

# The role of EQALM in the COMET project

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**COMET:**

Manufacturing of commutable calibrators and quality control materials for standardisation and post-market surveillance of IVD tests.

The overall aim of this project is to establish the necessary metrological infrastructure to provide calibration services to External Quality Assessment (EQA) providers and IVD manufacturers to evaluate and improve accuracy and harmonisation of medical test results. This will help the in vitro diagnostic industry meet the requirements of the In Vitro Diagnostic Medical Devices Regulation (IVDR) regarding calibration and performance verification of IVD tests.

# Why is EQALM involved?

## **Objectives COMET:**

Objective 1: Improved availability of commutable CRMs & EQA materials for high priority biomarkers

Objective 2: Identification of manufacturing processes leading to high commutability levels

Objective 3: Development of more efficient and cost-effective ways of conducting commutability studies

Objective 4: Novel approaches for EQA data aggregation

## Objective 1: Improved availability of commutable CRMs & EQA materials for high priority biomarkers

- Bilirubin
- Cyclosporine
- Parathyroid Hormone (PTH)
- Human Cytomegalovirus (hCMV)
- Estradiol
- Point of Care Test (POCT) for glucose
- panel of clinically relevant biomarkers: estradiol, testosterone, glucose, creatinine, urea, uric acid, sodium, potassium, chloride, calcium, total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol

## Why COMET?

1. To **improve the availability of fit for purpose** calibrators and **quality control materials** that can be used by in vitro diagnostic (IVD) manufacturers and **External Quality Assessment (EQA) providers** for establishing and verifying metrological traceability of clinical measurements for various measurands
2. To **identify manufacturing processes** for the production of calibration and **quality control materials of high commutability levels**.
3. To **develop more efficient and cost-effective ways of conducting commutability studies**
4. To **support post-market surveillance** of IVD tests by working in **close cooperation with EQA providers** and IVD manufacturers.
5. To **combine EQA data** obtained and to develop novel approaches for **EQA data aggregation** in order to **evaluate harmonisation of measurement results on an international basis**.
6. To facilitate the take up of the technology and measurement infrastructure developed in the project

## Benefits for EQALM:

- Recognition as an international expert organisation for EQA in laboratory medicine
- Building up experience in the production of well characterised (traceability, commutability) EQA materials together with a group of international experts from different disciplines.
- Building up experience in commutability studies → sharing materials for inclusion in commutability studies.
- Exploration of the EQALM Central database project → sharing data from EQA surveys .
- Involvement in developing protocols and publications.

no.	Participant Type	Short Name	Organisation legal full name	Country
17	Associated Partner - associated to all funded beneficiaries	EQALM	European Organisation for External Quality Assurance Providers in Laboratory Medicine	Switzerland

**EQALM** is an umbrella organisation for European EQA organisers in laboratory medicine. It currently has members from 29 European countries and 6 countries from outside Europe. EQALM will play a key role for the organisation of a large scale EQA scheme and the work on EQA data aggregation in WP4. EQALM will be associated to all funded beneficiaries.

