THE EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)

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

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Overview of the EDQM Biological Standardisation Programme

European Pharmacopoeia Training Session on Biologicals

4-5 February 2020

Catherine Milne, DBO, EDQM

Presentation Overview

- EDQM Biological Standardisation Programme
- Scope
- Why Focus on Biologicals?
- …and Standardisation
- Standardisation What Do We need?
- Goals of the EDQM BSP
- How Does the EDQM BSP Help?
- What EDQM BSP Does Not Do
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- Examples of BSP Projects Past and Present
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- Leaflet
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- Recent Example of a Succesful Study
- How to Participate in a BSP Project
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- Thanks

EDQM Biological Standardisation Programme (BSP)

- Exists since 1991
- Contract with EU since 1994 - coincides with the creation of the OMCL network
- Sponsors
  - Council of Europe /EDQM
  - EU Commission

Funded by the European Union and the Council of Europe

EUROPEAN UNION

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Implemented by the Council of Europe

Scope

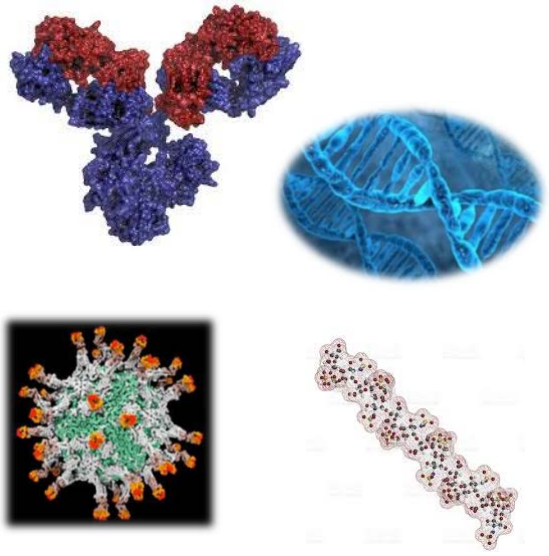
- **Biotech products** (Group 6, MAB, P4BIO)
  (hormones, cytokines, anticoagulants (heparins), mAbs…)
- **Blood products, contaminants** (Group 6B)
  (immunoglobulins, coagulation factors…)
- **Vaccines, sera for human use** (Group 15)
- **Vaccines, sera for veterinary use** (Group 15V)
- **Miscellaneous** (specific working groups)
  (allergens, endotoxins, mycoplasma…)

Why Focus on Biologicals? (1)

Nature of the products

Biological products are

- ✓ complex molecules, mixtures
- ✓ produced by a biological process
  - human, animal, recombinant…
  - purified , fractionated, concentrated,...
- ✓ inherent with biological variation reflecting molecular heterogeneity
- ✓ Characterised by their biological activity and structure/function



Why Focus on Biologicals? (2)

Nature of the control/characterisation tests

Tests	Variation sources
In vivo	
- direct : challenge assays, body temperature,...	- animal strain & individuals,…
- indirect : serology assays,...	- immunisation design,…
In vitro	
- cell culture assays	- cell lines & culture conditions,…
- immunoassays (ELISA, ToBI,...)	- reagents, testing conditions,…
- nucleic acid amplification	- sample preparation
- physico-chemical characterisation	- polydispersion, glycosylation,…
- specific activity	- conversion factors (IU-mg)
- ...	

→ inherent (biological) variation/heterogeneity
- of the samples
- of the reagents, references, readout systems, assay conditions,...

→ Historic reliance on animal models for routine testing

…and Standardisation?

Interest of standardisation

- Reliable, relatable results for manufacturers batch to batch
- Supports independent control by authorities and comparison of results
- Supports exchange and mutual recognition of control results
- Provides confidence in values for clinical use

Context

- Licencing decisions e.g. centrally authorised products
- Investigations e.g. adverse events, suspect adulterated or counterfeit product, …
- Exchange of products in global markets
  - Access e.g. stock shortages (due to production issues, emergencies: natural disasters or outbreaks,…)
  - continuity of treatments (for travellers, for use of related products…)

→ need for comparison & trust in results obtained by different laboratories

→ global exchange of data and medicines in the interest of public health

Standardisation: What Do We Need ? (1)

