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# Cell and Gene Therapy Center of Excellence Overview

July 2024

better solutions. innovative partners.

# Introducing the Research Consulting Organization (RCO): the new standard for success

## soaring beyond CRO

**We revolutionized the traditional model,** creating an entirely new system that redefines what's possible for you and your organization.

## custom by design

One size has never fit all. We're here to finally offer a custom alternative that fits your unique needs.
**A+ solutions scaled to your size.**

## excellence through innovation

Our industry is constantly changing, and if you don't evolve, you'll be left behind. **We've innovated a process that suits today's needs.**

## strategy-led solutions on a global scale

**We're changing standardized to strategized.** Our global reach powers the insights that are the key to your success.

- regulatory sciences
- clinical research solutions
- quality & compliance
- pharmacovigilance solutions
- medical information
- R&D technology

**1,160+** specialized degrees

**1,000+** active biotechnology, pharmaceutical, medical device, and diagnostic clients

**3000+** professionals

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# Cell and Gene Therapy Center of Excellence

## Cell and Gene Therapy COE team helps clients around the world accelerate their novel, advanced therapeutic products to the market

- Reducing Risk
- Ensuring Compliance
- Accelerating Access for Patients
- Ability to staff up with speed- locally and globally

### North America

Windsor, Ontario, CA
Bozeman, Montana, US
• Chicago, Illinois, US (3)
Ft. Washington, Pennsylvania, US
• Raleigh, North Carolina, US
San Diego, California, US
Washington, D.C., US

### Europe

Berlin, DE
Dublin, IE
Amsterdam, NL
Leiden, NL
Malmo, SE
Stockholm, SE
Buckinghamshire, UK
Cambridge, UK
Harlow, UK
• London, UK (2)
Richmond, UK

### Asia-Pacific

Hyderabad, IN
Melbourne, AU
Tokyo, JP

• Flagship Office

# Cell and Gene Therapy **Experience**

**Your partner for the development of advanced and novel therapies**


## Program Types

- CAR-T cells (autologous and allogenic),
- TILs (Tumor-infiltrating lymphocytes)
- AAVs, dual AAVs
- Gene-editing
- Vector-based gene transfer
- Stem cells, MSC and iPSCs
- Therapeutic vaccines
- Tissue engineering products
- γδ T cells

.

## Services

- Planning, Sourcing, Clinical development, Technology, Auditing, Reimbursement, Medical & Pharmacovigilance
- Scientific Advice with EMA, MHRA, PEI, MEB, etc
- ITF and INTERACT meetings
- Priority Medicines (PRIME) and Orphan Drug Designation (ODD)
- Genetically-modified Organism (GMO) applications
- (Conditional) marketing authorisation applications

## Therapeutic areas

- Oncology, hemato-oncology, tissue-agnostic indications
- Hematology: hemophilia B, hemophilia A, thalassemia, sickle cell disease, porphyria
- Inherited retinal disorders (IRDs)
- Autoimmune diseases
- Other rare diseases: paroxysmal nocturnal hemoglobinuria (PNH), phenylketonuria (PKU), GM2 gangliosidosis, Krabbe disease, etc

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# Consultants

# Paula van Hennik

**Group Head Medical and Regulatory Sciences**

https://www.linkedin.com/in/paula-van-hennik-O2454959/

- **Regulatory affairs – alternate CHMP member on behalf of the Dutch Medicines Evaluation Board** – *6.5 years experience*
  - ✓ In this committee, deciding on benefit/risk of (extension of) European marketing authorization applications and extensions, oncology, hemato-oncology and part of the benign hematology products were part of the portfolio, which included advanced (gene and cell) therapy products.
  - ✓ Specifically on cell and gene therapy: CAR-T cells, adoptive T-cell therapy, AAVs, lenti-viral based gene therapy.
  - ✓ Regulatory strategy from early development up to approval, amongst others EMA Scientific advice, Priority Medicines (PRIME) designation, (clinical) development plans (including PIPs), review of clinical trials protocols.
- **Regulatory affairs - (senior) clinical assessor at the Dutch Medicines Evaluation Board** – *4.5 years experience*
  - ✓ Focus on **Oncology** products, including **cell therapy** products.
- **Post doc and research group leader** – *3.5 years and 7 years experience, respectively*
  - ✓ Sanquin, Division Research, Amsterdam, The Netherlands.
  - ✓ Topic: molecular mechanisms of hematopoietic (stem) cell migration. Award of several competitive public research grants.
- **PhD** in Hematology (Medical Faculty, Erasmus University, Rotterdam, The Netherlands) on *in-vivo* and *in-vitro* hematopoietic stem cells assays.

