Biannual newsletter
September 2024

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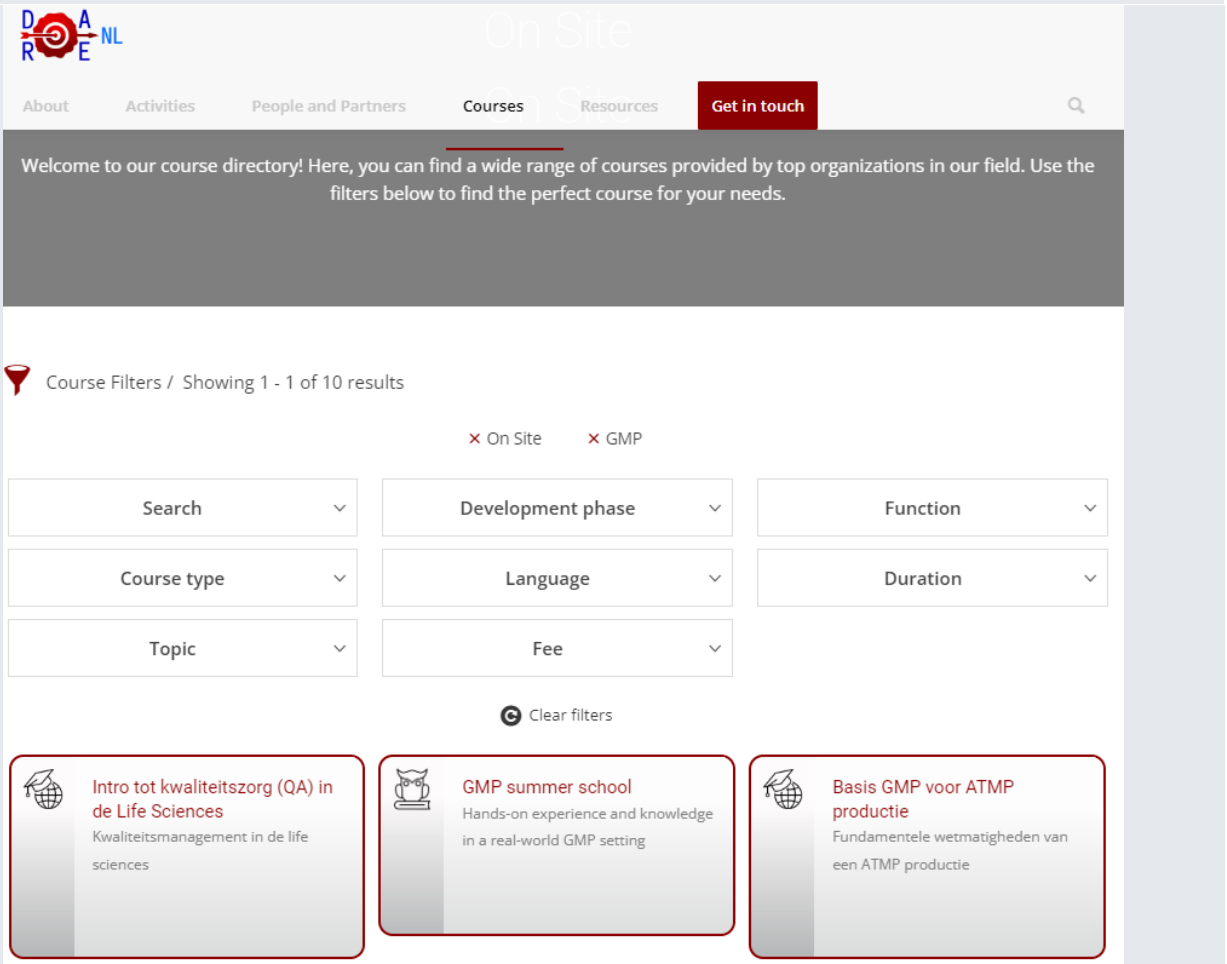


Online ATMP education tool launched

We are thrilled to announce a new online resource for ATMP professionals developed in WP1. This ATMP education tool is designed to streamline your search for high-quality training courses and make your professional development journey more efficient and tailored to your specific needs. The education tool offers a detailed inventory of ATMP courses from around the globe. Each course is catalogued with a description, link and details regarding location and costs.

Whether you are a scientist looking to improve your practical skills, a pharmacist seeking to expand your knowledge of regulatory aspects, or a patient representative aiming to deepen your understanding of ATMP development, our tool allows you to quickly find the most relevant courses by filtering based on topic, profession, product developmental stage and more.

In our commitment to providing the most comprehensive and up-to-date resource, we invite you to **share any useful courses**, workshops and trainings that may not yet be included in our inventory by filling this form. Your contributions will help us enhance this tool, making it an even more valuable asset for the ATMP field.

We also encourage you to **leave reviews** on the courses you attend. Your feedback will play a crucial role in prioritizing and ranking courses based on their relevance and content quality. This community-driven approach helps maintain a high standard of education and ensures that the most valuable courses are highlighted.

Spread the word & happy learning!

