Annex I – JRP protocol

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18RPT02 adOSSIG

Developing an infrastructure for improved and harmonised metrological checks of blood-pressure measurements in Europe

Start date: 01 June 2019

Duration: 36 months

Coordinator
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CMI

Glossary

aOSG	advanced oscillometric signal generator
BP	blood pressure
JWG	joint working group
NIBP	non-invasive blood pressure
MDD	Medical Devices Directive
MDR	Medical Devices Regulation
NMI	national metrology institute
DI	designated institute
ISO	International Organisation for Standardisation
OIML	Organisation Internationale de Métrologie Légale
SC	subcommittee
SM	sphygmomanometer
TC	Technical Committee
WHO	World Health Organisation
SSC	Smart specialisation concept

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Section A: Key data

A1 Project data summary

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Participant details:

a. Partners (participants who will accede to the Grant Agreement)

no.	Participant Type	Short Name	Organisation legal full name	Country
1	Internal Funded Partner	CMI	Cesky Metrologicky Institut	Czech Republic
2	Internal Funded Partner	BEV-PTP	Physikalisch-Technischer Pruefdienst des Bundesamt fuer Eich- und Vermessungswesen	Austria
3	Internal Funded Partner	GUM	Central Office of Measures	Poland
4	Internal Funded Partner	IMBiH	Institut za mjeriteljstvo Bosne i Hercegovine	Bosnia and Herzegovina
5	Internal Funded Partner	IPQ	Instituto Português da Qualidade, I.P.	Portugal
6	Internal Funded Partner	NSAI	National Standards Authority of Ireland	Ireland
7	Internal Funded Partner	PTB	Physikalisch-Technische Bundesanstalt	Germany
8	Internal Funded Partner	SMU	Slovenský Metrologický Ústav	Slovakia
9	External Funded Partner	UL	Univerza v Ljubljani	Slovenia

A2 Financial summary

	Internal Funded Partners	External Funded Partners	Unfunded Partners	Total
Labour (€)	343 581.24	33 520.00		377 101.24
Subcontracts (€)	7 000.00			7 000.00
T&S (€)	45 100.00	4 000.00		49 100.00
Equipment (€)				
Internally Invoiced Goods and Services (€)				
Other Goods and Services (€)	27 500.00	2 000.00		29 500.00
Large Research Infrastructure (€)				
Indirect (€)	20 809.06	9 880.00		30 689.06
Total eligible costs (€)	443 990.30	49 400.00		493 390.30
Total eligible costs as % of total costs	90 %	10 %	0 %	
EU contribution (€)	**443 990.30**	**49 400.00**		**493 390.30**
EU contribution as % of total EU contribution	90 %	10 %	0 %	
Months	80.8	9.2		90.0

The project plans to subcontract the development of the project website (A5.1.3) because the consortium does not have the technical expertise to create this. Essential clinical expertise in collecting real-life data (A2.1.2) will be subcontracted in case there are problems with the oscillometric signal database, which is necessary for the completion of the project.

A3 Work packages summary

WP No	Work Package Title	Active Partners (WP leader in bold)	Months
WP1	Advanced oscillometric signal generator for real-life signals	**PTB**, CMI, GUM, IMBiH, IPQ, SMU, UL	14.8
WP2	Development of procedures for testing sphygmomanometers with an aOSG	**CMI**, GUM, NSAI, PTB, SMU, UL	12.7
WP3	Procedure for calibration and recalibration of the aOSG	**UL**, CMI, GUM, IMBiH, NSAI, PTB, SMU	21.1
WP4	Smart specialisation concept	**CMI**, BEV-PTP, GUM, IMBiH, IPQ, NSAI, PTB, SMU, UL	13.8
WP5	Creating impact	**PTB**, all partners	19.6
WP6	Management and coordination	**CMI**, all partners	8.0
		Total months:	90.0

Section B: Overview of the research

B1 Scientific and/or technical excellence

B1.a Summary of the project

Overview

This project aims to improve the reliability and accuracy of blood pressure (BP) measurements by developing an advanced oscillometric signal generator (aOSG) and by establishing new calibration procedures and services for blood pressure metrology. Furthermore, the project will establish a competence centre for blood pressure metrology and create a network for blood pressure metrology consisting of NMIs, DIs, surveillance bodies and medical professionals.

Need

Hypertension affects almost half of the European population [1] and is responsible for 13 % of all non-accidental deaths [2]. Hypertension increases the probability of stroke, heart attack and kidney diseases, causing over 22 % of all heart attacks [3]. Effective treatment of hypertension is possible but, as it rarely shows symptoms, the key to successful treatment is early detection. Reliable and accurate BP measurements taken by sphygmomanometers (SM) are indispensable in the diagnostics of hypertension. Therefore, the periodic verification (i.e. metrological checking) of SMs is recommended by the professional medical community [4]; and even required by law in several European countries [5,6].

The European Council Directive 93/42/EEC, which focuses on medical devices, and the succeeding Regulation (EU) 2017/745 require lengthy and costly clinical trials before a new sphygmomanometer enters the market. These clinical trials are performed on human subjects to demonstrate adequate accuracy in different BP ranges. To pass clinical trials, sphygmomanometers are required to work with an average error not higher than ±5 mmHg. However, clinical trials are not performed on every manufactured device, but rather on single, well maintained specimens – frequently called *golden units*. Production devices enter the market (and everyday use) without in-depth testing and end-users must rely on the manufacturer's quality assurance. After entering the market, the devices are subject to mandatory calibrations and verifications in several European countries, but nowadays these procedures only check that the internal pressure sensor works within tolerance, they do not address other components (e.g. software).

Although the EU legislation allows market-surveillance bodies to initiate investigations and even request a clinical trial to be repeated in case of a presumably inaccurate device, due to the high costs and effort required for such investigations, violations are only detected by user complaints.

A sphygmomanometer entering the market can over- or underestimate the true blood pressure value by 5 mmHg and still meet the legal requirements. According to recent studies [1, 3, 7] underlining the importance of accurate BP measurements and adequate metrology, if all BP measurements deviated to such a degree, then over 65 million Europeans would be affected either by non-treated hypertension or side effects of unnecessary treatment.

An advanced oscillometric signal generator can generate oscillometric blood pressure signals indistinguishable from real real-life human signals. However, as there are currently no procedures for testing sphygmomanometers with advanced oscillometric signal generator, the development of such a reference device must be accompanied by the development of the corresponding procedures to use it for SM testing.