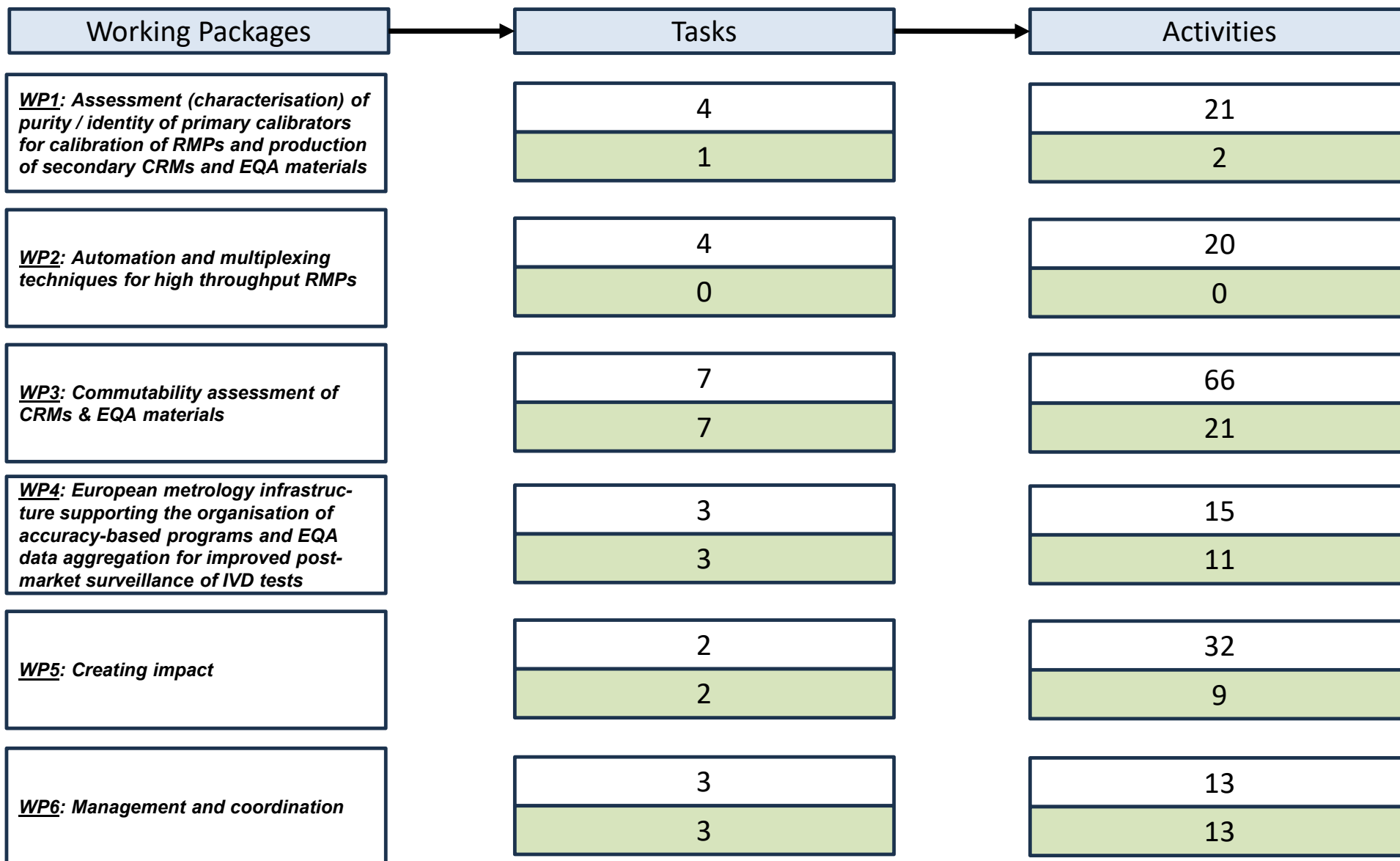


# What should be done by EQALM?

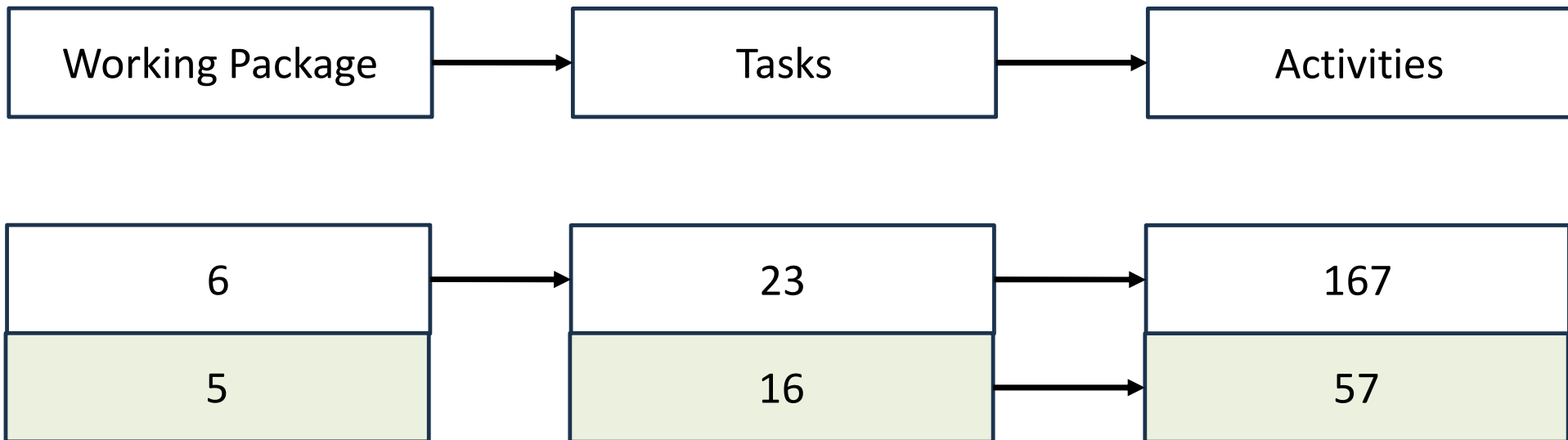
WP No	Work Package Title	Active Participants (WP leader in bold)
WP1	Assessment (characterisation) of purity / identity of primary calibrators for calibration of RMPs and production of secondary CRMs and EQA materials	<b>PTB</b> , LGC, LNE, INRIM, NIB, TUBITAK, MHRA, INSTAND, SPMD-RfB, UMK, CHUL, CHUM, <b>EQALM</b> , Roche, INVENT, HDS
WP2	Automation and multiplexing techniques for high throughput RMPs	<b>LGC</b> , PTB, Roche, CHUL, LNE, UGent
WP3	Commutability assessment of CRMs & EQA materials	<b>HDS</b> , UMK, CHUL, CHUM, Roche, Archem, INVENT, INSTAND, SPMD-RfB, <b>EQALM</b> , LNE, PTB, LGC, INRIM, NIB, TUBITAK, MHRA, UGent
WP4	European metrology infrastructure supporting the organisation of accuracy-based programs and EQA data aggregation for improved post-market surveillance of IVD tests	<b>Sciensano</b> , <b>EQALM</b> , HDS, INSTAND, SPMD-RfB, PTB, LGC, LNE, TUBITAK, UGent, UMK, Roche, INRIM, NIB, CHUL, MHRA
WP5	Creating impact	<b>LNE</b> , all participants
WP6	Management and coordination	<b>LNE</b> , all participants

## Project structure:





## Project structure (summary):



## Examples:

### Task 1.3: Purity and identity assessment of primary reference and quality assurance materials for hCMV

Activity number	Activity description	Participants (Lead in bold)
A1.3.1 M3	With support from CHUM, EQALM, SPMD-RfB, INSTAND, LGC, NIB, PTB, TUBITAK, INRIM and MHRA, UMK will identify and predict <b>target uncertainties</b> for primary and secondary reference materials and RMPs hCMV so that the medical need can be fulfilled. EQALM, UMK, CHUL and CHUM will provide clinical input, e.g., to define what uncertainties are needed to make relevant medical decisions. EQALM, SPMD-RfB and INSTAND will provide input as EQA providers. LGC, NIB, PTB, TUBITAK, INRIM, MHRA will provide input as reference materials producers and calibration laboratories.	<b>UMK</b> , MHRA, CHUM, EQALM, SPMD-RfB, INSTAND, LGC, NIB, PTB, TUBITAK, INRIM

Contribute



E-mail or questionnaire to EQALM members to ask for relevant information.

## Examples:

### Task 3.2: Commutability study #1: Multiparameter commutability study of secondary CRMs and EQA materials for a panel of clinically relevant biomarkers