Common - reference standards
- critical reagents

Chemical Reference Substances (CRS) ⟶ Physico-chemical tests

Biological Reference Preparations (BRP) ⟶ Biological assays (majoritarily)
Biological Reference Reagents (BRR)

Reference standards for use in biological assays

→ are usually assigned an arbitrary unitage :
'amount that induces a defined biological effect'

→ represent the average response
from a large number of assays from various laboratories

Standardisation: What Do We Need ? (2)

For biological assays common unitage is generally defined via a primary standard in International Units

International Standards (IS) are primary standards for biological activity

- Established through international collaborative studies – usually not method specific
- Assigned a value in International Units (IU), arbitrary units defined by the World Health Organization (WHO)
- Primary role to define the unit
- Stable formulation provides a long-term reference point for calibration of secondary standards for 'regular' use

Standardisation: What Do We Need ? (3)

Ph. Eur. Reference standards for Biologicals are:

- working standards for use in conjunction with the Ph. Eur. texts
- officially adopted by the Commission of the Ph. Eur.
- calibrated against the corresponding WHO IS (when existing)
- assigned with a content
  - in IU (when available)
  - in Ph. Eur. Units or other relevant units when no IS are established
  - mg/vial, chromatogram (e.g. CRS, BRP for system suitability)

The calibration of BRPs requires data from a large number of laboratories
→ need for coordinated international collaborative studies

Standardisation: What Do We Need ? (4)

Common validated methods

- transferable
- acceptable intra-laboratory variation
- acceptable inter-laboratory variation
- suitable for various products

And what would we like?

To REPLACE, REDUCE, REFINE the use of animals (3Rs) for quality control testing

- Scientific, ethical and practical motivation
- Develop better, more reproducible/precise tests with state of the art validation
- Humane use of animals
- Potential cost reduction and sustainability

Goals of the EDQM BSP

Support Quality Control of Biologicals

- Establishment of Ph. Eur. working standards (BRP/CRS) & reagents (BRR)
- Standardisation of methods for Ph. Eur.
- Application of 3R concept (refine, reduce, replace) to Ph. Eur. methods
- International harmonisation: collaboration with WHO, OIE and national authorities

How Does the EDQM BSP Help?

- **Provides a 'neutral' independent space for exchange**
  (anonymised participants /samples, central calculation)
  For:
  - Independent laboratories from national authorities e.g. OMCLs
  - Laboratories from different manufacturers
  - Qualified academic/other labs
  - National authorities and experts
- **Uses large scale collaborative studies to:**
  - Demonstrate the general applicability and recommended use of methods already validated in a 'local/small scale' context
  - Establish commonly assigned values for Ph. Eur. reference standards
- **Provides a key link between practical work of laboratories and the Ph. Eur.**
  - Successful methods and standards are included in the Ph. Eur. and have a legal standing
- **Focus on the European market with an eye on global participation and acceptance** (common reference material and method recognition where possible)

What EDQM BSP Does Not Do

- Method validation outside the QC field
- Method development from scratch
- Complete validation for individual products
- Method validation for single products or single manufacturers

Organisation

Steering Committee

Includes:

- Chairs of Ph. Eur. biological groups (6, 6B, 15, 15V)
- Interested parties' representatives
  - European Medicines Agency (EMA); BWP, IWP
  - EU Commission
- Co-opted experts (human and vet)
- EDQM Director
- Observer from World Health Organisation (WHO)

Project Leaders

- Nominated technical experts for a given study, bound by confidentiality agreements

EDQM DBO:

- Technical secretariat; coordination & management of projects

Method of Work – Overview (1)

1. Proposal for new BRP/method (from Expert Group, OMCL, manufacturer…)
   - ✓Relevant to the Ph. Eur.
   - ✓Mature method with validation package (no research/development required)
   - ✓Applicable to most products
   - ✓No proprietary method/reagents
2. Decision by Steering Committee
   - ✓Start of the project (if possible run jointly with WHO, US-FDA, USP to established harmonised/common reference standards and methods)
   - ✓Nomination of external expert as Project Leader
3. Launch of BSP project including collaborative study

Method of Work – Overview (2)