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## Robert Beall, PMP
## Vice President Cell and Gene Therapy Center of Excellence

Robert Beall, PMP @LinkedIn

Program and Project Management

- Manage global expansion efforts of the first globally approved CAR T Therapy
- Manage GMP design build for Gene Therapy Center
- Business plan for NIH Center for Cellular Engineering
- Business plan for NIH Center for Molecular Diagnostics Centers
- Business plan for cell therapy centers for regional hospitals
- Support development of hospital exemption for cell therapy
- Program and project planning for automated cell expansion platform
- Risk management for CDMO Cell and Gene Therapy manufacturing center build
- Remediation management for media manufacturer
- Lead author for ISPE's Good Practice Guide to Process Validation

**Simona Guidi**
**Senior Consultant**
simona@linkedin

Subject Matter Expert for CGT development & early stages.

- CMC and regulatory support for clinical development of CGT (cell, gene therapy and tissue engineered products)
- CGT Process&Analitical development support
- Support for design and compliance of CGT manufacturing sites
- Validation strategy design for CGT processes
- CGT CDMO selection and auditing

*Specific expertise: CAR-T, CAR-NK cells, iPSCs, Mesenchimal Stem/stromal Cells (MSCs) various sources, Liver Stem Cells (hLSCs), Neural Stem Cells (hNSCs), Adipose derived-Mesenchimal Stem/stromal Cells genetically modified, Viral Vectors for ex-vivo application, Keratinocytes, Fibroblasts and Chondrocytes on scaffold, Dendritic cells-based vaccine, Tumor educated macrophages (TEMs), Cardiac progenitors cells (CPCs).*


## Eleonora Casucci
## Vice President Quality and Compliance EU/UK/India and CEO of ProPharma MIA License B.V.

Eleonora Casucci@LinkedIn


- **Business Leader** – *5 years experience*
  - ✓ Business expansion in various geographies (EU, UK and India) and areas of expertise, amongst which Cell & Gene, Batch certification under ProPharma MIA in EU and UK, Clinical trial supply management.
- **Manager of Quality Assurance Operations and Qualified Person** – *8 years experience*
  - ✓ Blood and plasma products, orals dosages, sterile, biologics and gene therapy products for clinical studies
- **Validation Scientist** – *3 years experience*
  - ✓ **Process Validation for oral and sterile API**
  - ✓ **Validation Manager for newly constructed IMP cleanrooms and laboratories**

*Specific CGT expertise: DNA vaccines.*

**MSc in molecular biology**: thesis on design and development of a FISH's (Fluorescent In Situ Hybridization) assay application for quantification of identified bacterial cluster in wet samples

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# Service Overview

- Regulatory
- CMC
- Quality

# European Regulatory Science

**30 years of proven experience and success in European regulatory affairs**

- >10 MAAs per year → centralized, national, DCP, MRP
- >20 scientific advice meetings per year
- >100 CTA/IMPDs prepared and submitted per year

**45 new full service clinical trials per year**

**Frontrunners with CTIS with proven success**

**Demonstrated experience in medical writing, ensuring accuracy, consistency, and compliance**

- Strategic, responsive, and flexible medical writing / editing project support
- Protocol, IB, PIS/ICF, CSR, clinical disclosures
- Briefing package, ODD, PIP, MAA, SmPC

**Long-term client relationships with +80% work from repeat clients**

## ProPharma offers the leading breadth and depth of scientific knowledge of European regulatory frameworks needed to meet its clients' business objectives

# US Regulatory Science

## 40 years of FDA Regulatory Experience

Submissions include but are not limited to:

- FDA Meetings (Pre-IND, End of Phase 1/2, Pre-NDA, Type A, Type C, Type D, INTERACT, etc.)
- Drug Submissions (INDs and NDAs/BLAs)
- Medical Device Submissions (510(k), *De Novo*, PMA)
- Request for Designation
- Orphan Drug Designation (ODD) Applications
- Maintenance Submissions (Annual Reports, etc.)
- Post Approval Submissions (CBE-30, PAS, etc.)
- Risk Evaluation and Mitigation Strategy (REMS)

***Each year we conduct/submit approximately:***

*30 formal meetings with the FDA*

*12 medical device submissions*

*6 NDAs/BLAs*

*6 INDs*

*6 ODD applications*

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# European Regulatory Development Capabilities