Activity number	Activity description	Participants (Lead in bold)
A3.2.1 M2	With support from EQALM, INSTAND, SPMD-RfB, HDS, CHUM, UMK and UGent, LNE will establish a list of at least 4 measurands and a list of IVD-MDs for which commutability will be assessed. Various measurands will be considered, including but not being limited to estradiol, testosterone, glucose, creatinine, urea, uric acid, Na, K, Cl, Ca, total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol. EQALM, INSTAND, SPMD-RfB and HDS will use EQA data to identify i) the most frequently used assays and ii) measurands for which assays accuracy and/or comparability needs to be improved or monitored more closely. CHUM, UMK, UGent and HDS will advise on IVD-MDs and measurands worth including based on clinical needs. Using available leaflets and/or by approaching assay manufacturers, LNE, with support from PTB, LGC, TUBITAK and UGent, will perform a review of assays specifications to estimate sample uptake and precision of the selected IV-MDs. <b>At least 2 priority measurands will be selected for which reference method target values will be assigned in A3.2.8.</b>	<b>LNE, EQALM,</b> INSTAND, SPMD-RfB, HDS, CHUM, UMK, PTB, LGC, TUBITAK, UGent

Contribute



E-mail or questionnaire to EQALM members to ask for relevant information.



## Examples:

### Task 4.2: Organisation of a large-scale EQAS

Activity number	Activity description	Participants (Lead in bold)
A4.2.1 M14	Based on the list of measurands established in A3.2.1 and results from A3.2.8, <b>EQALM</b> with support from HDS, INSTAND, SPMD-RfB, UMK and LNE, will <b>select at least 2 measurands</b> for which a large scale EQAS will be designed, in which EQA materials of well-characterised commutability and target value assigned with RMPs will be distributed in different European countries by multiple EQA providers. <b>EQALM</b> will organise a <b>call for participation to European EQA providers</b> in order to identify those interested to access the materials. Based on responses, a target number of participants will be estimated. It is expected that the minimum number of participants will be 500.	<b>EQALM</b> , HDS, INSTAND, SPMD-RfB, UMK, LNE

Lead



EQALM is responsible for the execution of this task. E.g. by input from members. Call for participation.



## **Examples:**

**Task 4.3: Development of a framework for performance verification of IVD tests and harmonisation monitoring of clinical measurements through EQA data aggregation**



Important and crucial role for the EQALM Central Database !

Activity number	Activity description	Participants (Lead in bold)
A4.3.1 M3	With support from Sciensano, INSTAND, SPMD-RfB, HDS and LNE, EQALM will prepare a document describing possible solutions for establishing a framework for performance verification and harmonisation monitoring of IVD tests through EQA data aggregation.	<b>EQALM</b> , Sciensano, INSTAND, SPMD-RfB, HDS, LNE
A4.3.2 M12	<p>Sciensano will design and develop an SQL <b>database</b> in which data will be transferred using a PHP algorithm which will also be developed by Sciensano.</p> <p>With support of EQALM, SPMD-RfB, INSTAND and HDS, Sciensano will define different levels of detail according to which data will be analysed. This will be done based on information collected by EQA providers to identify what IVD-MD was used to report EQA results for a given measurand. Candidate information to be considered include but are not limited to the measurand (target analyte, matrix), measuring system / analyser, source of metrological traceability, reagent, calibrator, etc This work will be conducted in accordance with the state-of-the-art nomenclatures and coding systems for IVD-MDs, e.g., those established in JCTLM TF-Nomenclature and/or any other relevant guidelines.</p>	<b>Sciensano</b> , EQALM, SPMD-RfB, INSTAND, HDS

