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healthy all life long

QUALITY CONTROL OF VACCINES:

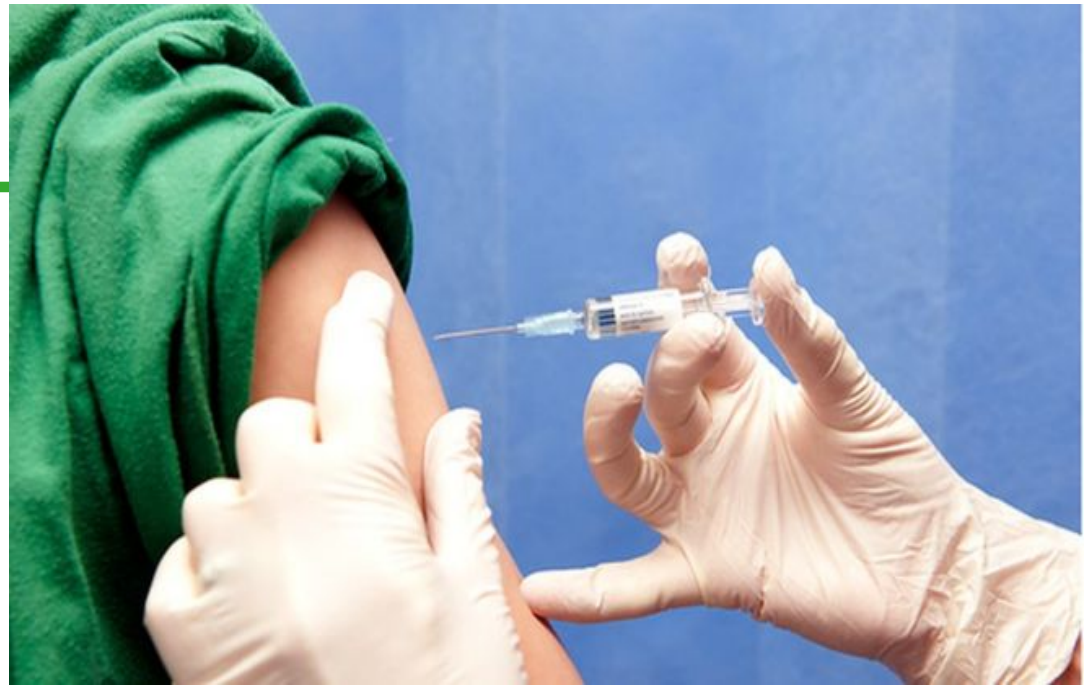
How do we ensure the safety and quality of vaccines ?