Existing difficulties of blood pressure measurements are exacerbated by an insufficient metrology infrastructure at NMI level. BP measurements require expertise in medical metrology but in practice these are frequently considered of secondary importance to pressure metrology. As a result, instead of establishing urgently needed true traceability for modern dynamic oscillometric instruments, only the surrogate of static pressure measurements is verified. This is insufficient for medical purposes. Using aOSGs for SM testing would solve the problem on the device level but aOSGs must be adequately, i.e. dynamically, verified. Therefore, the current potential of advanced oscillometric signal generators is limited by insufficient means to test them. To exploit their full potential, the complete traceability chain for advanced oscillometric generators needs to be established.

Most European NMIs lack the resources and/or know-how to address this issue because there is no harmonised approach. In particular, emerging NMIs suffer from not having a clear goal for their further development while synergetic sharing of resources is prevented by limited cooperation and a lack of strategies for further development.

Objectives

The overall aim of the project is to develop sustainable metrological research capabilities to provide traceability for blood pressure measurement in Europe. This will include the development of a new advanced blood pressure oscillometric signal generator and investigation of its possible role as an absolute blood pressure standard to carry out checks of the performance of (SMs).

The specific objectives are

1. **To develop an advanced oscillometric signal generator device** with the capability of accurately reproducing pre-recorded real-life oscillometric blood pressure pulses.
2. **To define the necessary requirements and test procedures** for the newly developed advanced oscillometric signal generator to become a reference standard to establish traceability for automated sphygmomanometers.
3. **To develop a procedure for the periodic recalibration of the newly developed advanced oscillometric signal generator** at the NMI level, including defining acceptable uncertainty limits of ±1.5 mmHg or better.
4. **To engage closely with regional and European stakeholders,** including regulatory and governmental bodies, medical experts, professional medical societies, standards developing organisations, metrological committees and device manufacturers to ensure that all medical, legal and metrological requirements regarding blood pressure measuring devices are met.
5. **To develop and implement a concept for smart specialisation in the field of traceable blood pressure measurements** and to integrate this concept with similar ones for other medical devices. To establish a single joint research capacity and to develop a strategy for the perpetuation and sustainability of this new capability and a strategy for offering calibration and research services to national or international customers including NMIs/DIs. Additionally, for each internal partner, to develop an individual strategy for the long-term operation and transnational use of this joint research capacity, and for the access to its calibration and testing services from their respective countries. The individual strategies will be discussed within the consortium, to ensure that a coordinated and optimised approach to the development of traceability in this field is developed which is suitable for Europe as a whole.

Progress beyond the state of the art and results

The project will expand the knowledge gained during the EMPIR Project 16RPT03 inTENSE, within which a competence centre on the intraocular pressure is being established. The first three objectives of the project aim to progress metrological testing of sphygmomanometers beyond the state of the art by creating an advanced test device, procedures and calibration methods. To this end, an advanced oscillometric signal generator (aOSG) will be developed which will be able to generate real life signals as opposed to the strictly periodic oscillometric signals generated by the current commercial blood pressure simulators. After its development, the aOSG will be tested as a possible standard for the recalibration and verification and in-depth performance checks of sphygmomanometers. The project will develop a dynamic procedure for testing sphygmomanometers with an aOSG as opposed to the static procedures representing the present state of the art.

The final two objectives aim at the establishment of joint research capacity, which will persist beyond the project lifetime and will support, promote and further develop advanced blood pressure metrology. Currently, a number of EU countries, e.g. Austria, Czech Republic, Germany, Slovakia, have regulations in effect requiring periodic metrological checks or (re-)verification for professionally used SMs to ensure consistent performance in the field. This project aims to create harmonised metrological checks for blood pressure measurements to ensure a homogeneous European market.

Advanced oscillometric signal generator device

The aOSG will allow in-depth performance checks and calibrations of the sphygmomanometers, which will reduce the necessity to use human subjects in clinical trials and reduce the financial and time costs of such trials.

The aOSG will be able to generate signals undistinguishable from real-life human signals. Technically it will be suited, therefore, to replace human subjects in clinical trials for conformity assessments of new SMs. Predictably, the medical community will not immediately accept such a radical paradigm change but a realistic initial goal for a wider usage of this device is to replace those human subjects who are ethically sensitive or at the highest risk during clinical trials, e.g. neonates, pregnant women, subjects with severe untreated hypertension.

Necessary requirements and test procedures

For the aOSG to be used in the in-depth performance check of oscillometric sphygmomanometers, test procedures for such an in-depth, dynamic testing of sphygmomanometers and technical and metrological requirements will be defined. These requirements and advanced test procedures will amend insufficient state-of-the-art static pressure testing and will allow the evaluation of performance of the whole sphygmomanometer rather than just the ability of pressure sensor to display static pressure correctly.

Procedure for the periodic recalibrations of aOSGs

Currently, the calibration of almost every pressure instrument is carried out by static pressure. The aOSG will generate oscillometric blood pressure signals, i.e. short rapid dynamic pressure pulses superimposed on slowly decreasing pressure. As the valid calibration of such a device is currently not possible at NMI level, the development of advanced dynamic calibration procedures is one of the necessary steps to allow the aOSG to work as intended.

Close engagement with regional and European stakeholders

This project will bring together the most relevant international metrological and medical institutions, producers of sphygmomanometers and market surveillance bodies, and make the project known and accessible to the wider community. In addition, the possibility of the future expansion of the competence centre scope will be investigated i) geographically beyond Central Europe and ii) thematically towards all quantities in medical device metrology.

Impact

Impact will stem from the two main goals of the project: the development of an advanced oscillometric signal generator (aOSG) and the establishment of the research and competence centre for blood pressure metrology. The outputs of this project will significantly progress blood pressure metrology beyond the current state of the art, improving reliability and accuracy of oscillometric blood pressure measurements achievable at all levels including NMIs, DIs, surveillance bodies, manufacturers of sphygmomanometers, medical professionals and patients.

Impact on industrial and other user communities

Development of an aOSG and advanced calibration procedures will allow easier and cheaper in-depth performance checks of new sphygmomanometers. This will ease development process of SMs for new and small manufacturers, offering them a chance to access the market at lower costs and thus encouraging the innovation.

