DNDi
Best Science
for the Most Neglected

GARDP

TRANSFORMING ACCESS TO MEDICINES THROUGH INTEGRATED DEVELOPMENT & MANUFACTURING

The DNDi-GARDP CMC platform

Every year, dozens of medicines that are submitted for regulatory approval are rejected—not due to safety or efficacy concerns, but due to shortcomings in the manufacturing development of the final drug product. The result is that medicines which are proven to be clinically effective are not available to people who need them. This is a common occurrence when drug developers fail to prioritize a critical component of research and development (R&D) known as chemistry, manufacturing, and controls, or CMC.

> "Minute details in medicine manufacturing can have serious consequences on the quality of a product and its regulatory approval. Even if the science behind a product is solid, it is critical to consider the chemistry, manufacturing, and control of the product early in R&D to ensure the final product is quality-assured."
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> **Dr Jicui Dong**
> Unit Head, Product Policies, Access and Manufacturing Support Unit, WHO

CMC involves the design, development, and scale-up of manufacturing processes for drug substances (e.g., active pharmaceutical ingredients, or APIs) and drug products (e.g., final tablets or granules). Implementing a robust CMC plan that is integrated into the scientific research and development of a drug is crucial to successful regulatory approval as well as to efficient and cost-effective manufacturing and access to a future product. CMC also plays an essential role in adapting drug formulations for the specific needs of patient groups like children and women, and for low-resource settings.

As non-profit organizations, DNDi and GARDP are leading the way in utilizing CMC expertise to advance the development, formulation, and delivery of treatments for neglected diseases and bacterial infections. While pharmaceutical companies may integrate CMC into their processes to ensure product quality and regulatory compliance, DNDi and GARDP have joined forces to apply CMC excellence and fill gaps in R&D and commercial models to address the unique needs of underserved populations. Through the joint DNDi-GARDP CMC platform, these organizations focus their resources and collaborative efforts on therapeutic solutions that are neglected by the commercial sector.

Jointly hosted by DNDi and GARDP, the CMC platform leverages the expertise and networks of two non-profit organizations to advance the cost-effective development and manufacture of safe and affordable medicines for neglected tropical diseases and bacterial infections in high-burden populations. The platform's team of staff works closely with a global network of experts to execute a wide variety of projects bridging product development and access for both repurposed drugs and new chemical entities.

