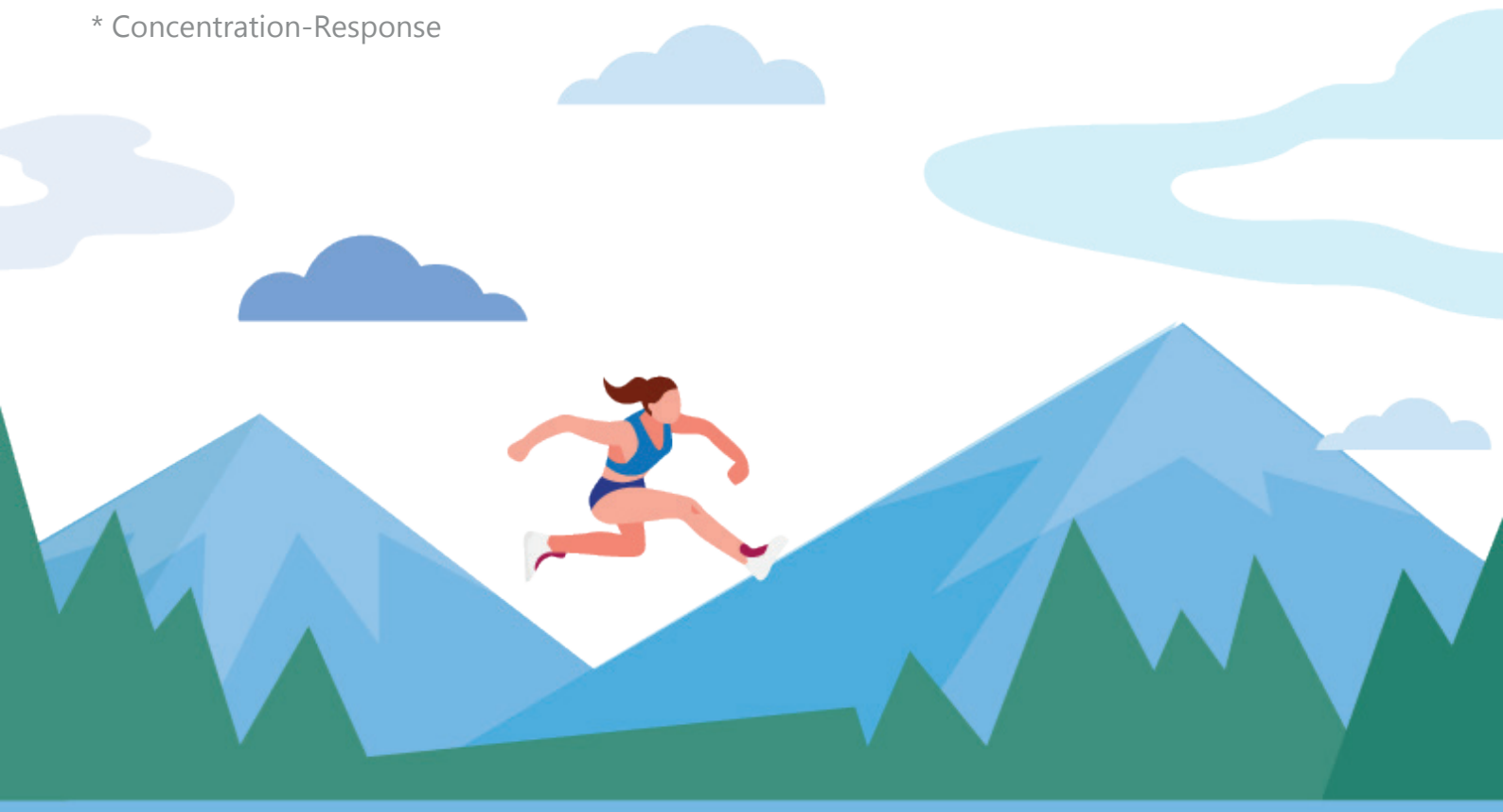
PhinC Development has been pioneer in the use of concentration-response modeling in early phase.