The research and competence centre will create a well-developed metrological infrastructure with advanced calibration services and will provide manufacturers with clear guidance, and hence legal certainty on how requirements can be met. Physicians and medical staff will be able to rely on the existing traceability chain, trust the measurement results are correct and methods are validated. Patients in clinics, practitioner offices, and home-care settings will have more confidence in the measured BP values, as the improved infrastructure will allow surveillance bodies and other legal entities to ensure adequate quality of the devices available on the market.

Impact on the metrology and scientific communities

This project will make metrology for advanced blood pressure measurements accessible to a broader range of countries. This will be achieved through the smart specialisation, by condensing expertise and knowledge at one site, while simultaneously making it accessible to others. A centre of excellence for blood pressure measurement (competence centre) will be established at CMI, which will be designed for the needs of Czech Republic and all European NMIs/DIs in this field who cannot or do not want to build and maintain this capacity for themselves. The project will create a network for blood pressure metrology consisting of NMIs, DIs, surveillance bodies and medical professionals, and a calibration laboratory providing dynamic pressure traceability will be established. Other European NMIs, particularly emerging NMIs and DIs, which are lacking the capabilities or the resources to provide the complete traceability chain for BP measurements, will be able to serve their national customers with less demanding metrological services, while relying on the competence centre for the higher-level ones.

Impact on relevant standards

The project will have an active participation in key sphygmomanometry and pressure related standardisation committees, international and European legal metrology organisations (e.g. ISO/TC 121/JWG7, OIML TC18 and IMEKO TC16). This participation builds on links already established by the consortium, which is highly influential in national and international metrology and standardisation committees, and will be used to facilitate greater awareness of the benefits of the project.

In the longer term, i.e. after the end of the project, the outcomes may contribute to the revision of different normative documents (e.g. IEC 80601-2-30 and OIML R 16-2). The partners are the principal editors of the German "Leitfaden für die messtechnische Kontrolle von Medizinprodukten mit Messfunktion" (Guidelines for Metrological Checks of Medical Devices with a Measuring Function), so the relevant project results will serve as input into this document.

Longer-term economic, social and environmental impacts

The European healthcare industry will primarily benefit from this project in the long term. The prevalence of hypertension is 44 % in Europe [1], which means more than 200 million adults are affected by this health problem. The required accuracy of automated sphygmomanometers in a clinical trial is ±5 mmHg but a consistent over- or underestimation of measured BP values by 5 mmHg would change the number of diagnosed patients by ~30 % in either direction [3]. At the end of the project, an aOSG will exist with uncertainty of better than ±1.5 mmHg and a dynamic traceability chain will be established. It can thus be ascertained that the initial ±5 mmHg uncertainty of a sphygmomanometer can be maintained without deterioration over the whole production and lifetime cycle of the device; a guarantee which cannot possibly be given today. Cautiously, assuming that for only 1 % of the patient misdiagnoses can be avoided in the future, the direct benefits of the project can be quantified as:

- 2 million EU citizens who will be spared a false positive or false negative diagnosis,
- 370 M€ per year which will be saved for the EU healthcare systems by avoiding the costs for unnecessary medication of healthy subjects and the even higher costs for undetected and untreated hypertension (estimated from 196 B€/a total costs for cardiovascular diseases in the EU in 2009 [8], 53 % of which are treatment costs, and a ~36 % share for hypertension treatment [9]).

B1.b Overview of the scientific and technical objectives

The overall objective of the project is to raise the quality and reliability of automated blood pressure devices in Europe and to progress beyond the current state of the art in blood pressure metrology.

The specific objectives of the project are:

1. **To develop an advanced oscillometric signal generator device** with the capability of accurately reproducing pre-recorded real-life oscillometric blood pressure pulses. (WP1)
2. **To define the necessary requirements and test procedures** for the newly developed advanced oscillometric signal generator to become a reference standard to establish traceability for automated sphygmomanometers. (WP2, WP3, WP4)
3. **To develop a procedure for the periodic recalibration of the newly developed advanced oscillometric signal generator** at the NMI level, including defining acceptable uncertainty limits of ±1 5 mmHg or better. (WP3)
4. **To engage closely with regional and European stakeholders**, including regulatory and governmental bodies, medical experts, professional medical societies, standards developing organisations, metrological committees and device manufacturers to ensure that all medical, legal and metrological requirements regarding blood pressure measuring devices are met. (WP4, WP5)
5. **To develop and implement a concept for smart specialisation in the field of traceable blood pressure measurements** and to integrate this concept with similar ones for other medical devices. To establish a single joint research capacity and to develop a strategy for the perpetuation and sustainability of this new capability and a strategy for offering calibration and research services to national or international customers including NMIs/DIs. Additionally, for each internal partner, to develop an individual strategy for the long-term operation and transnational use of this joint research capacity, and for the access to its calibration and testing services from their respective countries. To ensure that a coordinated and optimised approach to the development of traceability in this field is developed which is suitable for Europe as a whole.

B1.c List of deliverables

Relevant objective (Activity delivering the deliverable)	Deliverable number	Deliverable description	Deliverable type	Partners (Lead in bold)	Delivery date
Objective 1 (A1.4.4)	D1	Technical document on the development of the advanced oscillometric signal generator, able to withstand constant pressures up to 300 mmHg, generate pulses of 0.5-10 mmHg for frequency up to 10 Hz and determine the pneumatic frequency response in the frequency range 1-20 Hz	Technical document	**PTB**, GUM, CMI, IMBiH, IPQ, SMU, UL	Aug 2021 (M27)
Objectives 1–5 (A1.4.6)	D2	Validation report on applicability of the advanced oscillometric generator in market surveillance and/or clinical trials	Validation report	**PTB**, UL, CMI	May 2022 (M36)
Objective 2 (A2.3.3)	D3	Guidelines for the evaluation of automated sphygmomanometers using an aOSG and oscillometric data	Guidelines	**CMI**, GUM, NSAI, PTB, SMU, UL	May 2022 (M36)
Objective 3 (A3.2.3)	D4	Report on the development of an uncertainty model for the aOSG calibration with a target uncertainty ± 1.5 mmHg	Report	**IMBiH**, CMI, GUM, PTB, SMU, UL	Jul 2021 (M26)
Objective 3 (A3.3.4)	D5	Report on the aOSG calibration procedure enabling to obtain an uncertainty of ± 1.5 mmHg or better	Report	**UL**, CMI, GUM, IMBiH, NSAI, PTB, SMU	Mar 2022 (M34)
Objectives 4, 5 (A4.4.4)	D6	White Paper on the smart specialisation concept developed to ensure a coordinated and optimised European approach towards European metrology centre	White paper	**CMI**, GUM, IMBiH, IPQ, SMU, UL, PTB, NSAI, BEV-PTP	May 2022 (M36)
Objectives 1–5 (A4.3.4)	D7	Report demonstrating the qualified traceable measurement and extended calibration services for the aOSG and similar devices	Report	**CMI**	May 2022 (M36)
Objective 5 (A4.5.9)	D8	Agreed individual strategies for internal partners for the long-term operation and transnational use of the joint research capacity (competence centre) and for the access to its calibration and testing services from their respective countries	Documented strategies	**CMI**, GUM, IMBiH, IPQ, SMU, PTB, NSAI, BEV-PTP	May 2022 (M36)
(n/a)	D9	Evidence of contributions to or influence on new or improved international guides, recommendations and standards with a specific focus on the following guides and committees: CCM WGPV, IMEKO TC16. Examples of early uptake of project outputs by end-users	Reporting documents	**CMI**, all partners	May 2022 (M36)