3. Reporting and updates on project to BSP SC for advice and decisions on critical steps
   - ✓BSP SC meets face to face twice/year
   - ✓Written/exchange as needed
4. Approval of final report by BSP SC, relevant Ph. Eur. Group of Experts
5. Adoption by Ph. Eur. Commission (for BRP) – Ph. Eur. experts evaluate and prepare for inclusion in Ph. Eur. texts (methods/new BRPs)
7. Publication in Pharmeuropa-Bio & SN

Special Considerations

- Studies can take a long time (in particular method validation) – requires stamina, perseverance and adaptability
- Assay standards: in most cases IS is needed for calibration
- Whenever possible collaboration with WHO/NIBSC for simultaneous establishment of IS & BRP
- As far as possible study participants include a mix of OMCL and Industry labs from Ph. Eur. member states/observers
- Respect of the 3Rs in study design

Focus on Step 3: The Collaborative Study

- Aims at
  - Confirming the suitability of and calibrating / assigning a unitage to a candidate RS
  - determining the transferability of a method and general applicability
- Includes
  - A pool of international participants : OMCLs, manufacturers, authorities
    variable number of laboratories depending on methods (<10 *in vivo*, up to 50 *in vitro*)
  - a common protocol, reagents (as needed) & reporting sheets
  - a central analysis of the datasets
  - a review of the study report at successive levels:
    participants, relevant group of experts, BSP Steering Committee, Ph. Eur. Commission
  - a publication

Focus on Step 3: The Collaborative Study Phases (1)

Phase 1- Preparation with Project Leader(s)

- Procure candidate starting material
- Produce batch(es) of candidate standard
- Pre-test in small number of labs
- Stability studies

- Elaborate study protocol
- Interaction with statistician for study design
- Invite participant laboratories
  - OMCLs, manufacturer (EU and other)
- Prepare for shipping (permits etc.)

Focus on Step 3: The Collaborative Study Phases (2)

Phase 2 – Collaborative study with all participants

- Distribute common samples
  - calibrants : current WHO IS and/or Ph. Eur. Ref. Standard
  - candidate replacement batch(es)
  - *additional samples, critical reagents*
- Distribute common study protocol
  - materials and methods
  - special instructions
  - reporting sheets
  - deadlines and contact details
- Return of results and central analysis
  - Assignment of a unitage to the candidate
  - Evaluation of assay variation
  - Consider continuity with IS and previous BRP
- Draft study report - anonymised data sets

Focus on Step 3: The Collaborative Study Phases (3)

Phase 3 – Reporting Phase *with manufacturers (primarily)*

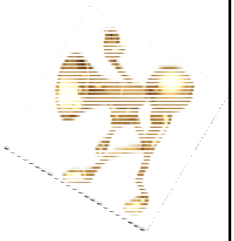
- **Optional phase based on specific need and study outcome**
  e.g. new reference standard, new method
- Collect and analyse data from routine production lots
  - Provides additional input on suitability
  - Helps to determine criteria for inclusion in Ph. Eur., specification setting

Dissemination of Results

BSP studies results are:

Reported to:

- Study Participants - pre-check of draft report before further distribution
- BSP Steering Committee
- Involved Expert Groups
- Ph. Eur. Commission

