Technical Operations
Supply Chain - Global Artwork

End to End Labelling

Automated Artwork, Automated Leaflets, and all Packaging Components

Chiara Tchokothe, Nuclear Medicine Head of Global Artwork
Berlin
October 06, 2023

NOVARTIS | Reimagining Medicine

Agenda

- Brief introduction
  - ✓ The Theragnostic Principle: Treat what you See
  - ✓ Mechanism of radioligand therapy
- Production and supply chain for radiopharmaceuticals
- Real logistic example
- What does Global Artwork in Nuclear Medicine mean?
- Nuclear Medicine Global Artwork Organization
- Artworks and packaging
- Artwork and variable data (Vial, Lead Shielding, Key fact)
- End-to-end process

Brief Introduction

- Advanced Accelerator Applications is pioneer in targeted Radioligand Therapy (RLT) and precision Radioligand Imaging (RLI). The current portfolio includes also Molecular Imaging (MI) with PET (Positron Emission Tomography).
- This platform **includes in scope also clinical and medical supply,** in addition to commercial supply and artworks for non-production and technical purpose.

The Theragnostic Principle: Treat what you See

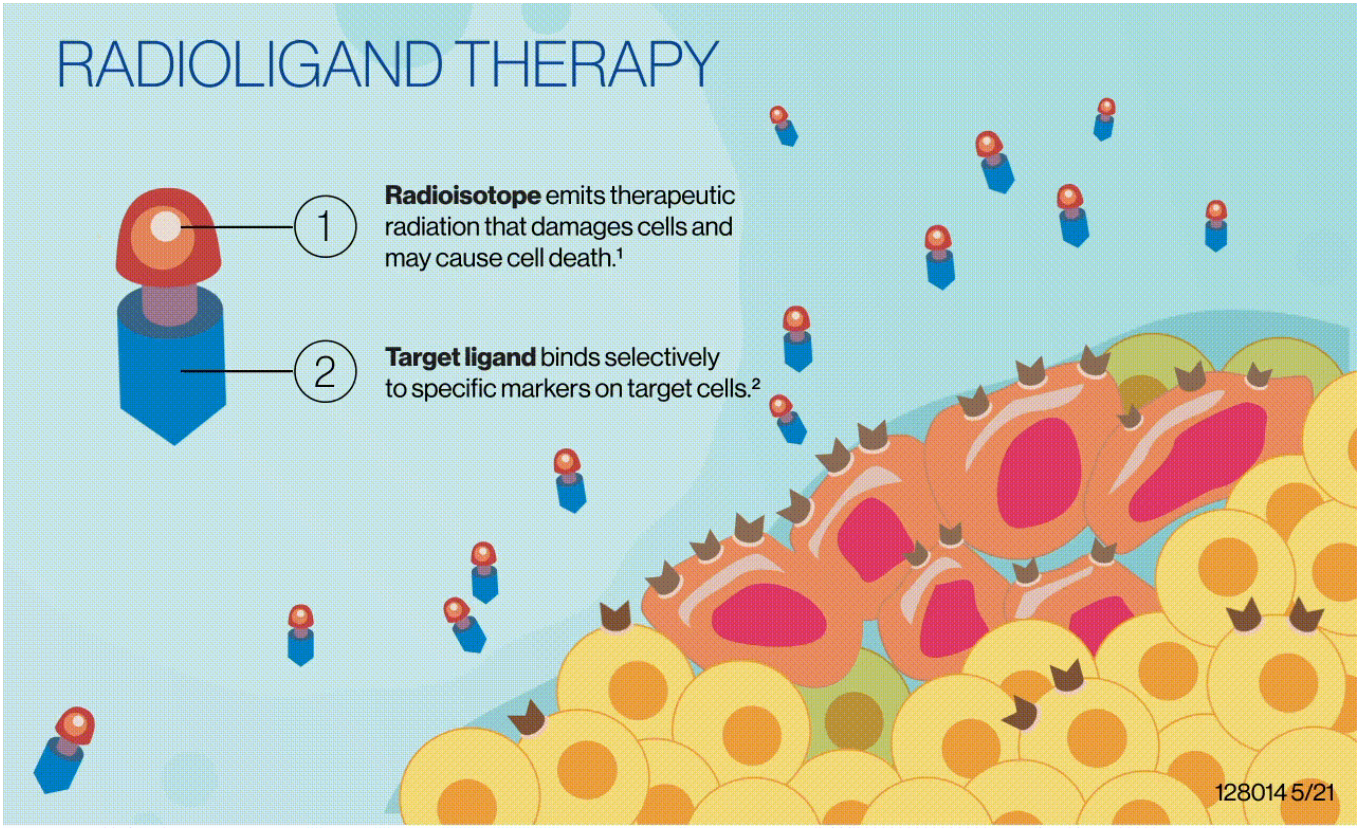
DIAGNOSTIC (RLI / MI)