## Clinical Trial Authorisation (CTA)

- Drafting and submission of the CTA and IMPD
- Responses to questions
- Ethics and GMO submissions
- Protocol and study report writing

## Scientific Advice

- Priority Medicines (PRIME), ITF & ILAP
- Briefing book (nonclinical, clinical and CMC)
- CHMP and national agency advice
- Support and preparation for agency meetings

## Cell and Gene Therapies

- Complete regulatory, nonclinical, clinical and CMC support
- ATMP classification, RMAT designation, plus INTERACT and ITF meetings

## Regulatory Strategy/Roadmap

- Existing precedent for approvals
- Overall registration, orphan and paediatric strategy; exclusivity planning
- Submission planning and gap analysis

## Paediatric Investigation Plans

- Overall content and strategy (clinical, nonclinical and CMC) – waivers and deferrals
- Responses to questions
- Modifications and compliance check

## Orphan Designation

- Prevalence Assessment
- Dossier drafting and responses to questions
- COMP scientific advice
- Similarity and significant benefit assessment & maintenance strategy

## Marketing Authorisation Applications

- All pre-submission activities
- Pre-submission Agency meetings
- Global CTD Modules 1–5 medical writing – including clinical, nonclinical and CMC
- Procedure and responses to questions

## Chemistry, Manufacturing & Controls

- IMPD drafting; IND to IMPD conversion
- Scientific and technical support, including gap analysis and overall strategy
- Work across regulatory submissions – paediatric, orphan, scientific advice CTAs etc.
- Compile Module 2.3 and 3 content for the MAA
- Provide technical and regulatory expertise within technology transfer projects
- Expertise across small molecule, biologics, vaccines, gene therapy, cell therapy and other innovations

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# Trusted Partners to Deliver Successful Outcomes

Number of CMC Due Diligence Projects/Year — 2+

Products Supported to First GMP Batch/Year — 5+

IMPDs/Year — 5+

CMC Scientific Advice Conducted/Year — 10+

CDMO Selection Projects/Year — 6+

Tech Transfer Projects (inc. CMO | CDMO | CRO Selection) — 200+


150+ — Total Number of Products Supported in the Past 2 Years

80+ — Total Number of Biological Products Supported in the last 2 Years (peptides, proteins, vaccines, ATMP, combination therapies)

70+ — Number of Small Molecules supported in last 2 years

50+ — Number of Validation Studies (Analytical | Process)/Year

20+ — Validation Master Plans/Year

1K+ — Number of Collective Risk Assessments (Elemental | Tox Impurities | Process | Nitrosamines, etc.)

**ProPharma's EU/UK-based team of 35+ experienced CMC consultants brings unparalleled expertise to every client and project, averaging 20+ years of experience in local/global pharma | agencies | CMOs and 5+ years in consultancy services**