Koen Brusselmans

Sciensano Symposium 8/12/2022 BEL Brussels

.be

Importance of vaccination

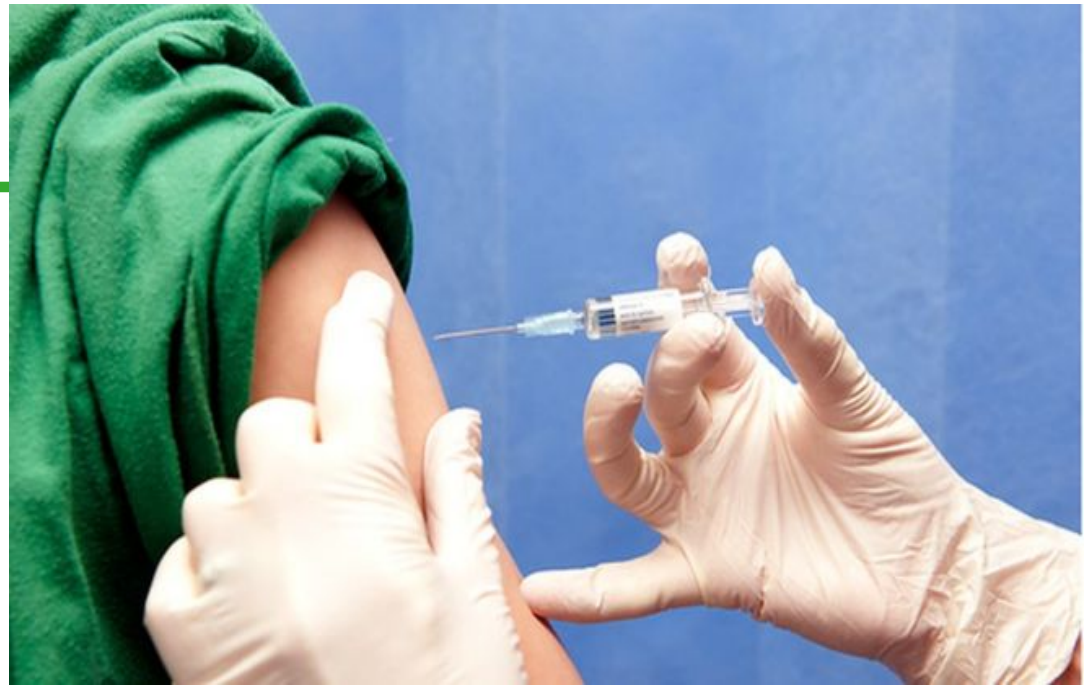


- After access to clean water > vaccination = most important factor for saving lives worldwide.
- Vaccines: widely used.

  Belgium: +1 million vaccine doses / year.

- Vaccines: to prevent disease (not for treatment) > administered to healthy people.

Importance of vaccination



- After access to clean water > vaccination = most important factor for saving lives worldwide.
- Vaccines: widely used.

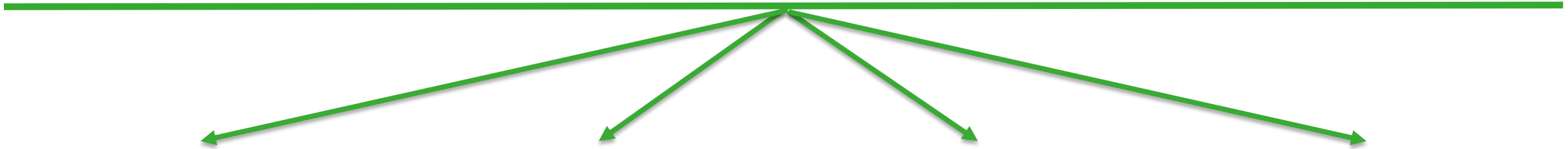
  Belgium: +1 million vaccine doses / year.
- Vaccines: to prevent disease (not for treatment) > administered to healthy people.
- **Vaccines need to be <u>safe + efficacious.</u>**

Vaccines have the most stringent quality control system of all medicinal products in Europe.

High level of vaccine hesitancy / antivax sympathy

Important to properly explain and communicate to the broad public how the quality and safety of vaccines is ensured.