THERAPEUTIC (RLT)

PRRT = Peptide Receptor Radionuclide Therapy RLT = RadioLigand Therapy

NOVARTIS | Reimagining Medicine

Mechanism of radioligand therapy



References: 1. Jadvar H. Targeted radionuclide therapy: an evolution toward precision cancer treatment. *AJR Am J Roentgenol.* 2017;209(2):277-288. **2.** Jurcic JG, Wong JYC, Knox SJ, et al. Targeted radionuclide therapy. In: Tepper JE, Foote RE, Michalski JM, eds. *Gunderson & Tepper's Clinical Radiation Oncology*. 5th ed. Elsevier, Inc; 2021;71(3):209-249.

Production and supply chain for radiopharmaceuticals

Radioligand Therapy (RLT) and Molecular Imaging (MI)

Key points

- A dose is specific to a time and day of injection or to a patient (for non-commercial supplies) and is made to order and “just in time” manufactured.
- A batch may include multiple doses (hence multiple Artwork Identifiers) for individual patients, for different clinics and/or different countries.
- A dose is produced after a patient has been identified and the order is placed.
- Products have **very short shelf-lives** (e.g. up to a few days).
- Product stocks do not exist.
- Artworks and labels are tested and printed directly at the production sites, there is no external printing house involved.
- Multiple variable fields are present in the Artwork and those are regulatory relevant placeholders.

Real Logistic example

An individualized treatment: Each vial is produced on demand and just in time

Manufacturing Facility in Turin	Milan airport	Zurich airport	Asia - Latam	Clinical site
Day 1 :09:00 AM Manufacturing	Day 1 :03:00 PM Depature LX1639	Day 1 :09:00 PM Depature LX160	Day 2 :08:30 AM Arrival	Day 3 :09:00 AM Arrival Expiry date

Responsibility

Advanced Accelerator Applications, a Novartis Company	Airport	Importer

Direct shipment from our facility to the hospital or a clinical site

NOVARTIS | Reimagining Medicine

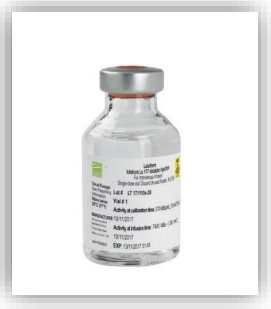
What does Global Artwork in Nuclear Medicine mean?

- The global artwork team is the Process Owner and Strategic Lead for the global artwork process for radiopharmaceutical products.
- It is also the operational expert team that manages the end-to-end process for all incoming artwork changes for the entire product portfolio. This includes but is not limited to:
  - ✓ Ownership and maintenance of **artwork identifiers** (AW ID)
  - ✓ Creation of **artwork files** (incl. pre-sets and templates)
  - ✓ Managing **GxP documentation**, driving artwork reviews and approvals, incl. site printing test (critical for **variable data** fields)
  - ✓ Launches, text changes, non-production (mock-up's) and technical changes. The scope includes the creation of **commercial & non-commercial artworks** for clinical and medical[1] supply.
  - ✓ SME in global projects, such as **printing systems** and **data transfer**

[1]Global Medical Affairs (GMA) programs such as Managed Access Program (MAP), including Individual Patient Request (IPR), Individual Government Request (IGR), Research Collaborations and Investigator Initiated Trials (IIT).