A4.3.3 M35	<p>For at least two IVD manufacturers and at least one measurand, Sciensano will use the SQL database established in A4.3.2 to incrementally <b>aggregate data</b>. First, available EQA data from SPMD-RfB, INSTAND and HDS will be used to verify the suitability of the database built in A4.3.2. Based on results from A4.1.3, A4.1.4 and A4.2.4, EQA data will be aggregated at different levels of detail defined in A4.3.2 so that as much data as possible can be aggregated at the lowest level of detail (e.g., IVD manufacturer without any other information), while lower amounts of data will be aggregated for higher levels of detail (e.g., IVD manufacturer, analyser, reagent, calibrator, etc). The design of the database and/or the procedure for EQA data aggregation will be updated incrementally based on data characteristics and possible limitations being encountered. With support from EQALM and LNE, Sciensano will:</p> <ul style="list-style-type: none"> <li>• <b>evaluate potential limitations</b> stemming from defining peer groups according to the usual conventions employed by EQA providers,</li> <li>• evaluate the benefits of aggregating EQA data obtained from the same EQA material (A4.2.4) or different EQA materials (A4.1.3)</li> <li>• establish a <b>list of information to be collected</b> from participants about their measuring system for each measurand to enable suitable description and/or classification into homogeneous groups for which EQA data from measuring systems will be representative of performance for a stated measurement procedure. EQALM, SPMD-RfB, INSTAND and HDS will advise regarding what information EQA providers can and are willing to provide.</li> </ul>	<p><b>Sciensano,</b> EQALM, SPMD-RfB, INSTAND, HDS, LNE</p>
A4.3.4 M36	<p>Using results from A4.3.3, Sciensano, EQALM, SPMD-RfB, INSTAND, HDS and LNE will prepare <b>recommendations</b> describing the benefits, barriers and routes for wider use of large scale and systematic aggregation of EQA data. Recommendations will describe the minimum information needed to collect data that provides the ability to aggregate results from different EQA providers and create useful outputs. The recommendations will elaborate on possible strategies to support the development of a <b>permanent infrastructure</b> centralising the collection of EQA data and their analysis at the European level.</p> <p>Once the recommendations have been agreed by the consortium, the coordinator on behalf of Sciensano, EQALM, SPMD-RfB, INSTAND, HDS, LNE will then submit it to EURAMET, as <b>D8 "Recommendations for the development of novel approaches for External Quality Assessment (EQA) data aggregation, including benefits, barriers, and routes for a wider use on an international basis."</b></p>	<p><b>Sciensano,</b> EQALM, SPMD-RfB, INSTAND, HDS, LNE</p>