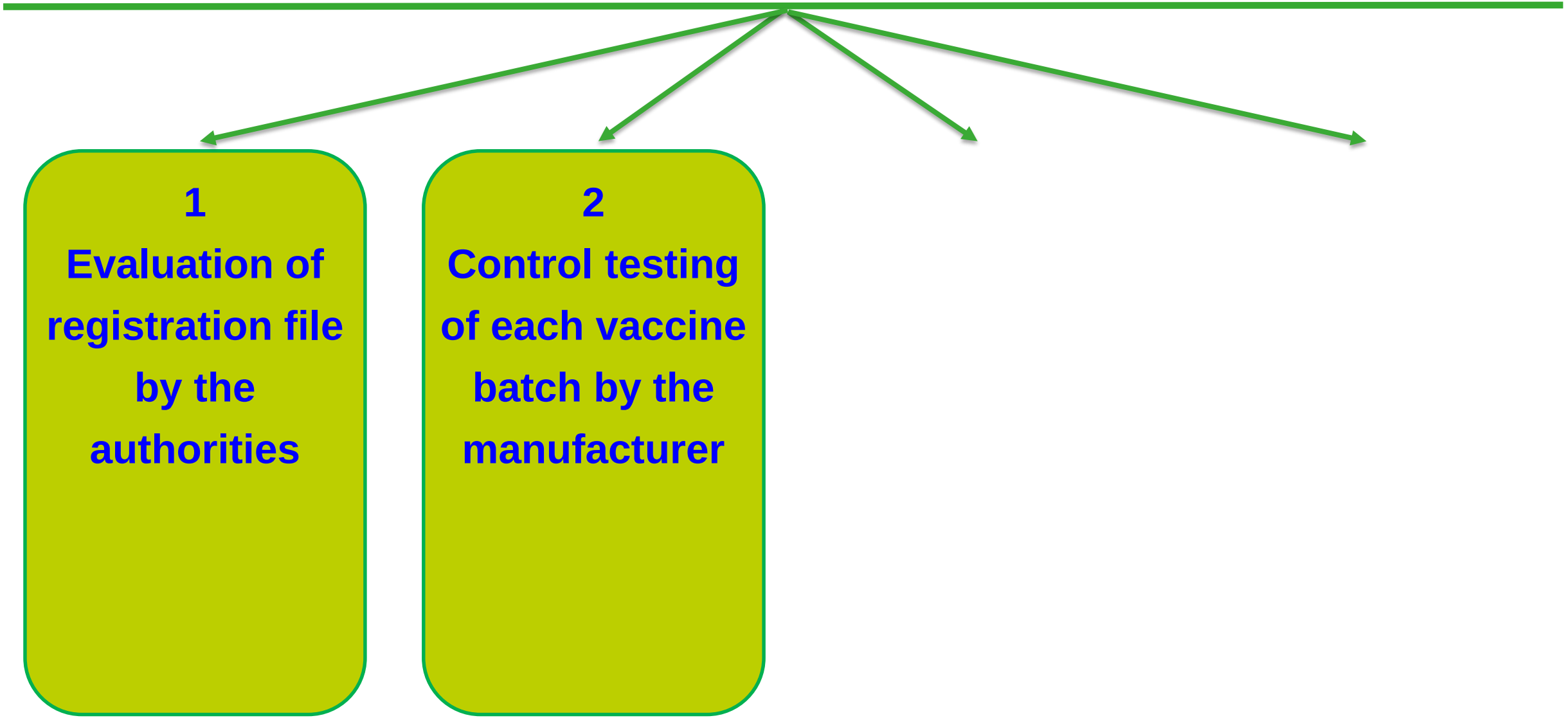
EU: 4 levels of quality control for vaccines