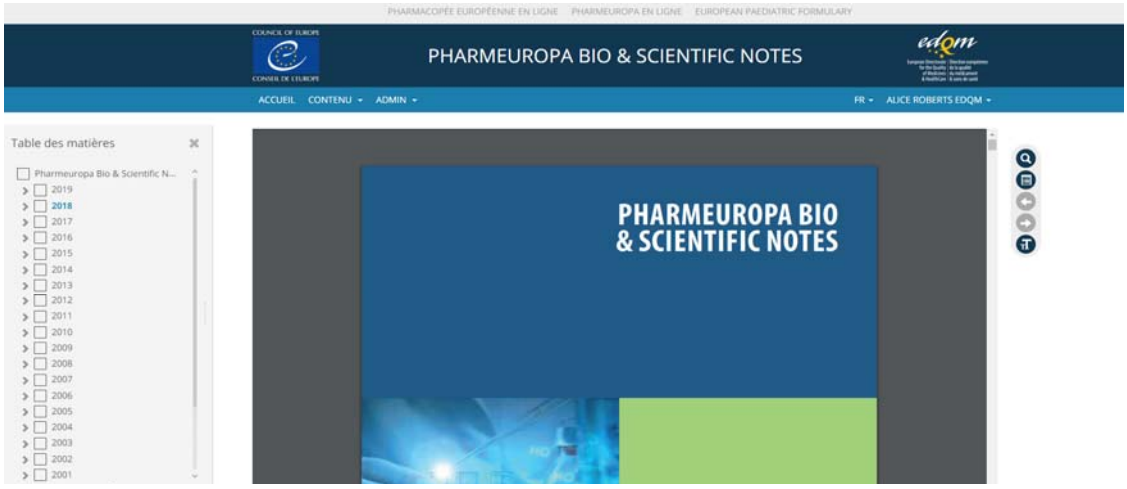


Published in:

- Pharmeuropa-Bio & Scientific Notes
- Peer reviewed scientific journals (some studies)

In some cases (e.g. new methods, issue of global interest) a symposium is organised by EDQM

Pharmeuropa Bio & Scientific Notes

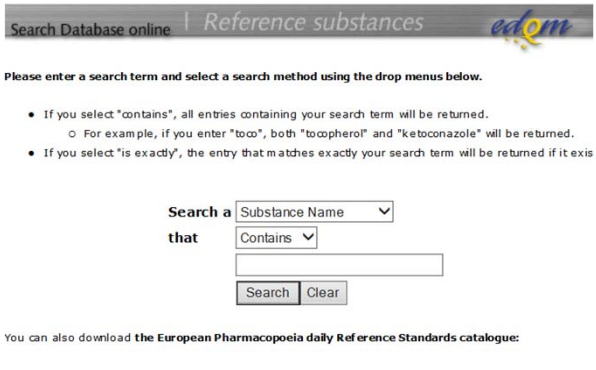


Complete study report with all methodological details published in electronic format, FREELY ACCESSIBLE VIA EDQM WEBSITE

Accessibility of BRPs and Leaflets

BRPs/BRRs/CRS are available via the EDQM catalogue and can be searched for on-line

https://crs.edqm.eu/



Examples of BSP Projects Past and Present (1)

160 BSP projects

123 projects on BRP/CRS/BRR establishment
about 100 batches of more than 60 different BRP/CRS
BRPs/CRS monitored throughout their lifetime

- Human vaccines — Antigens, toxoids, toxins; Antisera,... — mumps, [illegible], acellular/whole cell pertussis, influenzae b, poliomyelitis (OPV, IPV), HBV, HCV,...
- Veterinary vaccines — Antigens; Challenge; Antisera,... — rabies, equine influenza, clostridia, swine erysipelas, Newcastle disease, tetanus toxoids,...
- Blood products — Immunoglobulins; Clotting factors; Contaminants,.. — normal and specific Ig (tetanus, hepatitis,...); coagulation factors VII, VIII, IX, albumins,...; HAV & HEV RNA, prekallikrein...
- Biotech products — Erythropoietin, somatropin, heparins, etarnercept, infliximab…
- Miscellaneous — Mycoplasma strains, allergens, endotoxins…

ALL BRP/CRS prepared for use in context of Ph. Eur. texts

Examples of BSP Projects Past and Present (2)

Validation of improved & alternative 3R methods

43 projects on method validation
>25 projects on 3R methods - to refine , reduce, replace animal use

- Human vaccines — serology methods, alternative 3R
  - diphtheria, tetanus, acellular...
  - hepatitis A, rabies...
  - Inactivated... pyrogenicity & antigen content,...
- Veterinary vaccines — alternative 3R *in vitro* assays
  - Clostridium tetani, swine erysipelas, Newcastle disease,...
  - improved agglutination method, alternative 3R potency assays
  - isoagglutinins direct method, Tetanus immunoglobulins,...
- Biologicals — alternative 3R & improved physico-chemical tests
  - somatropin, heparins, erythropoietin, INF alfa-2,...