DARE-NL consortium meeting 2024

The second consortium meeting on 20 September was attended by 155 participants from organizations such as Dutch and Belgian academia, CBG, IGJ, FAST and >20 companies. Eleven companies sponsored the meeting and attended in person, providing live demonstrations. Check out the pictures for an impression.

Engaging presentations on novel therapies, quality control and education were followed by interactive discussions between expert panels and the audience, including the patient and scientific advisory board members. The expert roundtable discussion also facilitated a stage for connection between academia, industry, regulatory authorities and many more professions present. The key take aways will soon be shared with all attendees and members.

The DARE-NL team also convened on 19 September to evaluate project progress, which involved impactful discussions with many actions items that we will follow-up on. Thanks to everyone involved for your contributions to the project!

The meeting was an excellent opportunity to network, exchange ideas and spark new collaborations to shape the future of ATMP development in the Netherlands. Excited about the synergy the DARE-NL meeting has empowered, preparations have again started for the meeting next year. Let us know if you have ideas or would like to contribute in any way!

DARE-NL progress highlights

WP1: Setup of DARE-NL data, training and valorization platform

Lead: Emma de Pater, Erasmus Medical Center

The ATMP education platform is under development

The overview of available ATMP-related courses based on interviews and meetings in DARE-NL has been combined with an overview prepared by the ISCT, sorted by product development phase as well as profession and published as an interactive tool on the DARE-NL website. The tool will be most valuable for the ATMP community and beyond if it represents an up-to-date courses collection – so submit new courses –, becomes commonly used – so spread the word – and provides course evaluations – so **leave reviews** for courses you have followed.

A collaboration with Hogeschool Avans has been setup to develop courses tailored to ATMP developers. A national ATMP workshop for and by operators is organized with ATMP operators from all centers that develop ATMPs.

A business plan for a sustainable DARE-NL infrastructure is in development

A draft DARE-NL sustainability model has been discussed with the IP

management committee and KWF and sent for feedback to the SC, SAB and PAB members. Valuable input was provided at the evaluation meeting on 19 September and will be further worked out.

WP2: Harmonizing GMP processes for the manufacturing of cancer-specific ATMPs

Lead: Trudy Straetemans, University Medical Center Utrecht

Harmonized qualification documentation starts to take shape (WP2.1/2.2)
The **qualification of suppliers** is an ongoing process and will be continued based on the information present in the ATMP working party. Suppliers used by at least three centers have been audited within the ATMP working party since before DARE-NL started. The reports from these audits have been transferred to DARE-NL Zenya. A harmonized procedure for the qualification of suppliers is also available in Zenya. The procedure for raw material risk assessment has been finalized and will be available for authorization in Zenya soon.

The first harmonized procedure has been published (WP2.3)
Lists of generic procedures and common equipment have been collected, discussed and published in the shared MS Teams environment. The first **harmonized standard operating procedure** on excursions of environmental monitoring has been finalized. The next procedure selected to harmonize is the Aseptic Process Validation policy, for which the writing and reviewing procedure is ongoing.
A template to share **inspection results** has been finalized: all inspections are scheduled, filled in the form template, reviewed by another center and elaborated upon request. Data from the most recent inspections have already been shared.
A **survey on ATMP facilities** organization and technologies was setup together with GoCART, T2Evolve, EBMT and NXTGEN-hightech and run by

the EBMT from June - September. The analyses will be shared for publication by the teams involved.

WP3: QC harmonization and assay development

Lead: Inge Jedema, NKI/AVL

Development and implementation of QC assays is ongoing (WP3.1/3.2)
The overview of QC assays currently used, outsourced and (centrally) desired has been finalized and will be shared in Zenya. Validation of the **cell counting** method was chosen as the first method to be validated. This will start with a validation of the manual (hemocytometer) method, including a comparison of the accuracy of the method execution by different labs using beads as reference sample. The next step will be the validation of automated cell counting method(s) according to the new EP 2.7.29 guideline. NKI and Radboudumc have created a draft template, the first part (including assessment of comparability of accuracy of manual counting method with reference beads) having been performed over summer.
An overview of existing round robin quality assessments (e.g. TBNK flowcytometry) will be made to assess what can be leveraged and what needs to be developed.

Inventory of QC requirements in the EU, USA, and UK is ongoing (WP3.3)
The leaders of WP3, WP6 and WP3.3 had a brainstorm meeting on how to **streamline the interaction** with EMA and national authorities like CBG. Marcel Hoefnagel (CBG) presented on this topic at the DARE-NL consortium meeting on 20 September. A connection was initiated with Join4ATMP, a new European consortium with similar interests.

WP4: Setup of a Dutch academic GMP vector manufacturing platform

Lead: Edwin Bremer, University Medical Center Groningen

GMP-ready lentiviral production platform is under development (WP4.1)
Generation of the master cell bank (MCB) and working cell bank (WCB) and adaptation of HEK293 producer cells to high density bioreactor culture have been completed. Tech transfer for MCB/WCB manufacturing has been initiated. QC testing for MCB/WCB will be outsourced. The transfer plasmid has been designed and is distributed among interested DARE-NL partners. **Tech transfer** of LV manufacturing to GMP facility has been initiated.