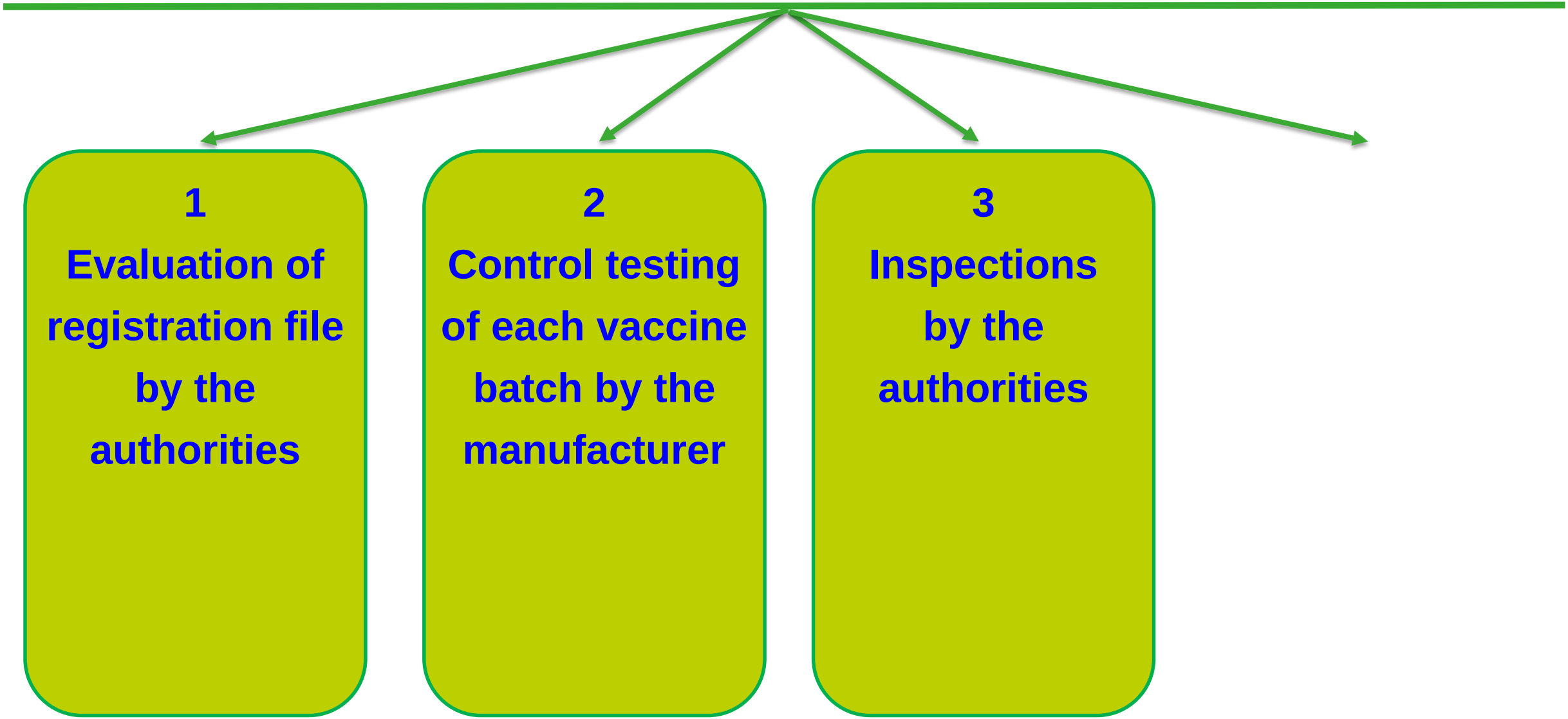
1

Evaluation of registration file by the authorities

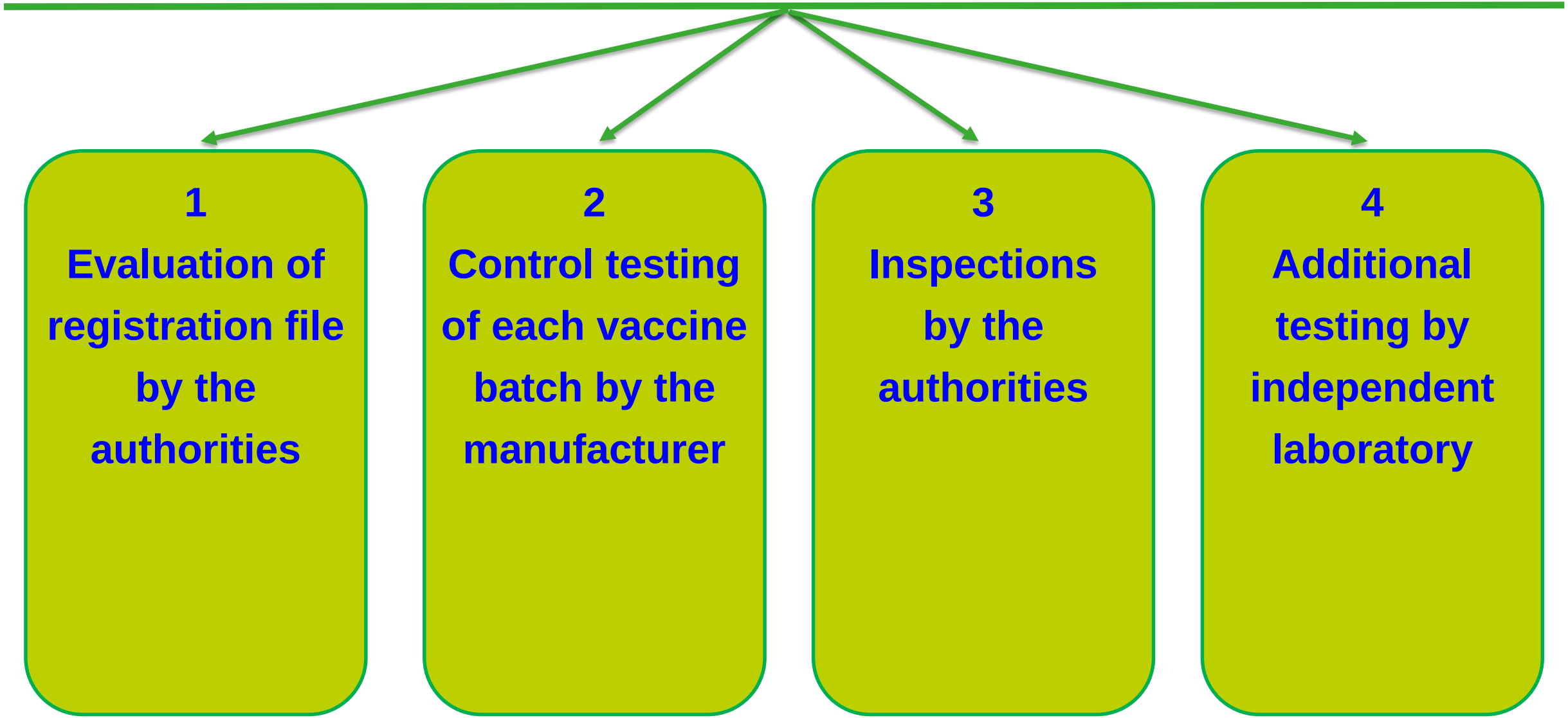
EU: 4 levels of quality control for vaccines



EU: 4 levels of quality control for vaccines



EU: 4 levels of quality control for vaccines



EU: 4 levels of quality control for vaccines

1

Evaluation of registration file by the authorities

2

Control testing of each vaccine batch by the manufacturer

3

Inspections by the authorities

4

Additional testing by independent laboratory

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Evaluation of registration file

Before a vaccine can be used, the company has to submit the registration file to the competent authorities (FAMHP, EMA).

afmps fagg
agence fédérale des médicaments et des produits de sa
federaal agentschap voor geneesmiddelen en gezondheidsproducten

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

The authorities perform an evaluation of the registration file.

During review procedure: questions are raised, additional information is requested.

Only when all data are found acceptable, the vaccine is approved.

Vaccine registration file: 3 parts

1: Quality

- manufacturing process
- vaccine composition
- control testing

2: Pre-clinical

- absorption
- metabolism
- toxicology

3: Clinical

Data from clinical studies in humans

- efficacy
- safety

Quality part of vaccine files evaluated by Sciensano (in collaboration with FAMHP)