THE DNDI-GARDP CMC PLATFORM: INNOVATION AND QUALITY ASSURANCE IN DRUG DEVELOPMENT & MANUFACTURING

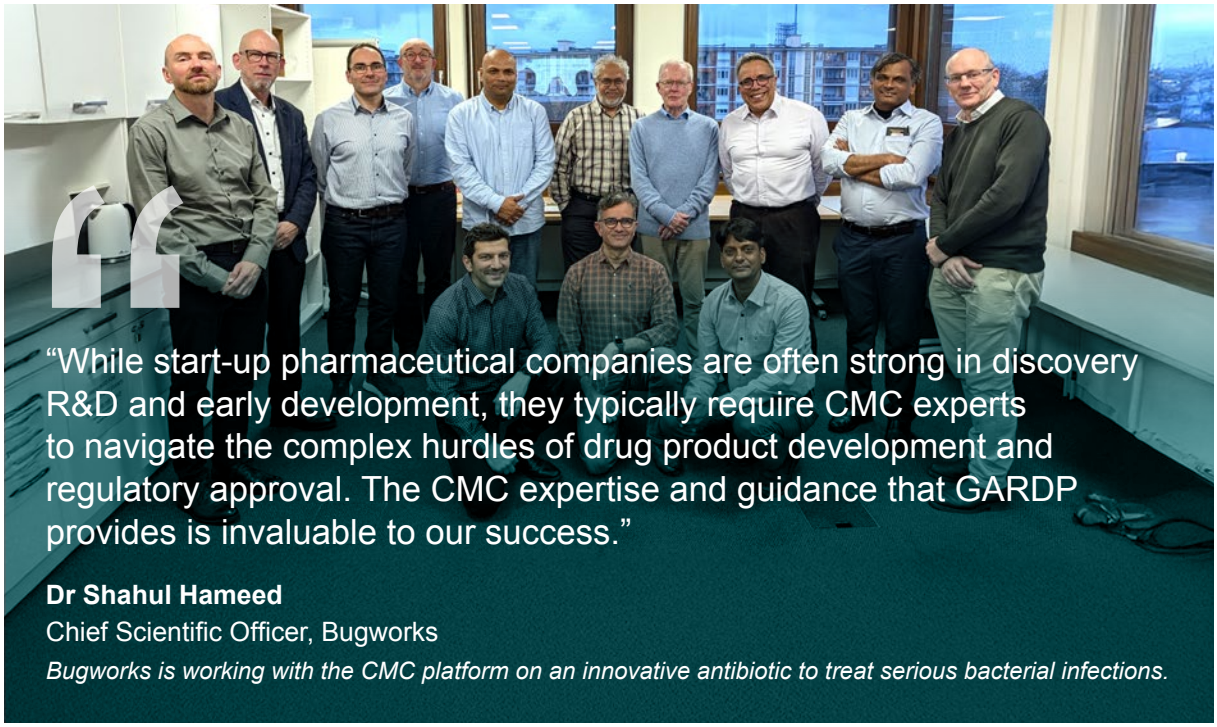
Types of pharmaceutical products

- APIs, investigational product
- Commercial product for registration
- Industrial product for distribution

1. Provide CMC expertise throughout product development
2. Design and develop adapted formulations
3. Ensure rigorous manufacturing (clinical trial supply, commercial product, technology transfer)
4. Develop quality-assured and cost-efficient manufacturing processes
5. Support for registration, prequalification and/or inclusion in treatment guidelines

- **Safe, affordable, and accessible treatment formulations**
- **Quality-assured regional manufacturing**
- **Authorization by health regulators**

The platform serves the R&D portfolios of both organizations across product development and access, enabling cost-saving synergies and the replication of best practices at every stage. The platform also addresses a crucial need by providing its services to select private sector partners and other not-for-profit organizations, which may have limited capacity and experience in formulation development and cost-efficient manufacturing practices, including low-volume production for neglected patient populations.



"While start-up pharmaceutical companies are often strong in discovery R&D and early development, they typically require CMC experts to navigate the complex hurdles of drug product development and regulatory approval. The CMC expertise and guidance that GARDP provides is invaluable to our success."

Dr Shahul Hameed
Chief Scientific Officer, Bugworks
Bugworks is working with the CMC platform on an innovative antibiotic to treat serious bacterial infections.

PLATFORM ACTIVITIES

1 **Provide CMC expertise throughout product development**

Potential treatments in development may demonstrate therapeutic efficacy, but lack a viable path to becoming affordable and accessible therapies for patients worldwide. The CMC platform helps identify which drug candidates have the greatest public health potential, and it contributes to decision-making at pivotal stages in the development process through development cost evaluation, commercial cost-of-goods analysis, and market landscaping.

2 **Design and develop adapted formulations**

The right formulation is critical to drug safety and efficacy, as well as patient access. The CMC platform selects and adapts formulations that are practical to administer in low-resource settings and appropriate for key patient groups.

3 **Ensure rigorous manufacturing (clinical trial supply, commercial product, technology transfer)**

The majority of medical products are manufactured in a handful of countries, leaving some regions especially vulnerable to shortages. The CMC platform works with manufacturing partners in underserved regions to establish and scale up manufacturing processes, including through technology transfer, to bolster affordable regional supply.

4 **Develop quality-assured and cost-efficient manufacturing processes**

Neglected diseases and treatments for vulnerable groups often have small patient populations that require low-volume drug production. The CMC platform develops and optimizes manufacturing processes that are appropriate even for low volumes, helping to reduce manufacturing costs and potentially improve affordability for patients and health systems. The processes adhere to good manufacturing practice (GMP) and environment, health, and safety (EHS) guidelines, including quality control procedures and responsible waste disposal.

5 **Support for registration, prequalification and/or inclusion in treatment guidelines**

There are several avenues to enable access to products in the DNDi and GARDP portfolios, including: 1) direct submission to national regulatory authorities; and 2) submission for WHO Prequalification (PQ) to facilitate access in countries participating in the WHO PQ collaborative registration procedure. The CMC platform furnishes essential information to support both submissions as well as update treatment guidelines.