n/a	D10	Delivery of all technical and financial reporting documents as required by EURAMET	Reporting documents	CMI, all partners	May 2022 (M36) + 60 days

B1.d Need for the project

The average hypertension prevalence in Europe is 44 %, with regional and community extremes as high as 60 % [1]. Hypertension causes 13 % of deaths and over 22 % of all heart attacks in Europe [2], also it increases the probability of stroke, heart attack and kidney diseases. According to the state of the art [3]: "*Underestimating true blood pressure by 5 mmHg would mislabel more than 20 million Americans with pre-hypertension when true hypertension is present. It has been predicted that the consequences of an untreated 5 mmHg of excessive systolic blood pressure would be a 25 % increase over current levels of fatal strokes and fatal myocardial infarctions for these individuals [10]. Conversely, overestimating true blood pressure by 5 mmHg would lead to inappropriate treatment with anti-hypertension medications in almost 30 million Americans, with attendant exposure to adverse drug effects, the psychological effects of misdiagnosis, and unnecessary cost [7]*". For the EU, the percentages are similar, and the absolute numbers reach in total over 65 million Europeans.

Effective treatment of hypertension is possible but, as it rarely shows immediate symptoms, the key to successful treatment is early detection. Reliable and accurate BP measurements taken by sphygmomanometers are the indispensable foundation of hypertension diagnostics.

Non-invasive methods of BP measurement can be divided into two main groups, manual (auscultatory) and automated (oscillometric, for all practical purposes) methods. Manual auscultatory method determines BP values directly by simultaneous i) reading of pressure value in the cuff on the patient's limb and ii) observation of the so-called Korotkoff sounds. Although the auscultatory method is considered the "gold standard", its correct utilisation requires the measurements to be performed by medical professionals and therefore this method is not appropriate for automated or home-care measurements. Although medical professionals are aware of the challenges occurring when using the auscultatory method (e.g. terminal digit preference) they are mostly on the operator training level and hence easy to avoid. The automated oscillometric method observes pressure pulses in an inflated cuff. Devices using this method represent the vast majority of electronic devices entering the market today, as they do not require skilled observers, avoid the "white-coat effect", can be used for long-term and home monitoring, and allow for fully automated BP monitoring on intensive care units. However, the relationship between oscillometric pulses and systolic and diastolic BP values is complex. The algorithms used to estimate BP values are based on empirical data, gained from clinical studies by each manufacturer separately. There is no standard procedure or algorithm and the proprietary internal software of automated SMs is not disclosed, neither to the public nor to regulatory bodies or test houses. Although commonly used, oscillometric sphygmomanometers are known to occasionally indicate inaccurate values due to algorithmic and software issues. These issues are aggravated with patients who need accurate measurements the most, i.e. those with cardiac and circulation problems [11].

Manufacturers of blood pressure measuring devices are required by European legislation to demonstrate conformity to the essential requirements as defined in the Council Directive 93/42/EEC concerning medical devices, and Regulation (EU) 2017/745 of the European parliament and of the Council on medical devices. Practically, this boils down to a demonstration of compliance with the respective harmonised or otherwise relevant standards, e.g. the ISO 81060 series requiring the manufacturer to perform lengthy and costly clinical trials prior to entering the market with each new device. These clinical trials are performed on human subjects (including special groups like neonates, pregnant women, people with untreated hypertension, etc.) to demonstrate adequate accuracy in various BP ranges. To pass clinical trials, the devices are required to work with average error not higher than ±5 mmHg and standard deviation not higher than 8 mmHg. Therefore, the sphygmomanometer can fulfil all legal requirements with respect to accuracy and yet the measurement results may still be inaccurate enough to cause inappropriate treatment (as mentioned above). Regarding the average blood pressure value in Europe, 136/83 mmHg, considered as pre-hypertension, it is obvious that accurate and correct blood pressure measurements are very important [1]. Experts from academia, medicine and surveillance bodies confirm the need for accurate and precise measurements and measuring instruments [12-15].

Due to the inconvenience caused to the involved subjects and the high costs of clinical trials, a new approach is urgently required. An advanced device (aOSG), capable to generate oscillometric signals undistinguishably from life human signals, is needed to reduce, and in the long run eliminate, the need to employ human subjects to assess the accuracy of a given SM model. An aOSG capable to produce absolute BP reference values is particularly imperative when clinical tests need the inclusion of certain human subjects at high risk (e.g. severe hypertension, testing of SM for neonates).

The EU legislation allows market-surveillance bodies to initiate investigations, up to requesting the repetition of clinical trials, in case of a presumably inaccurate device. However, this scrutiny is prevented by the high costs and effort of such a reinvestigation. Hence violations are only detected in very rare and extreme cases.

Although EURAMET TC-M stated already in 2012 in Dynamic Area Roadmap that there is a need to develop new methods, facilities and transfer standards for dynamic pressure, especially where high accuracy is required, the research in this field covered mostly *industrial* pressure metrology. Because metrology for BP measurements within Europe is mostly assigned to classical pressure metrology departments, it is equally undeveloped in most countries. Although metrological checks, verifications or calibrations of sphygmomanometers are required by law in several countries, the metrology world can only provide tools and methods adequate for manual devices, i.e. static pressure calibrations. There are no services available for traceable dynamic pressure calibration to serve the blood pressure metrology. To overcome the current problems of insufficient traceability chain, transfer to dynamic pressure traceability is necessary for new oscillometric standards.