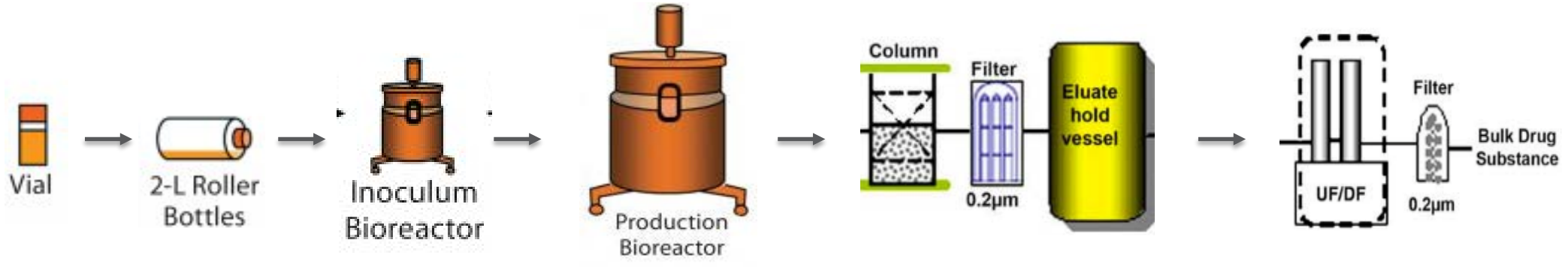
Content of registration file: Quality part

Information on:

vaccine production facilities

Information on:

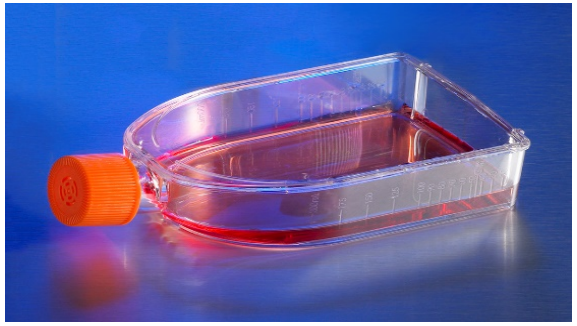
all different steps of the vaccine production process.



Upstream process Production purification/filling

Content of registration file: Quality part

Information on: quality of all materials used during vaccine production

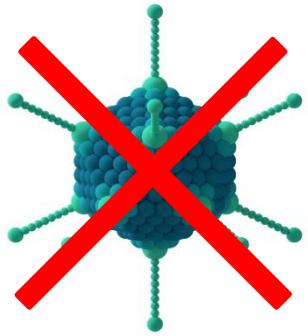


Cells to grow vaccine

Reagents (purity, content)

Equipment (filters,…)

Vials
Syringes
(leachables)



Absence of microbial and viral contamination

Content of registration file: Quality part

Vaccine specifications:

- Fixed panel of quality parameters.
- Should be analysed on each vaccine batch.
- Using validated test methods.

Quality parameter	Acceptance criteria
Antigen content / activity	
Purity	
Integrity	
Residual protein impurity	
pH	
Sterility	

Content of registration file: Quality part

Vaccine specifications:

- Fixed panel of quality parameters.
- Should be analysed on each vaccine batch.
- Using validated test methods.
- **Strict acceptance limits (clinically qualified > safe and efficacious).**

Quality parameter	Acceptance criteria
Antigen content / activity	**15 µg- 25 µg**
Purity	> 99 %
Integrity	> 95 %
Residual protein impurity	< 20 ng / dose
pH	6,2 – 7,2
Sterility	sterile

Content of registration file: Quality part

Vaccine specifications:

- Fixed panel of quality parameters.
- Should be analysed on each vaccine batch.
- Using validated test methods.
- Strict acceptance limits (clinically qualified > safe and efficacious).

- **Results from several lots:**
  - **at release**
  - **at end of their shelf life (> stability).**

Quality parameter	Acceptance criteria
Antigen content / activity	15 µg- 25 µg
Purity	> 99 %
Integrity	> 95 %
Residual protein impurity	< 20 ng / dose
pH	6,2 – 7,2
Sterility	sterile

Companies cannot deviate from the content / conditions of the registration file.

EU: 4 levels of quality control for vaccines

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Additional testing by independent laboratory

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Control testing by company

- Every single vaccine batch has to be tested by the manufacturer.
  - Vaccine batch = yield of a single production run in a fermentor that is purified and filled in vials / syringes.
- Testing according to specifications in registration file:
  - Using fixed testing panel.
  - Using validated methods.