Activity	Description	EQALM activity	Lead / Contribute	Start Date	End Date	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11	M12	M13	M14	M15	M16	M17	M18	M19	M20	M21	M22	M23	M24	M25	M26	M27	M28	M29	M30	M31	M32	M33	M34	M35	M36		
						S24	O24	N24	D24	J25	F25	M25	A25	M25	J25	J25	A25	S25	O25	N25	D25	J26	F26	M26	A26	J26	J26	A26	S26	O26	N26	D26	J27	F27	M27	A27	M27	J27	J27	A27			
WP1	Production of primary calibrators			M1	M18																																						
1.3	Purity and identity assessment of primary reference and quality assurance materials for hCMV																																										
A1.3.1	Predict target uncertainties	Input based on EQA results	Contribute	M1	M3																																						
A1.3.2	Define the measurand	Clinical input + input based on EQA results	Contribute	M1	M3																																						
WP2	High throughput of RMPs			M1	M30																																						
-	-	-		-	-																																						
WP3	Communtability			M1	M36																																						
3.1	New approaches for commutability assessment of CRMs & EQA materials																																										
A3.1.5	Report on commutability/value assignment etc.	Input for report	Contribute	M15	M30																																						
A3.1.6	Guideline on sample manufacturing and key causes limiting commutability of CRMs and EQA materials	Input for guideline	Contribute	M15	M30																																						
3.2	Commutability study #1 : Multiparameter commutability study																																										
A3.2.1	List of measureands and IVD-MDs	Input based on EQA results	Contribute	M1	M2																																						
A3.2.5	Source and/or produce CRMs and EQA materials	Invitation to EQA providers	Contribute	M3	M8																																						
A3.2.10	Report on commutability of CRMs and EQA materials etc.	Input for report	Contribute	M12	M14																																						
3.3	Commutability study #2 : neonatal bilirubin																																										
A3.3.1	List of measureands and IVD-MDs	Input based on EQA results	Contribute	M1	M2																																						
A3.3.5	Source and/or produce CRMs and EQA materials	Invitation to EQA providers	Contribute	M3	M8																																						
A3.3.10	Report on commutability of CRMs and EQA materials etc.	Input for report	Contribute	M22	M24																																						
3.4	Commutability study #3 : therapeutic drugs																																										
A3.4.1	list of IVD tests	Input based on EQA results	Contribute	M1	M2																																						
A3.4.5	Source and/or produce CRMs and EQA materials	Invitation to EQA providers	Contribute	M3	M8																																						
A3.4.10	Report on commutability of CRMs and EQA materials etc.	Input for report	Contribute	M22	M24																																						
3.5	Commutability study #4 : PTH																																										
A3.5.1	list of immunoassays	Input based on EQA results	Contribute	M1	M2																																						
A3.5.5	Source and/or produce CRMs and EQA materials	Invitation to EQA providers	Contribute	M3	M16																																						
A3.5.10	Report on commutability of CRMs and EQA materials etc.	Input for report	Contribute	M22	M24																																						
3.6	Commutability study #5 : hCMV																																										
A3.6.1	list of IVD tests	Input based on EQA results	Contribute	M1	M2																																						
A3.6.5	Source and/or produce candidate primary and secondary materials	Invitation to EQA providers	Contribute	M3	M16																																						
A3.6.6		Protocol commutability study	Contribute	M3	M16																																						
A3.6.10	Report on commutability of CRMs and EQA materials etc.	Input for report	Contribute	M22	M24																																						
3.7	Commutability study #6 : POCT for glucose			M1	M36																																						
A4.1	Post-market surveillance of IVD tests through retrospective value assignment of reference method target values to commutable EQA materials																																										
A4.1.1	Selection of EQA materials for target value assignment	Support in selection	Contribute	M13	M14																																						
A4.1.3	Collection of EQA data	Collection of EQA data	Lead	M13	M25																																						
4.2	Organization of a large scale EQA scheme																																										
A4.2.1	Selection of measurands / call for participation	Selection of measurands / call for participation	Lead	M13	M14																																						
A4.2.2	Source of EQA materials	Organisation large scale EQA survey	Contribute	M15	M20																																						
A4.2.5	Distribution of EQA materials	Support distribution / data collection	Contribute	M24	M31																																						
A4.2.6	Analysis of results / preparation of manuscript	Analysis of results / preparation of manuscript	Lead	M13	M36																																						
A4.2.7	List of CRM's and EQA materials	Support for preparing the list	Contribute	M13	M30																																						
4.3	Framework for performance verification and harmonization monitoring of IVD tests through EQA data aggregation																																										
A4.3.1	Document on performance verification and harmonisation verification through data aggregation	Preparation of document	Lead	M1	M3																																						
A4.3.2	Design and elaboration of SQL Database	Input for data analysis	Contribute	M4	M12																																						
A4.3.3	Incremental data aggregation	Support in evaluation	Contribute	M13	M35																																						
A4.3.4	Preparation of recommendations	Input for recommendations	Contribute	M35	M36																																						
WP5	Creating impact			M1	M36																																						
5.1	Dissemination and communication																																										
A5.1.4	Presentations at relevant congresses and symposia	EQALM Symposium	Contribute	M1	M36																																						
A5.1.7	Dissemination to the wider community	Quality assurance-related newsletters	Contribute	M1	M36																																						
A5.1.12	Liaise to HALMA	Liaise to HALMA	Contribute	M1	M36																																						
A5.1.16	Stakeholder workshop for EQA providers	Organisation workshop	Lead	M1	M36																																						
5.2	Exploitation and uptake																																										
A5.2.2	Database of CRMs & EQA materials	Publication at EQALM website + inform members	Contribute	M1	M36																																						
A5.2.4	New ways for of organizing commutability studies	Communication with EQA providers	Contribute	M1	M36																																						
A5.2.5	Permanent organization promoting standardization and post-market surveillance of IVD tests	Communication with EQA providers	Contribute	M1	M36																																						
A5.2.6	Preparation of application notes	Support in preparation	Contribute	M1	M36																																						
A5.2.8	Stakeholder workshop for EQA providers	Organisation workshop	Lead	M1	M36																																						