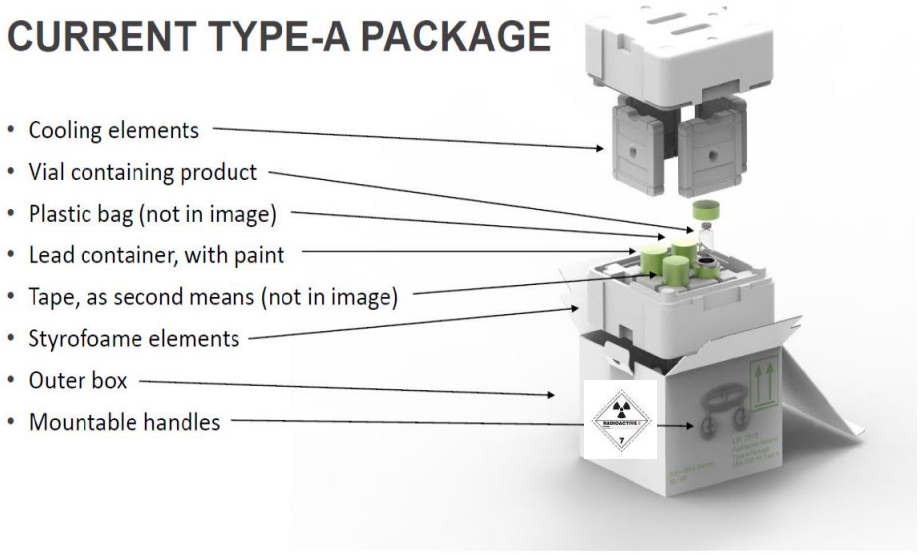
Artworks and packaging

VIAL



LEAD SHIELDING

TYPE A for transportation



Leaflets are folded and placed inside the Type A transportation package

Type A package includes a label that complies with international transportation regulations for radioactive goods, and is not part of any regulatory dossier, hence is not regulatory relevant.

Artwork and variable data

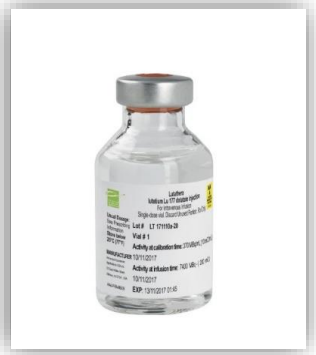
- Due to the nature of radiopharmaceuticals, the variable data is more extensive and complex and includes from 7 up to 12 data fields on vial labels and lead shielding labels.
- For this reason, the variable data formatting is visualized on the artworks for these components. Therefore, artworks are always designed including two pages, one with and one without the variable data formatting visualized.

✓ The version **with variable data placeholders** is used for:

- submission to HA via RA dossiers where formatting is visualized in support of regulators review & approval
- serves as guidance when calculation of the variable data in the position of the label, must be transferred to the printing system

✓ The version **without variable data placeholders** is used to be implemented at the manufacturing printing system

Artwork and variable data
Vial



[redacted] 370 MBq / mL
[redacted] or injection /
[redacted] pour injection
Solution for Intravenous Infusion after Dilution /
Solution pour perfusion intraveineuse après dilution
Single-dose / Unidose
DIN 02484552

RAYONNEMENT
DANGER - RADIATION

Manufacturer / Fabricant :

Lot: {LTYYMMDDX-nn}
Vial: {X} **Volume:** {Y} mL
Activity at calibration time /
Activité à l'heure du calibrage: 370 MBq / mL
(10 mCi / mL) - {DD/MM/YYYY hh:mm UTC}
Activity at infusion time / Activité au moment de la perfusion: {Z} MBq - {T} MCi
{DD/MM/YYYY hh:mm UTC}
EXP {DD/MM/YYYY hh:mm UTC}