Successful candidate methods included in Ph. Eur. texts by Ph. Eur. expert groups

Uses of BSP References in the Ph. Eur. (1)

Physico-chemical tests ------> CRS/ BRP

- content in mg/vial
- chromatogram(s)/spectrum

Identification Tests	liquid chromatography (2.2.29.)	Erythropoietin for physicochemical tests CRS
Molecular size distribution	Zone electrophoresis (2.2.31)	Erythropoietin for SEC system suitability CRS
Related proteins	Capillary electrophoresis (2.2.47),	Heparin Low-molecular mass for calibration CRS
Impurities	peptide mapping (2.2.55.)	Somatropin CRS
assay for protein	PAGE (2.2.31.)	Somatropin/desamidosomatropin resolution mix CRS
...	SEC (2.2.30.)	Human immunoglobulin for molecular size BRP
	...	Human immunoglobulin for electrophoresis BRP
		Human albumin for electrophoresis BRP
		.....

→ as reference solution for comparison of profile, mobility,...

→ for system suitability

Uses of BSP References in the Ph. Eur. (2)

Biological assays / tests ⟶ Biological Reference Preparation (BRP)

- content in IU, titre,.../ampoule or vial
- *In specific unit e.g. cfu/mL, arbitrary Ph. Eur. unit (when no IU)*

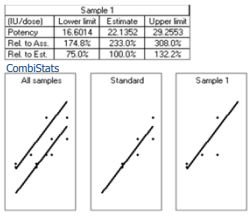
Potency System Suitability Contaminants

→ **Examples for the determination of a biological activity**

Standard for potency assay

e.g. Tet, Dip, IPV, infliximab, rabies vet, FVIII, FIX....
(2.7.8, 2.7.6, 0214, 2982, 2844, 2846..)

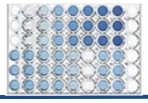
BRP calibrated in IU/vial (U/vial,...)
Method described in Ph. Eur.
Run sample together in the same test as the calibrator



Statistical analysis compares sample to reference to express relative potency in standardised units
Validity criteria in monograph

Reference Sera (in IU if possible)

e.g. Bordetella pertussis mouse antisera (ELU/vial)... (2.7.16)



Allows expression of results in calibrated comparable units

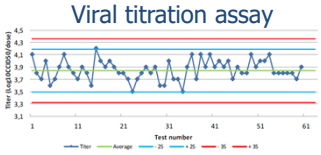
Uses of BSP References in the Ph. Eur. (2)

→ **Examples for system suitability/limits/evaluating level of contaminants**

Measles, mumps, rubella, varicella
(0162, 0213, 0538, 0648, 1057, 2442)

BRP established with viral units (PFU)/vial

Viral titration assay

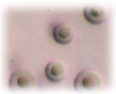


Method performance monitored for consistency with independent reference
Validity criteria in monograph

Mycoplasma – 5 reference strains
(2.6.7)

Low passage reference strains for culture method
BRP established with CFU/mL

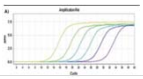
- Suitability of culture media
- Inhibitory substances
- Positive control



Qualifies the test reagents and conditions to ensure method performance and representative Results
Validity criteria in monograph

NAT assays (HAV, HCV, HEV RNA, B19 DNA) (1646) BRP calibrated in IU against IS

- Positive control



Acceptable level and validity criteria in monograph

anti-D, **antiA/antiB**, **PKA in albumin**, **Endotoxin…**(2.6.26, 2.6.20, 2.6.15, 2.6.14…)

- Positive/negative control
- System calibrators

Acceptable level and validity criteria in monograph

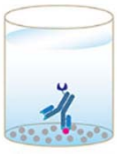
Uses of BSP References in the Ph. Eur. (4)

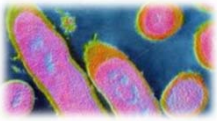
Biological Reference Reagents (BRRs, *BRPs**)

- Critical reagents needed for the performance of the method
- Often linked to *in vitro* methods e.g. specifc mAbs for immunochemical methods but also others

Examples:

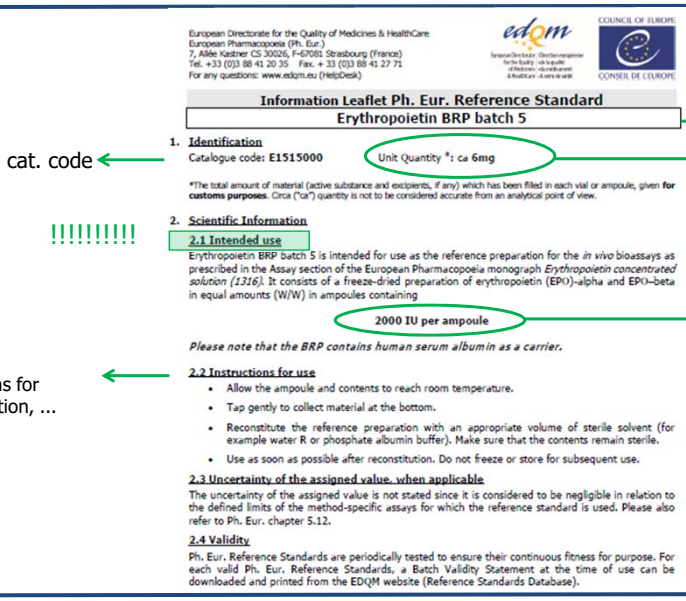
- Coating antigens – hepatitis A *in vitro* assay, Erysipelas coating antigen
- Newcastle Disease vaccine – mAbs for coating and detection
- Challenge strains e.g. swine erysipelas bacteria





* Historic nomenclature

Leaflet (1)



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For any questions: www.edqm.eu (HelpDesk)

Information Leaflet Ph. Eur. Reference Standard
Erythropoietin BRP batch 5

1. **Identification**
Catalogue code: **E1515000**
Unit Quantity *: ca **6mg**

*The total amount of material (active substance and excipients, if any) which has been filled in each vial or ampoule, given **for customs purposes**. Circa ("ca") quantity is not to be considered accurate from an analytical point of view.

2. **Scientific Information**

2.1 Intended use

Erythropoietin BRP batch 5 is intended for use as the reference preparation for the *in vivo* bioassays as prescribed in the Assay section of the European Pharmacopoeia monograph *Erythropoietin concentrated solution (1316)*. It consists of a freeze-dried preparation of erythropoietin (EPO)-alpha and EPO-beta in equal amounts (W/W) in ampoules containing

2000 IU per ampoule

Please note that the BRP contains human serum albumin as a carrier.

2.2 Instructions for use

- Allow the ampoule and contents to reach room temperature.
- Tap gently to collect material at the bottom.
- Reconstitute the reference preparation with an appropriate volume of sterile solvent (for example water R or phosphate albumin buffer). Make sure that the contents remain sterile.
- Use as soon as possible after reconstitution. Do not freeze or store for subsequent use.

2.3 Uncertainty of the assigned value, when applicable

The uncertainty of the assigned value is not stated since it is considered to be negligible in relation to the defined limits of the method-specific assays for which the reference standard is used. Please also refer to Ph. Eur. chapter 5.12.

2.4 Validity

Ph. Eur. Reference Standards are periodically tested to ensure their continuous fitness for purpose. For each valid Ph. Eur. Reference Standards, a Batch Validity Statement at the time of use can be downloaded and printed from the EDQM website (Reference Standards Database).

official name

cat. code

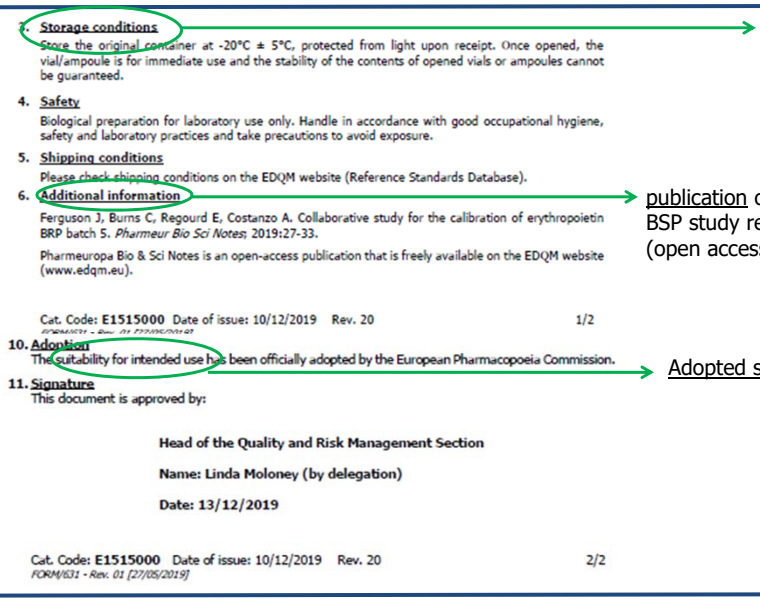
approx. content
only for customs

!!!!!!!!!!

assigned potency !!!!!!!!!!

instructions for reconstitution, ...