# How is this organised by EQALM?

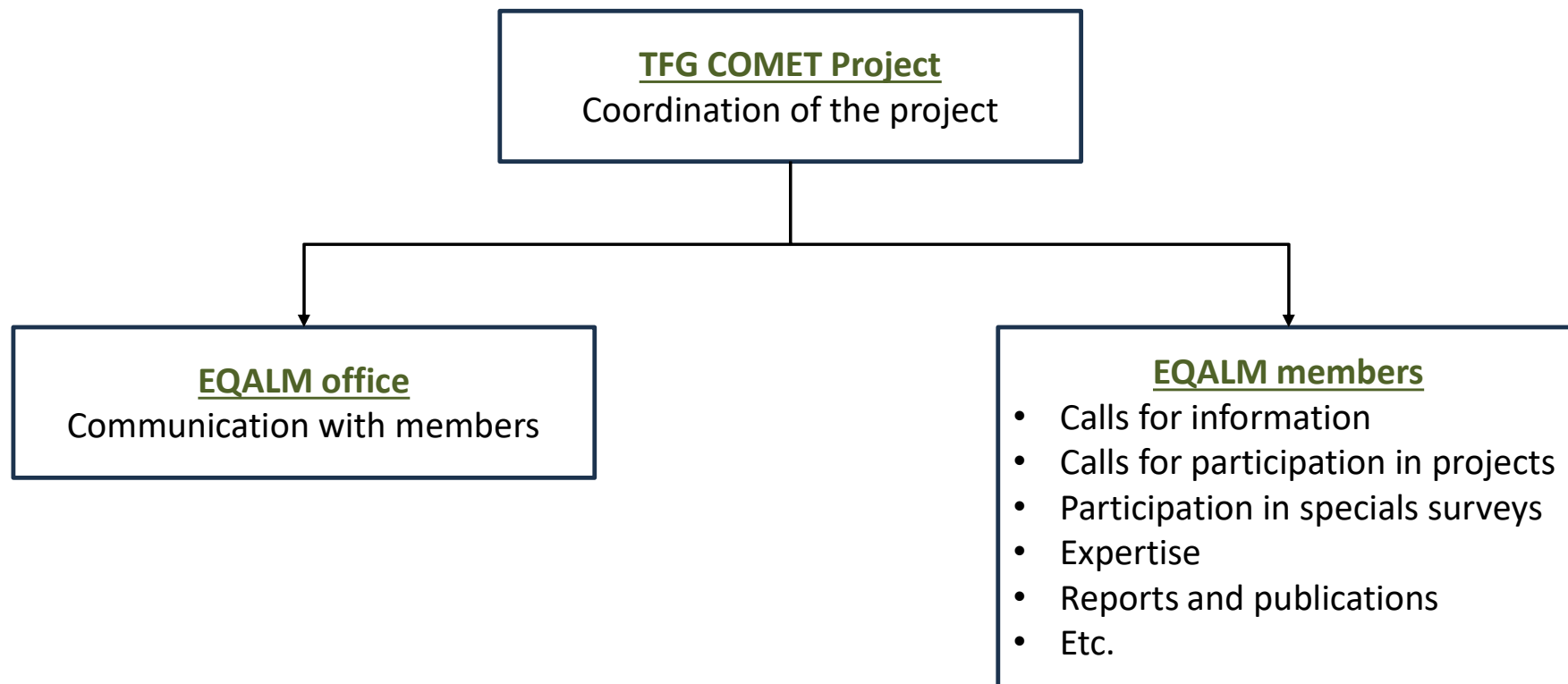


## Task and Finish Group COMET project:

- Piet Meijer (chair) – as chair of the WG Central Database
- Gro Gidske (member) – as chair of the board.
- Gitte Henriksen (member) – as chair of the scientific committee.
- Wim Coucke (member) – as liaison for the EQALM Central Database.

Sciensano (Belgium) is funded partner in the project to make involvement of the EQALM Central Database possible.

EQALM remains owner of the content / output. EQALM rules for data exchange and ownership remains active.



## **Benefits for EQALM members:**

- Contribute in the selection of targets and IVD tests covered in the project
- Get insights in the most appropriate formats of EQA materials to evaluate results accuracy and harmonization
- Get commutable EQA materials value assigned with reference methods at no cost
- Develop the EQALM central database and feed it with EQA data originating from materials of proven commutability



# **PARTICIPATION OF EQALM IN THE COMET PROJECT IS A JOINED EFFORT!**