Quality parameter	Acceptance criteria
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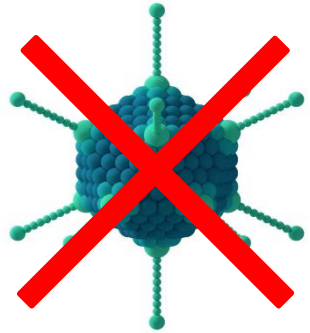
Control testing by company

- Every single vaccine batch has to be tested by the manufacturer.
  - Vaccine batch = yield of a single production run in a fermentor that is purified and filled in vials / syringes.
- Testing according to specifications in registration file:
  - Using fixed testing panel.
  - Using validated methods.
  - **Results should comply with specifications limits** (clinically qualified, approved by authorities).
- **Vaccine batches outside limits cannot be released.**

Quality parameter	Acceptance criteria
Activity / content	**15 µg- 25 µg**
Purity	**> 99 %**
Integrity	**> 95 %**
Residual protein impurity	**< 20 ng / dose**
pH	**6,2 – 7,2**
Sterility	**sterile**

Control testing by company

- Vaccines containing inactivated viruses /bacteria > additional specifications
- E.g. influenza or poliovirus vaccine
  - Test for possible residual live virus or bacteria.
  - If toxic compounds are used for inactivation:
    > test for possible residuals (e.g. formaldehyde).



⇨ **Only vaccine batches that fully comply with all specifications, can be released.**

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Inspections

- All vaccine production sites have to be inspected:
  - before vaccine approval.
  - post-approval, every 2-3 years.

- Inspectors verify if manufacturing and control testing by company is:
  - compliant with the registration file
  - compliant with the GMP legislation (Good manufacturing practices).
    - Production process and testing.
    - Quality of materials.
    - Proper recording and full traceability during vaccine manufacturing.

⇨ *Sciensano participates in GMP inspections (vaccines) performed by FAMHP.*

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Control testing by OMCL

- EU legislation (EU directive 2001/83/EC):
  - allows member states to implement additional level of quality control.
  - only for vaccines and plasma-derived products.
- In most EU member states (including Belgium), this testing is mandatory.
  Before a vaccine batch can be released to the market, every batch
  - has to be tested by the company.
  - **has to undergo an additional testing by an independent laboratory (OMCL)**
- OMCL: Official medicines control laboratory.
- **Belgian OMCL =** sciensano

Control testing by OMCL

- **European OMCL network: coordinated by EDQM (European directorate for quality of medicines).**

- EDQM and OMCLs define for each type of vaccine the mandatory OMCL tests.

  Selection of most important quality parameters: *activity, purity, integrity*.

edqm

European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE

Control testing by OMCL

- OMCL performs independent testing.
- If test results are compliant with specifications:
  - > **batch release certificate**.
- If results are not compliant:
  - > non-compliance certificate.
  - > batch must be destroyed.

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Quality of Vaccines and Blood Products

ISO 17025 Accreditation

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EU OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE FOR IMMUNOLOGICAL PRODUCTS

EU/EEA OFFICIAL CONTROL AUTHORITY BATCH RELEASE CERTIFICATE – Finished Product

Examined under Article 114 of Directive 2001/83/EC as amended by Directive 2004/27/EC (Immunological Medicinal Products) and in accordance with the Administrative Procedure for Official Control Authority Batch Release.