Existing difficulties of blood pressure measurements are exacerbated by an insufficient metrology infrastructure at NMI level. BP measurements need expertise in medical metrology but most European NMIs lack the resources and/or know-how to address this issue as there is no harmonised approach to this part of metrology. It is frequently considered of secondary importance to pressure metrology when a dedicated health department is missing. In particular, emerging NMIs suffer from not having a clear goal for their further development while synergetic sharing of resources is prevented by limited cooperation and unclear strategies for further development. As a result, instead of establishing urgently needed true traceability for modern dynamic oscillometric instruments, only the surrogate of static pressure measurements is verified. This is insufficient for the medical purpose. Using OSGs for sphygmomanometer testing would solve the problem on the device level. Little is gained, however, as long as aOSGs themselves cannot be adequately, i.e. dynamically, verified. At present, the potential use of advanced oscillometric signal generators is therefore limited by insufficient means to test them. To exploit their full potential, the complete traceability chain for advanced oscillometric generators needs to be established.

This project aims to develop metrological research capabilities in the field of non-invasive dynamic BP measurement. It focuses on the cooperation of experienced NMIs (such as PTB) and academia with less experienced partners (e.g. CMI, BEV-PTP, GUM, IMBiH, IPQ, NSAI, SMU) to enable knowledge transfer and sharing to establish coordinated approach toward the project's goal. The cooperation and coordination within the newly established competence centre will enable to address the needs of the project as a whole. Additionally, a Europe–wide research and metrological traceability network for medical devices in general will be established and maintained beyond this project.

B1.e Progress beyond the state of the art

Advanced oscillometric signal generator device

Current state of the art

There are many commercially available blood pressure simulators on the market. These devices are potentially suitable as transfer (relative) standards, i.e. they have a potential to be used in calibration and verifications but are not suitable for total in-depth performance checks of sphygmomanometers, where absolute standards are required. The signals generated by commercial simulator models are different from type to type; therefore, each sphygmomanometer simulator combination gives different BP readings. Consequently, there is no absolute oscillometric blood pressure standard available on the market.

Progress beyond the state of the art

The project will develop an aOSG, a device capable of accurately reproducing pre-recorded real-life oscillometric data. Unlike its commercially available counterparts, the aOSG will not replay the same signal (or set of signals) for every tested device, but will rather create unique signals for each tested sphygmomanometer taking into account dynamic variables like deflation rate, cuff size etc. The development of the aOSG will be accompanied by the development of test procedures for sphygmomanometer testing and dynamic pressure calibrations using the aOSG.

Necessary requirements and test procedures

Current state of the art

Currently, there are ISO/IEC standards [16, 17, 18] and OIML recommendations [19] defining performance requirements for sphygmomanometers. Protocols to check the accuracy of automated SMs have also been published by the European [20, 21], British [4] and German [22] Hypertension Societies. These documents were developed for mechanical devices and work well for them. However, for modern automated oscillometric

devices these test methods are insufficient and calibrations and tests based on above mentioned documents only examine if the internal pressure sensor works within tolerances. The sensor is tested by static pressure that has very little in common with real dynamic blood pressure. The algorithms to determine a systolic and diastolic BP value from a measured oscillometric curve are never even looked at.

A number of EU countries, e.g. Austria, Czech Republic, Germany, Slovakia and Slovenia, have regulations which require periodic metrological checks or (re-)verification for professionally used SMs to ensure consistent performance in the field. Once again, verification is limited to static pressure testing, therefore only ensuring that the pressure sensor works correctly, while nothing is learned about the correctness of the BP readings.

The relevant standards and EU legislation require extensive and costly clinical trials before a new sphygmomanometer enters the market. Additionally, it is required to obtain CE marking to demonstrate adequate accuracy of ± 5 mmHg, and standard deviation not higher than 8 mmHg. This value, however, applies only to the clinically tested so-called golden unit; it cannot be guaranteed over the whole production and lifetime cycle of the devices. Production devices are only assumed to be identical to the clinically tested ones and end-users must rely only on manufacturers' quality control.

Currently, regulatory bodies questioning the correctness of a CE marking on a presumably inaccurate automated sphygmomanometer, that already entered the market, need to re-initiate a full investigation including clinical trial to clarify the case. Due to the costly and time-consuming process involving testing on human subjects, such an action has never been heard of.

Progress beyond the state of the art

The aOSG will become the absolute oscillometric signal standard and hence be able to complement and in the long run possibly replace human test subjects during clinical trials. By design, it will be optimal tool for in-depth performance evaluation of sphygmomanometers. Today, such assessments require clinical human subject testing with given minimal number of test subjects and required specific BP values. As several of these combinations can be rare and hard to find or the inclusion of such subjects may be ethically problematic, the inclusion of the aOSG in such trials would provide valuable support. Examples of issues are: the need to test subjects with severe hypertension, where such a diagnosis leads to immediate treatment and therefore the original BP value is no longer available; testing of SM for neonates, where the required reference measurements can be complicated or life-threatening and are always ethically sensitive.

With the availability of the aOSG it is expected that the overall uncertainty/accuracy of measurement by sphygmomanometers will remain at approx. ±5 mmHg, which is today only the maximum average error during the clinical trials of SMs. Although the project will not lower the uncertainty per se, it can be expected that the new approach to the sphygmomanometer in-depth testing and traceability will allow the uncertainty to be maintained without deterioration over the whole production and lifetime.

Procedure for the periodic recalibrations of the aOSGs

Current state of the art

Valid calibrations, metrological and in-depth checks of sphygmomanometers require test equipment to be calibrated. For oscillometric blood pressure signals, i.e. combination of two dynamic pressure forms, this means a valid dynamic pressure calibration. As above, the current state of the art of calibrating simulators still rely on verifying static pressure indications and therefore fails to meet that requirement.

Beyond the state of the art

Significant progress beyond the state of the art will be achieved in advanced pressure calibration tool and services with a target uncertainty of ±1.5 mmHg. These procedures will be primarily developed for the aOSG produced within the project, but once the calibration chain is established, possible adaptations for similar devices can be easily made.