AAA-V-CA-905-03

Artwork and variable data
Lead shielding

NOVARTIS | Reimagining Medicine

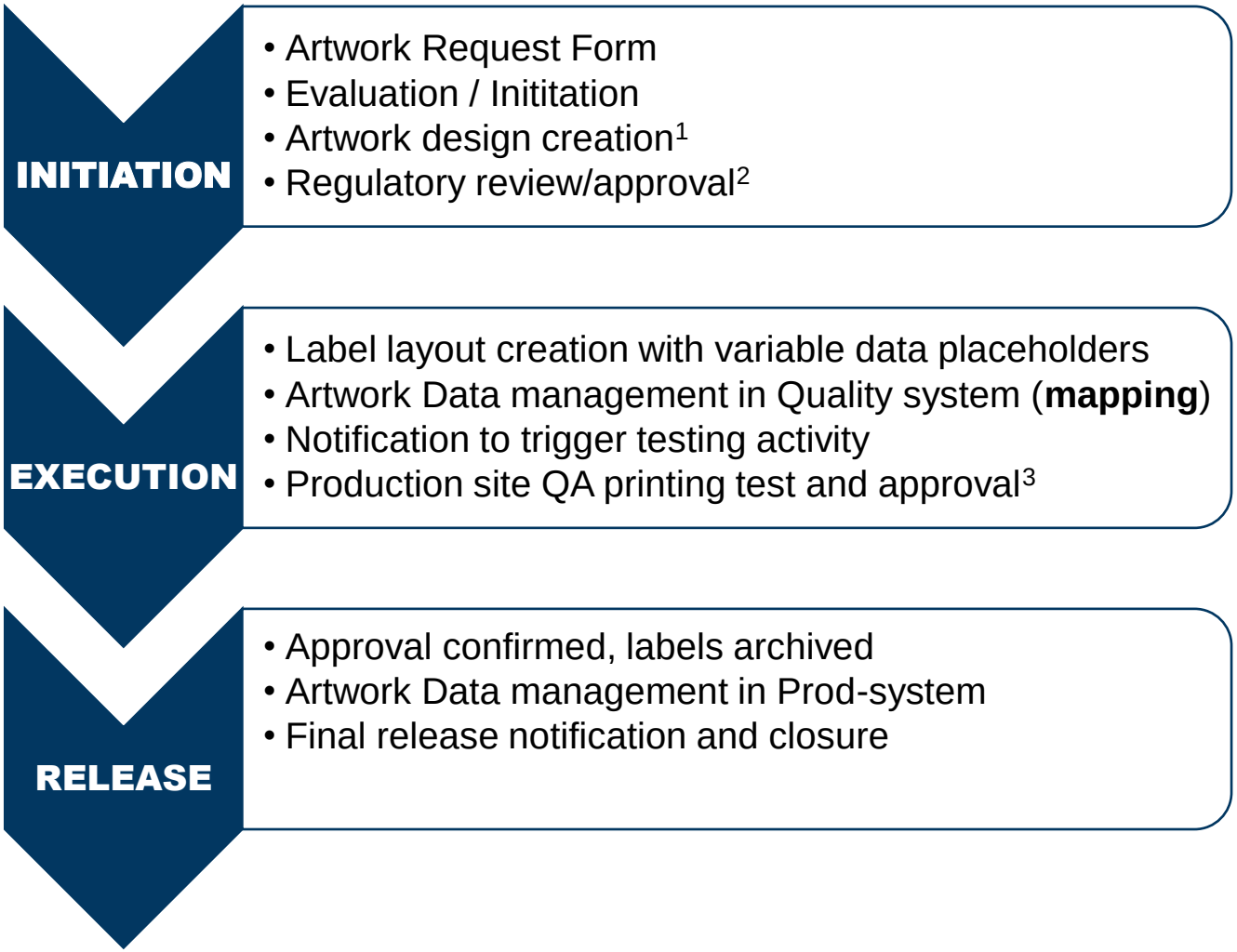
Artwork and variable data
Key fact

When the artwork is tested and fully approved and labels are going to be printed, all the data embedded into an order (such as injection time, location for time-zone calculation, injection cycle, patient id, etc. etc.) are information collected via production system designed within our facilities.

This system collects the data and fetches the AW ID available for a specific product > scope > market, to populate and fill the
variable data placeholders, previously designed by the Global Artwork team.

The Global Artwork team is responsible to establish a proper **mapping** configuration of the matrix product/scope/country/AW ID in line with regulatory requirements.

End-to-end process (high-level)



[1] Artwork creation in-house + external

[2] Regulatory approved artwork required to initiate technical review

[3] When artworks impact more than one site, all sites perform printing tests

Thank you

NOVARTIS | Reimagining Medicine