- Use of C-R* models through intensive ECG from FIH to ICH E14 TQT studies
- According to ICH E14 guideline revision in 2015
- Advantage: C-R analysis consider all the ECG collected simultaneously with systemic exposure to the drug
- Use preliminary C-R models, predict QT-interval prolongation and adapt regulatory ECG studies if necessary
- Approach sufficiently powerful and suitable in FIH

In partnership with

BANOOK GROUP

* Concentration-Response



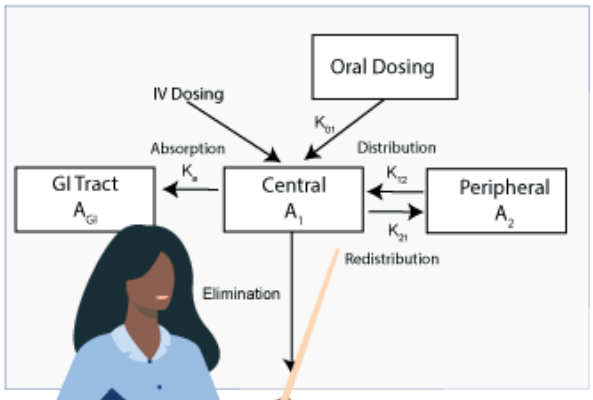
PHARMACOKINETICS STATISTICS

PhinC Development pharmacokineticists provide precise analysis of data, whatever the purpose of your pharmacokinetic (PK) studies.

PhinC Development covers all PK analysis requirements, including:

- Dose and time linearity studies
- Drug-drug interactions
- Gender and age impacts on the drug metabolism and pharmacokinetic (DMPK) of drugs
- Impact of hepatic or renal insufficiency on pharmacokinetic
- Bioequivalence studies

Calculations of PK parameters are performed according to standard international definitions. Calculations are then followed by in-depth interpretation by senior scientists.



CDISC COMPLIANCE

As many sponsors can attest, the preparation of CDISC-compliant datasets is time-consuming and costly. It is important to consider current and future data regulations when planning studies for your development program.

The main challenge is first to efficiently coordinate with all stakeholders in the CDISC process: data management, bioanalysis and regulatory submission.

Hence, **we always suggest involving experienced PK scientists early in the process, to ensure good communications between players and to avoid having the different teams working in isolation**.

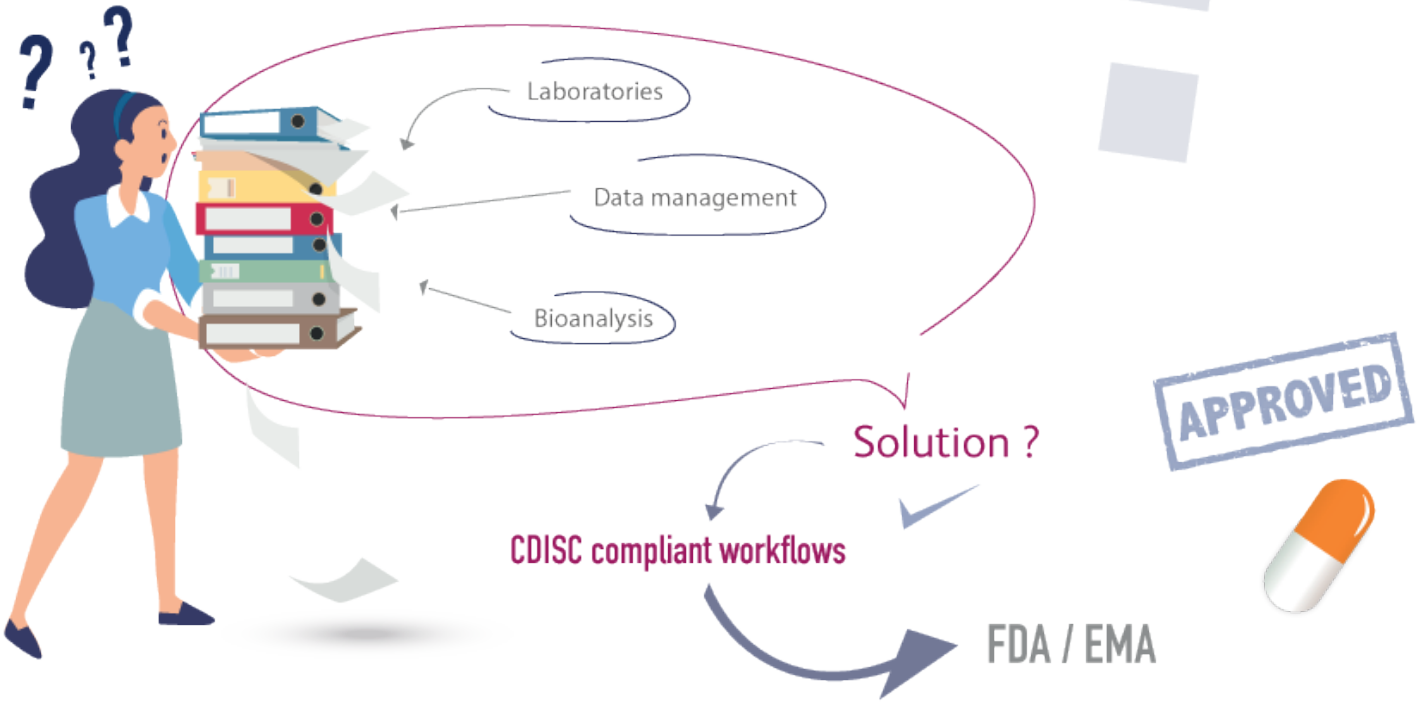
We developed CDISC compliant PK workflows aiming both to consider all the specificities of the PK analyses and to match with the different types of working organization with data management, bioanalysis and regulatory affairs.