Leaflet (2)



7. **Storage conditions**
Store the original container at -20°C ± 5°C, protected from light upon receipt. Once opened, the vial/ampoule is for immediate use and the stability of the contents of opened vials or ampoules cannot be guaranteed.

4. **Safety**
Biological preparation for laboratory use only. Handle in accordance with good occupational hygiene, safety and laboratory practices and take precautions to avoid exposure.

5. **Shipping conditions**
Please check shipping conditions on the EDQM website (Reference Standards Database).

6. **Additional information**
Ferguson J, Burns C, Regourd E, Costanzo A. Collaborative study for the calibration of erythropoietin BRP batch 5. *Pharmeur Bio Sci Notes*; 2019:27-33.

Pharmeuropa Bio & Sci Notes is an open-access publication that is freely available on the EDQM website (www.edqm.eu).

Cat. Code: **E1515000** Date of issue: 10/12/2019 Rev. 20 1/2

10. **Adoption**
The suitability for intended use has been officially adopted by the European Pharmacopoeia Commission.

11. **Signature**
This document is approved by:

Head of the Quality and Risk Management Section

Name: Linda Moloney (by delegation)

Date: 13/12/2019

Cat. Code: **E1515000** Date of issue: 10/12/2019 Rev. 20 2/2
FORM/631 - Rev. 01 [27/05/2019]

storage conditions
(unopened vials)

publication of the
BSP study report
(open access)

Adopted suitability **for intended use**

Designed For Purpose

The BRPs/CRS are established for an intended purpose

The collaborative studies are designed to verify the suitability for that purpose only and sufficient information is provided in the study report and leaflets to use the BRP/CRS in that context

- Can I use the BRP to calibrate something else/in a different method than that in the Ph. Eur. ?
- Can you tell me if there is X, Y or Z in the formulation because I want to use the BRP for…'insert favourite research project here'…?

Users are advised not to use the BRP/CRS/BRRs outside the scope of intended use

Consult the leaflet carefully and be sure it is the right tool for the job

A Few Words About Method Development For 3Rs

Important goal and a commitment of the Ph. Eur. and EDQM/COE

Several important considerations….

- Complex task
- Global 'blunt' measure (life/death) → specific parameters/parts of system
- Paradigm shift may be required (globally applied specification vs consistency approach)
- Critical mass on consensus to embark can be long in coming
- Not always possible to directly compare to existing test
- Usually requires access to specific reagents that may not be freely available
- Should as far as possible be relevant for all products on the market
- Not always a straight line from idea to fruition

Recent Example of a Successful Study (1)

BSP130 – *Clostridium septicum* - *in vitro* replacement of *in vivo* methods

- co-sponsored with EPAA (European Partnership for Alternative Approaches to Animal Testing)
- **BSP Project Leaders**: Keith Redhead (formerly at MSD-AH), Lukas Brukner (formerly at IVI), Botand Siklodi (Ceva)

The European Partnership for Alternative Approaches to Animal Testing

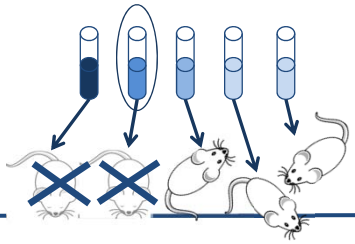
Clostridial vaccines – major group of veterinary vaccines sold world wide for farm animals - Compromise less than 5% of veterinary vaccines but responsible for over 40% of animal use for QC testing

Antigen *Clostridium* ***septicum***, a common component of veterinary vaccines – Proof of Concept for other strains

Grow organism → Remove cells → Active toxin (T) → Inactive toxoid (T,A) → Formulated vaccine

QC tests Minimal lethal dose (**MLD**) for toxicity (T) testing
Total combining power (**TCP**) for antigenicity (A) testing

Traditional MLD, TCP differ in set up and objective but both use mice as final read-out for toxicity



Goal:
- replace mice with cell culture (vero cell assay) for read out

Recent Example of a Successful Study (2)