Close engagement with regional and European stakeholders

Current state of the art

Although hypertension and issues with automated blood pressure measuring instruments are common in all European countries, there is currently no joint research capability nor network among NMIs that could effectively share the knowledge, develop necessary tools, methods and provide adequate calibration services.

Beyond the state of the art

This project will bring together the most relevant international metrological and medical institutions, producers of sphygmomanometers and market surveillance bodies, and make the project's outcomes known and accessible to the wider community. In addition, the possibility of future expansion of the competence centre

scope will be investigated: geographically beyond Central European countries and thematically towards all quantities in medical device metrology.

Concept for smart specialisation in the field of traceable blood pressure measurements

Current state of the art

Smart specialisation, which is being pushed by the EU, is currently not applied in the field of blood-pressure measurement at the NMI level. The feasibility of smart specialisation concept in the field of medical metrology is the focus of EMPIR project 16RPT03 inTENSE focused on intra-ocular pressure metrology (capacity building and strengthening, new measurands and international cooperation). The goal of that project is to establish a competence centre for intraocular pressure (IOP) metrology at CMI.

Beyond the state of the art

Parallel to the development of the aOSG, there will be a substantial part of the project focused on development and implementation of smart specialisation concept (SSC) for traceable oscillometric BP measurement and research in Europe. This will be a foundation for a long-term partnership, i.e. beyond the end of this project, in dynamic blood pressure metrology. The smart specialisation will allow the involved NMIs and DIs to optimally utilise the limited national capacities in a smart division of labour and resources. Upon the implementation of the smart specialisation concept, many NMIs will be relieved of the burden of being equally undeveloped in this particular field of metrology and will be able to focus their limited resources and capacities on other, and for them more important or profitable, fields. Simultaneously, this will allow NMIs/DIs to stay active in the field even if they do not have the experience, capacity or resources to do so at a full scale, e.g. an NMI which has the experience and equipment to calibrate pressure sensors but not the medical know-how required for advanced BP metrology, can keep the first part of the business and outsource the second part within the competence centre.

The smart specialisation concept will create a network of NMIs, DIs and universities that will be able to support and advise blood pressure metrology in Europe at all levels, from manufacturers, test offices, laboratories and market surveillance bodies to end-users, such as the medical community and patients. In addition, this network can be incorporated into the European centre for medical device metrology, planned to be established after the project.

B2 Potential outputs and impact from the project results

B2.a Projected early impact on industrial and other user communities

This project will improve the quality and reliability of automated blood pressure measurements by lowering uncertainties of measurement and establishing new test and calibration methods. This will have immediate impact on the whole chain, from manufacturers of sphygmomanometers to market surveillance bodies and healthcare professionals and patients. Both the newly created competence centre for blood pressure metrology and the aOSG will impact industry and end-user communities.

The new aOSG will enable manufacturers to perform in-depth performance checks of automated sphygmomanometers whenever needed; e.g. during the sphygmomanometers development and in case of software changes or problematic performance in certain blood pressure range. The manufacturers of sphygmomanometers will highly benefit from the new aOSG that will be able to reproduce very accurately real-life signals. This device can be used during clinical trials to substitute hard-to-find subjects required by the relevant standards (e.g. neonates, highly hypertensives).

The most important group of beneficiaries will be patients and medical professionals. The aOSG will increase confidence in the accuracy and reliability of blood pressure measurements, thus improving diagnosis and therapy. Besides more accurate readings, this will reduce the cost and effort for the society and EU healthcare systems.

Regional authorities will have a more realistic testing of sphygmomanometers than nowadays. The research capacity developed in this project will be able to adapt to technological or regulatory changes in the future and therefore support the regulatory stakeholder group.

The competence centre will be able to provide guidance, metrological expertise and calibration services for automated sphygmomanometers. The competence centre will last beyond the project and will subsequently become a part of the European centre for medical device metrology.

B2.b Projected early impact on the metrological and scientific communities

Within the project a competence centre for advanced blood pressure metrology will be established at CMI, which will be able to serve the whole region. The centre will provide traceable calibration services for aOSGs and similar devices and provide support for the whole chain of BP measurements. The centre will further expand the idea of a harmonised approach to blood pressure metrology, despite varying regulatory requirements and despite the absence of a EURAMET 'TC Health' or a comparable metrological authority in this field. Not only the stakeholder groups in the participating countries, but also the NMIs/DIs involved will benefit as resources will be shared and competence concentrated at one place.

Consortium and stakeholders will develop an effective communication and cooperation network that will allow the metrological partners to stay in close contact with both their customers, public or private test and calibration offices, and legislators and regulatory authorities.

The standard operating procedures and the good practice guidelines for sphygmomanometer testing using aOSGs and calibration procedures which will be developed and published by the consortium will provide smaller and less experienced NMIs/DIs from within or beyond the consortium with a clear route which they can follow. The establishment of the service centre will allow all smaller NMIs/DIs to leave this segment and focus their limited resources and capacities on other, and for them more important or profitable, fields. This new approach will help them to provide all metrology services required by national regulations or desired by the socioeconomic needs of their countries without the risk of violating the regulations or being unable to provide services due to limited resources.

Simultaneously, the centralised service at CMI will allow NMIs/DIs to stay active in the field even if they do not have the experience, capacity or resources to do so at a full scale, e.g. an NMI which has the experience and equipment to calibrate pressure sensors but not the medical know-how required for advanced blood pressure measurements, can outsource services from the competence centre.

B2.c Projected early impact on relevant standards

The project will have an active participation in key sphygmomanometry and pressure related committees, international and European legal metrology organisations such as ISO/TC 121/JWG7, OIML TC18 and IMEKO TC16. This participation builds on existing links and will be used to facilitate greater awareness of the benefits of the project. In the longer term, the outcomes of this project may contribute to the revision of different normative documents (e.g. IEC 80601-2-30, OIML R 16-2).

The German "Leitfaden für die messtechnische Kontrolle von Medizinprodukten mit Messfunktion" (Guidelines for Metrological Checks of Medical Devices with a Measuring Function) is the de-facto standard in Germany and Austria. As the project partners are its principal editors, relevant results will serve as input to this document.