Discover our Flow chart for PK Analysis

Some advantages:

- Standardizing analysis and reporting of data
- Facilitating pooling of data for future analyses such as PK population modeling
- Facilitating study data review by regulators
- Improving transferability of study results (including PK)

You are new to standards or new to CDISC?



QUALITY AT PHINC

QUALITY ASSURANCE

Essential for drug developers and health authorities. We have established all the necessary measures to guarantee totally secure data for our clients. We care about information security and physical protection, which is set up, monitored and optimized in strong interaction with our dedicated QA service.

DATA PRIVACY (GDPR)

PhinC Development provides you with permanent control and reliability of Information Technology (IT) which insure you the highest level of data security, from study analysis to archiving. We set up:

- GDPR compliance
- Control access permission
- Competence and maintenance of the servers
- Guarantee of the continuity of the activity using a Disaster Recovery Plan (DRP)

IT SYSTEMS

A policy of validation of computerized systems was implemented as soon as the company was created, following the 21 CFR Part 11 (Code of Federal Regulations) standard (and associated recommendations) and according to the GAMP (Good Automated Manufacturing Practice) guidelines. Thus all of our critical systems are validated and maintained according to the best practices of the industry and current regulatory expectations.

OUR TEAM, MULTIDISCIPLINARITY, EXPERTISE & DIVERSITY

Beyond the wide experience and multidisciplinarity of our scientists, we promote Diversity, Openness and Gender equality.

Any organisation aiming to be truly diverse needs to go way beyond targets and laws relating to equality. Smart businesses know they need diversity of backgrounds, life experiences and viewpoints at every level of their organisation so that they can attract, retain and make the most of people's abilities.

At PhinC Development, our aim is prioritizing diversity and investing resources and training approachs to make sure our teams have all the necessary means to succeed. Hence we:

- Ease access to the team's experience and its multi-disciplinary expertise
- Offer a multiple training sessions
- Provide all the necessary tools to ease the start
- Support throughout the process of initiation to the tools
- Ensure the well-being and safety at workplace

OUR VALUES

The values of a company are moral and societal principles on which the company is based to evolve and make strategic decisions, they reflect its vision. PhinC Development vision is directly inspired by the principles and professional ethics that have bound the 4 co-founders for almost 20 years.

PhinC Development really makes a point of respecting basic ethical guidelines, starting with its commitment to:

- Providing the right level of interpretation of analyses that the company performs and making sure that they are fully understood
- Delivering effective advice and results to our clients in a strictly fair, transparent and confidential manner
- Limiting overall exposure to investigational medicinal products for subjects participating in preclinical and clinical studies
- Being, in our daily practices, compliant with the applicable guidelines (EMA, FDA, ICH, GCP) and quality control practices
- Anticipating and declaring any conflict of interest that might occur

Moreover, we strive for raising awareness, setting an example and leave a positive footprint in this world. Indeed, not everyone has a good opportunity in life and that is why we must act.

In this respect, we are involved with humanitary associations that support the education for disadvantaged children but also help low-income families in Asia.

Furthermore, we are doing our best to reduce our carbon footprint, preserve nature and protect our fragile environment. To this end, at the end of each project, we plant trees to preserve, restore and create forests all over the world in collaboration with *Reforestaction*. We have also limited our movements and mainly use public transports.

CONNECT WITH US!

CONTACT US TODAY TO GET
A QUALIFICATION APPOINTMENT

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