Pre-BSP: Method development – MSDAH validated method accepted by regulators

2013 - dedicated EPAA workshop brings together interested parties and sets 'critical mass' in motion

BSP-SC endorses project start in June 2013 → 3 study phases over 6 years

Phase 1	Preliminary protocols developed Study samples collected and prequalified *in vivo* and *in vitro*	• Lab work carried out in 1 lab (PL:K.R.)
Phase 2	Collaborative validation of *in vitro* MLD and TCP Concordance with *in vivo* tests established	• 11 labs from 7 countries participate • 6 batches of toxin and 6 of toxoid tested • Common antitoxin and toxin provided • Rationalised design to minimise animal use
Phase 3	Optimisation of *in vitro* protocols Qualification of new samples (PL: B.S.) TCP and MLD refined/adapted (MLD→*TNE+)* New samples collected and pre-qualified New collaborative study – *in vitro* only	• 14 labs from 11 countries participate • 6 batches of toxin and 6 of toxoid tested • Common antitoxin and toxin provided

Recent Example of a Successful Study (3)

Conclusions

- Assays can be successfully transferred
- Good comparison *in vivo* - *in vitro*
- Vero cells 1000x more sensitive than mouse
- Both TNE+ and TCP *in vitro* are better than *in vivo* at discriminating toxins/toxoids of different strengths
- Both have better intra-lab precision and reproducibility than *in vivo*

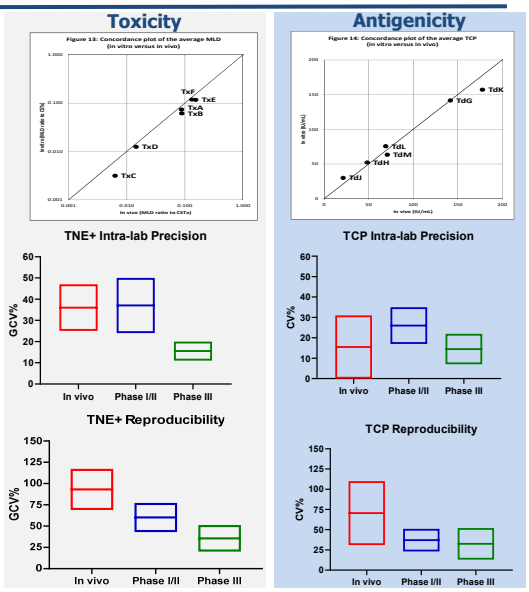
Recommend *in vivo* → *in vitro* in Ph. Eur.

Group 15V are preparing revised text(s) to be published in Pharmeuropa for public comment, following preliminary consultation with industry

Symposium planned for December 2020 at EDQM

Focus on implementation for *C. Septicum* and other strains

- Interested manufacturers, OMCLs, regulators; Europe and international, encouraged to attend



How to Participate in a BSP Project ?

✓ *evaluate a proposed new method/standard*
✓ *contribute to the calibration of a new batch of reference standard*

- As participant
  - laboratory from manufacturer / OMCL
    - if you perform the test
    - if you use the Ph. Eur. RS
- As project leader
  - expert in the field
    - with access to a laboratory
    - with wide knowledge of products / methods
    - if you developed a new method
- As donator of starting material
  - manufacturer

→ Check the EDQM website for ongoing / future studies (BSP work programme)
→ Contact the EDQM/DBO/BSP (via Helpdesk on the EDQM website or direct contact)

Conclusion

BSP contributes to the Ph. Eur.

- Validation of methods (particularly 3Rs)
- BRP/CRS/BRR that support the application of Ph. Eur. methods

And in a wider sense

- To the standardisation of biological medicines
- To public health protection

Many Thanks to All Supporters

Past and Present

BSP Steering Committee Members
Project Leaders
Project Participants
Donators of Material
International Collaborators

EDQM DBO Team

Scientific Project Administrators: Marie-Emmanuelle Behr-Gross, Angèle Costanzo, Sébastien Jouette, Natalia Sinitskaya, Eriko Terao
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Head of Section: Catherine Milne
Head of Division: Michael Wierer
Head of Department: Laurent Mallet

..and EDQM collaborators
DLab, DRSL, DAF, ITPD, PRDD….

Thank you for your attention

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