Successful establishment of GMP-ready retroviral production platform (WP4.2)
A production cell line and plasmid with full freedom to operate (FTO) have been established preGMP; **GMP transfer** is ongoing.

Establishment of process controls is under development (WP4.3)
The majority of QC tests for the lentiviral vector is performed in-house; adventitious virus will be outsourced.

WP5: Identification and implementation of new technologies for the development and GMP-compliant manufacturing of ATMPs

Lead: Harry Dolstra, Radboud University Medical Center

Roadmap for new technologies implementation is under development (WP5.1)
Inventories of technologies and reagents currently used and developed for non-viral ATMP engineering have been shared in Zenya. An inventory of commercial prices for GMP-grade CRISPR reagents has been performed. Due to the high prices, efforts to find a solution suitable for academic centers are ongoing. Options include reasonably priced commercial offers and in-house

production (one academic center or A15 production unit). A roadmap for the implementation of new technologies is under development.

Route for manufacturing GMP-grade reagents is designed (WP5.2/5.3)
Since CRISPR/Cas9 has been identified as the most critical raw material, the new ATMP ingredients focused on are CRISPR/Cas9-related reagents. A joint **roadmap** for the cost-effective purchasing or production of CRISPR/Cas9 reagents is under development. The roadmap will detail how to approach clinical translation, taking into account the EMA guidelines for cell and gene therapy.

WP6: Regulation, health economics, health technology assessment and patient access

Lead: Pauline Meij, Leiden University Medical Center

Overview of manufacturing, evidence, HTA and regulatory pathways for early phase product development is in progress (WP6.1)
The framework for the regulatory roadmap will be presented at the **WP6 workshop** in the UMCU on 17 October. Efforts to publish the roadmap in a comprehensive manner on the website are ongoing. DARE-NL comments have been submitted on the EMA guideline on Quality, Non-Clinical and Clinical Requirements for Investigational ATMPs in Clinical Trials and the EU public consultation "Health Technology Assessment- joint clinical assessment of medicinal products"

A stakeholder sandbox has been established (WP6.3)
A list of topics for discussion in the RSNN Special Interest Group ATMPs has been deduced from the interviews held with all partners in WP6 and the RSNN-SIG ATMP meetings. The second RSNN-SIG ATMP workshop with the topic 'Shaping the potential of ATMP-NL' was held on 11 June. This marks the **completion of milestone 6.3**: Create stakeholder sandbox. Discussions with stakeholders will remain an ongoing activity.

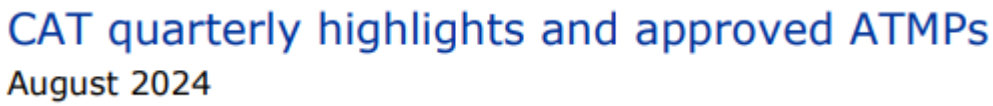
An HE and trial registry for ATMPs are in development (WP6.4/6.5)
A **symposium** on the setup of ATMP registries is organized by WP6 together with CCMO, IKNL and the patient advisory board. The database will be tested hands-on by DARE-NL researchers, clinicians and patient representatives in a workshop setting at the symposium, which is aimed to take place in January 2025.
The patient advisory board members are invited to all relevant meetings/workshops/reviews, receive annual progress report summaries and review all annual reports and the sustainability model.

Publication highlights in the field of ATMPs

COGEM explores how many new gene therapies are in the pipeline and what the associated costs, dilemmas and choices are. A report on the instruments the government has to keep gene therapies affordable and available (in Dutch, COGEM, June 2024).

The Dutch Ministry of VWS requested a QuickScan of the proposals for the revision of the EU General Pharmaceutical Legislation to assess whether the draft legislation is fit to assess innovative medicines for marketing authorization, and whether there are possibilities to achieve a positive impact on innovation and access to medicine (ZonMw, April 2024).

The approach of DARE-NL (in Dutch, Ned Tijdschr Hematol, March 2024).



Quarterly highlights and approved ATMPs by the Committee for Advanced Therapies

ATMP landscape: what happens in the network

DARE-NL has recurring meetings with FAST to keep each other updated and discuss initiatives with mutual interests. DARE-NL actively contributes to the ATMP guidebook for all stakeholders under development.

The management teams of DARE-NL and at.las got together to look into possibilities to collaborate. This started with the incorporation of the at.las e-courses and GMP summerschool in the DARE-NL education tool and at.las membership.

Harry Dolstra and Emma de Pater each presented DARE-NL achievements in a GoCART Coalition session at the 50th annual EBMT meeting in Glasgow, UK. The presentations were very well received in a great overview of national ATMP networks together with presentations on the Spanish TeraV network, the Italian life science hub, the Swedish SWECARNET and the home-brewn CARTs made in Germany.

Calendar:

see Teams (members) & website

Mailing list and newsletter

You can indicate your DARE-NL topics of interest here to be informed on the latest developments in the selected fields of interest.
If you are a DARE-NL member and do not select specific topics of interests, you are included in newsletters and communication of developments for all WPs.
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We love to receive contributions for the newsletter at info@dare-nl.nl.