Trade name:	INFANRIX HEXA
International non-proprietary Name / Ph. Eur. name / common name:	Diphteria, Tetanus, Pertussis (Acellular Component), Poliomyelitis (Inactivated), Hepatitis B (rDNA) with separate Haemophilus Type B Conjugate Vaccine (Adsorbed)
Batch numbers appearing on the package and other identification numbers associated with this batch[1]:	Final packaging lot: A21CD367 DTPa-IPV-HepB lot: AC21B693D Hiberix component lot: AHIBD300B

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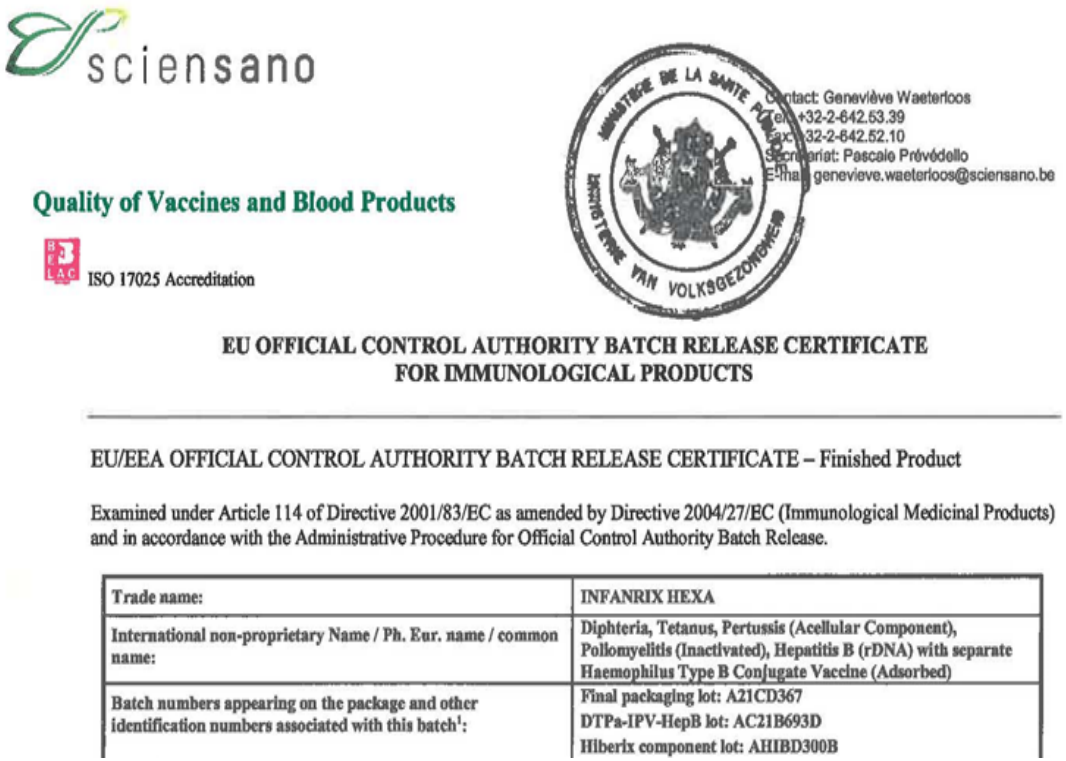

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To release a vaccine batch to the market:

Test results from both the manufacturer and the OMCL must comply with the acceptance limits of the vaccine specifications.

OMCL testing > additional guarantee for vaccine quality, safety and efficacy.

OMCL network

- OMCL laboratories in more than 20 EU countries.
- OMCLs: - operate under a strict quality system.
  - inspected by other OMCLs and EDQM.
  - can only use validated methods for vaccine testing.
- Batch release certificates granted by OMCL > mutual recognition.
  Certificates are valid in all EU member states.
- Companies can choose an OMCL (choice depends on available expertise).
- Sciensano (BE OMCL): one of most important OMCLs in EU for vaccines.

Vaccines tested by Sciensano (BE OMCL)

More than 30 different vaccines from 6 different vaccine manufacturers.

year	**# vaccine lots tested (certificates)**
2018	**1122**
2019	**969**
2020	**951**
2021	**1280**

Conclusion: 4 levels of vaccine quality control

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Evaluation of registration file by the authorities

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Control testing of each vaccine batch by the manufacturer

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Inspections by the authorities

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Additional testing by independent OMCL

Vaccines have the most stringent quality control system of all medicinal products in Europe.

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