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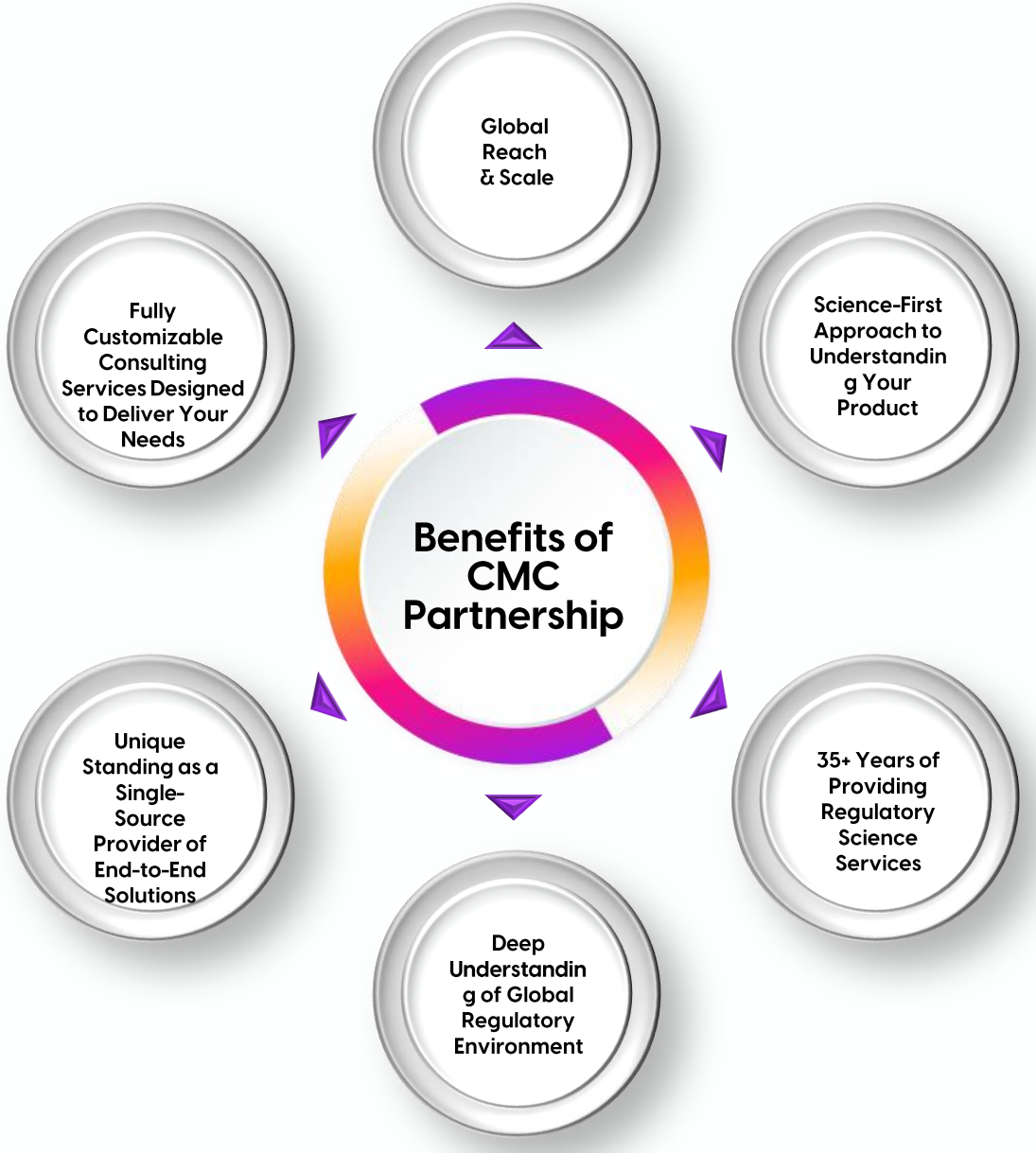
# 360° CMC Capabilities

- Guidance and Advice to Enable Process and Formulation Development + Analytical Development
- Process Optimization Expertise, Scale-Up and Quality by Design
- Expertise and Experience with the Facility, Equipment and Process Validation Lifecycle
- Leadership and Contributions with Technical and Regulatory Expertise within Technology Transfer Project
- Drive and Support the evaluation of Suitable Contract Research Organisations (CROs) and Contract Manufacturing Organisations (CMOs)
- Conduct Due Diligence and GxP Audits
- Support Compilation of Briefing Books for Scientific Advice(s) during Different Development Phases
- Prepare, Coordinate and Participate in meetings with Health Authorities
- Perform Regulatory CMC Gap Analyses and Strategy
- Mitigation and Remediation to Assure Regulatory Compliance
- Compile and Review CMC Documentation throughout Different Phases of the Product Lifecycle
- Support Regulatory Submissions for Clinical Trial Applications (IMPD, IND), Aarketing Authorization Applications (BLA, NDA & MAA), and Post-Approval Activities, including Line Extensions



# Quality and Compliance Consulting Service

## Custom-tailored approach according to your needs and goals. Our expertise and experience mean you can expect "quality the first time".

### Compliance and Quality Assurance (CQA) Services

**Global GxP compliance and qualification audits (including Data Integrity and CSV)**
- All GxP areas supported, global capabilities –we can take care of your complete audit schedule

**Mock Regulatory Inspections; Mock audits, Training and Remediation**
- Our success rate with inspections speaks for itself

**GxP QMS GAP analysis, SOP development, optimization and management**
- Offer includes an eQMS solution
- A compliant QMS is a critical element for obtaining a MIA and WDA

**Scalable QA resources**
- Can run your entire QA unit or provide you with QA resources to supplement existing QA team

PROACTIVE ⟷ REACTIVE

| Preventive | Maintenance | Remedial |
|---|---|---|
| • Quality Gap Analysis<br>• Vendor Qualification<br>• Mock PAI / Readiness<br>• Internal Audit | • Standard Audit<br>• GCP<br>• GMP<br>• GDP<br>• GVP<br>• CSV<br>• Other | • For-Cause Audits<br>• Consent Decree Support<br>• Respond to Regulatory Authority Observations |

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