Standards Committee / Technical Committee / Working Group	Partners involved	Likely area of impact / activities undertaken by partners related to standard / committee
ISO/TC 121/SC 3/ JWG 7	PTB	PTB is convenor of JWG 7 - Non-Invasive sphygmomanometers. This working group has developed several standards on non-automated non-invasive sphygmomanometers, automated non-invasive sphygmomanometers and on clinical investigation of automated sphygmomanometers. Simulators are required for several tests in the standard on automated non-invasive sphygmomanometers and will be the focus of a new technical specification. Due to technical advancements, these standards are revised regularly. This working group meets twice a year to discuss the revisions of published standards and the development of new technical specifications. In its convenor role, PTB will lead all these discussions and present this project and its results. Feedback will be sought on the results presented to this technical committee.
OIML TC18 / SC1	PTB, BEV-PTP, CMI, IPQ	PTB is secretary, BEV-PTP, IPQ are members and CMI is observer of the TC18 "Medical Measuring Instruments". This committee communicates mostly by e-mail and ad-hoc meetings. PTB, with the assistance of BEV-PTP, CMI and IPQ, will update the committee on the project's targets and results, and seek feedback on those. The recommendation R 16-2: Non-invasive automated sphygmomanometers, which requires the use of simulators for the testing of automated sphygmomanometers is under revision. PTB is actively taking part in this work.

IMEKO TC16	CMI, PTB, SMU	CMI is scientific secretary, and PTB and SMU are members of TC16 "Pressure". The area of dynamic BP measurement will be highlighted within this committee. IMEKO TC16 meets every 2 – 3 years in connection with IMEKO events. The group will be updated on the project's targets and results by CMI, or PTB and SMU. Cooperation on the dissemination of these results will be requested from this committee and from IMEKO TC13 Medicine.
EURAMET TG Health	CMI, GUM, IMBiH, IPQ, SMU, UL, PTB, NSAI, BEV-PTP	The consortium will contact this task group to explore cooperation within the framework of the smart specialisation concept. The consortium will keep EURAMET regularly updated about the project's plans and progress whilst simultaneously learning about their views on the project's planned activities, their possible experience in this respect and their recommendations. The consortium will seek support and endorsement for the European centre for medical device metrology from EURAMET whilst offering to take their recommendations and requests into account when building it.
CCM WGPV	CMI, PTB	CMI and PTB are members of the "Comité consultatif pour la masse et les grandeurs apparentées" – "Groupe de travail pression-vide". The area of dynamic BP measurement will be highlighted within this committee. The WGPV meets every 3 years (May 2020). The group will be updated on the project's targets and results by CMI or PTB on its next meeting.

B2.d Projected wider impact of the project

The main project impact on stakeholders will be achieved through improved blood pressure measurements and the competence centre for BP metrology, which will be established at CMI and act as a service provider for other European NMIs and DIs. Larger NMIs will be able to outsource the work to CMI without compromising the service for their customers, thus freeing valuable resources and allowing them to focus on other areas of research. Countries with NMIs/DIs that are lacking the capacity to develop and provide high-level BP metrology on their own will for the first time get access to this service, provided by CMI and mediated by their national NMI/DI, which will in turn benefit both their society and economy.

The competence centre will be a step towards a wider competence centre for the whole field of medical metrology. The centre will able to provide metrological services to European NMIs and Dis, and metrological advice to stakeholders.

The concept of a shared metrological workload as pursued by this project has the potential to profoundly change the metrological landscape in Europe. Traceable calibration of medical devices is a promising area of metrological activity, but it is not an easy field for newcomers to enter, because competence and know-how in the metrology of physical quantities might not be enough. Instead, a fair amount of medical competence and connections within the respective medical community are required. The competence centre at CMI will contribute with medical expertise while the basic physical-quantity metrology could remain at the local NMI/DI.

The new competence centre for BP metrology at CMI will provide a network to all stakeholders from governmental and regulatory authorities to manufacturers of sphygmomanometers, and calibration and test offices. New guidance documents on in-depth dynamic testing of electronic sphygmomanometers will be produced, and the traceability for aOSGs will be established. These will help public and private calibration offices to provide services according to the latest state of the art. It will also ensure a uniform and high-quality metrological service in all participating European countries.

Economic impact:

The aOSG to be developed in this project will reduce the need to employ human subjects to assess the accuracy of blood pressure measuring devices. This is particularly important when clinical tests require the inclusion of high-risk subjects e.g. neonates and severe hypertensives, thus reducing cost and time. The manufacturers, authorities responsible for CE marking, market surveillance bodies and medical societies performing clinical trials will benefit from easier, more affordable and faster clinical trials.

Socio-economic impact:

Cautiously assuming that for only 1 % of 200 million adults in EU diagnosed with hypertension [1], misdiagnosis can be avoided in the future, the direct economic impact of the project can be quantified as 370 M€ per year. This is a significant cost saving for EU healthcare systems, which will be able to avoid the costs for unnecessary medication of healthy subjects and the even higher costs for undetected and untreated hypertension [8].

Social impact:

More reliable measurements and advanced tools and standards for oscillometric blood pressure measurements will be available by the end of this project. Additionally, the metrological requirements will be unified for a number of states and possibly for all of the EU and associated states. This will provide EU citizens with better, more reliable and less uncertain measurements. As a result, and in agreement with the above cautious assumption of only 1 % improvement of diagnosis, 2 million EU citizens will be spared false positive or false negative diagnosis.

B2.e Data management

The project chooses to 'Opt-in' to the open access data requirement.

The consortium was authorised by the Newcastle University to use their database of pre-recorded oscillometric signals for the purpose of this project (a letter of authorisation exists and will be submitted if required). Data were collected outside the project and this database will not be made accessible taking into account the envisaged licensing terms for their use by the consortium.

The project will make its research data Findable, Accessible, Interoperable and Reusable (FAIR) in order to ensure that it is soundly managed. The consortium will produce a suitable Data Management Plan (DMP) which will describe the data management plans for all of the data sets that will be collected, processed or generated by the project. The DMP will cover the following aspects:

- the handling of research data during and after the end of the project;
- specification of the data that will be collected, processed or generated;
- the methodology and standards (including data security and ethical aspects) that will be applied;
- plans for data curation and preservation (including after the project).

An outline DMP will be created within the first month of the project and agreed by the consortium. The consortium intends prepare a first draft of the DMP for discussion at the project kick-off meeting. Each subsequent project meeting will include an agenda item on the DMP.