OVERVIEW OF THE DNDI-GARDP CMC PLATFORM

Why is this platform needed?

Basic CMC is integral to all drug manufacturing development, but additional CMC investments are needed to address the unique needs of underserved populations.

What does the platform do?

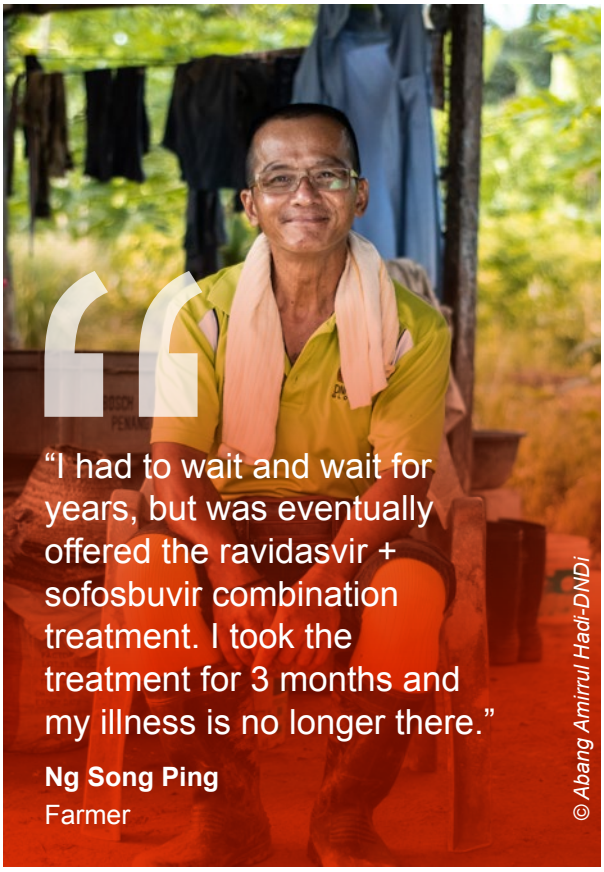
It carries out CMC activities to support the development and manufacture of investigational, commercial, and industrial drug products in DNDi's and GARDP's portfolios. It also provides its services to select private-sector partners and other not-for-profit organizations.

The ultimate goal?

To deliver safe, affordable, and accessible treatments for patients suffering from neglected tropical diseases and bacterial infections.

CASE STUDY 1
ACCELERATING PATIENT ACCESS TO A NEW HEPATITIS C TREATMENT

Hepatitis C is one of very few diseases that could be eliminated globally with tools that exist today, provided there is political will to do so. Although new safe and highly effective direct-acting antivirals (DAAs) for hepatitis C have been available since 2013, these products have largely been unaffordable for patients in low- and middle-income countries. DNDi partnered with Egyptian and Malaysian pharmaceutical companies to develop, scale up, and register ravidasvir, a new DAA for hepatitis C. The CMC platform provided technical expertise for product and process development, clinical trial supply, registration dossier preparation and CMC interactions with regulatory agencies. Ravidasvir was registered and first launched in Malaysia in 2022, and is now included in the World Health Organization's Essential Medicines List.



CASE STUDY 2
TECHNOLOGY TRANSFER TO ENABLE ANTIBIOTIC ACCESS

Although low- and middle-income countries tend to shoulder the greatest burden of drug-resistant infections, they often lack access to the "last-resort" Reserve antibiotics that can treat such infections. In 2022, the Japanese pharmaceutical company Shionogi signed a voluntary license and technology transfer agreement with GARDP to enable the manufacture and commercialization of cefiderocol, a Reserve antibiotic for adults with certain Gram-negative bacterial infections who have limited treatment options. The CMC platform is collaborating with CHAI on a technology transfer from Shionogi to GARDP's manufacturing sublicensee in India, Orchid Pharma. The platform has provided critical support to establish and scale up the drug development (API and final product) and manufacturing practices to enable access to quality-assured cefiderocol in a range of low- and middle-income countries.