The consortium agrees to deposit its open access data sets in suitable repositories. These will be located by the consortium using the Registry of Research Data Repositories (http://www.re3data.org/). Possible examples include Zenodo (https://zenodo.org/), which will allow the consortium to deposit both publications and data, and the EUDAT B2SHARE tool (https://b2share.eudat.eu/) which includes a license wizard for data licence selection.

In order to follow current best practice on data management further information will be obtained by the consortium from the Digital Curation Centre (http://www.dcc.ac.uk/dmponline), ScienceMatters (https://www.sciencematters.io/) and the Research Data Alliance (http://rd-alliance.github.io/metadata-directory/). The project will also seek to follow current best practice guidance on open data such as that from the Open Data Institute (https://theodi.org/).

As a minimum, the consortium will ensure that the data selected for open access:

- can be linked to and is available in a standard, structured format (e.g. JSON, XML, ASCII or TIFF), so that it can be easily shared;
- is consistently availability over time, so that end users can reliably use it;
- is stored self-descriptively or with a link to the publication/document (e.g. identified with a DOI) that accurately describes the data format and parameters used.

The selection of data to be openly accessible will be made on a case by case basis and agreed by the consortium. This will include ethical aspects and data security such as for the protection of IP for any project outputs that are considered to be commercially exploitable. In such cases, it may be necessary to withhold all or some of the data generated. This will be decided by the relevant partner(s) and managed by the DMP, the Consortium Agreement and if appropriate the project's exploitation plan.

B3 The quality and efficiency of the implementation

B3.a Overview of the consortium

The consortium combines the capabilities of eight EURAMET NMIs complemented by one university as external funded partner who will provide academic experience. The specific key competences of the partners are as follows:

CMI is the national metrology institute and the highest authority of the Czech Republic for metrology and testing telecommunication devices. In the field of medical instruments metrology, staff has experience with sphygmomanometers, IOP metrology and laboratory assessment. The laboratory is well equipped with appropriate equipment.

CMI will coordinate the project (WP6), lead WP2 and WP4, and will actively participate in all project goals.

BEV-PTP is the national metrology institute and legal metrology authority in Austria. The tasks in the field of metrology are carried out by the Metrology Service and by the verification offices. Calibrations, tests, seminars and expertise are provided within the frame of the Physico-technical Testing Service, a restricted legal entity. BEV-PTP has profound experience and knowledge in metrology of medical instruments, and it is well equipped with appropriate test benches.

BEV-PTP will participate in the smart specialisation activities (WP4) and impact activities (WP5).

GUM is the Polish official standards body, which ensures conformity and accuracy of the national measurement standards and their traceability to international measurement standards. GUM is also responsible for issuing conformity certificates within the system of the International Organisation of Legal Metrology and carrying out legal metrological control, and recognising the due control carried out by the relevant foreign metrological institutions as equivalent to the legal metrological control in the Republic of Poland.

GUM will participate in advanced traceability activities (WP3), smart specialisation activities (WP4) and impact activities (WP5).

IMBiH is the national metrology institute of Bosnia and Herzegovina. IMBIH brings in expertise in legal metrology, uncertainty evaluation, statistical methods, pressure metrology, and conformity assessment (verification) of measuring instruments covered by legal metrology. IMBIH, in coordination with other partners, will work as an active participant in realisation of the objectives of the project. IMBIH was involved in numerous EMRP and EMPIR projects.

IMBiH will participate in uncertainty evaluation (WP3), smart specialisation activities (WP4) and impact activities (WP5).

IPQ is the Portuguese National Metrology Laboratory and manages and promotes the development of the quality system, and legal framework for quality in Portugal, which includes the metrology subsystem. The mission of IPQ is to ensure accuracy and traceability of the measurements in Portugal. IPQ is responsible for national measurement standards, for the traceability of Portuguese reference standards, for technical support to legal metrology activities, for the realisation of national calibration laboratories comparisons and for participation in relevant international comparisons. IPQ has much experience in metrological traceability in the field of health instruments.

IPQ will participate in market research activities (WP1), smart specialisation activities (WP4) and impact activities (WP5).

NSAI is Ireland's official standards body. NSAI operates under the National Standards Authority of Ireland Act (1996) and incorporates Ireland's National Metrology Laboratory (NML) which is a division of NSAI. NSAI is responsible for establishing, maintaining and developing the national measurement standards for physical quantities and their dissemination to Irish users.

NSAI will participate in developing test procedures (WP2) and calibration procedures (WP3). NSAI will also contribute to the dissemination of the project's outputs to relevant stakeholders.

PTB has a long-standing expertise in the field of medical metrology as a specific branch on its own, as it runs a Medical Metrology/Medical Devices department since 1975. PTB coordinated EU-FP6 project "A simulator for oscillometric blood-pressure signals", and they developed a sophisticated blood-pressure simulator as well as test devices for other medical instruments with a measuring function. PTB created metrological guidelines for medical instruments and participated in many international projects. For years, PTB has been providing CMI traceability for intraocular pressure measurements.

PTB will lead WP1 and WP5 and is significantly involved in all objectives of this project.

SMU is the national metrology institute and the highest authority of the Slovak Republic for metrology. SMU has developed several methodologies for testing oscillometric sphygmomanometers. Specifically, SMU has over 15 years of experience in using calibration procedures on sphygmomanometers. The demonstrated experience will be used within this project to develop equipment, to conduct measurement analysis and to ensure the metrological excellence in this field.

SMU will participate in developing test procedures (WP2), in advanced traceability (WP3), smart specialisation activities (WP4) and impact activities (WP5).

UL is part of the University of Ljubljana, Faculty of Electrical Engineering. The Laboratory of Metrology and Quality has expertise in theory of measurements, measuring techniques and instrumentations, physical measurements (electromagnetic quantities, thermodynamic temperature, relative humidity in gases, material moisture, pressure) and biomedical instrumentation measurements (optical magnetometers, ear thermometers, non-invasive blood pressure monitors, psychophysiological parameters). The laboratory is accredited as an ISO/IEC 17020 control laboratory for sphygmomanometers. UL focuses on metrology of non-invasive blood pressure monitors and NIBP simulators since 2005.

UL will lead WP3 and is significantly involved in all objectives of this project.

Section C: Detailed project plans by work package

C1 WP1: Advanced oscillometric signal generator for real-life signals

The aim of this work package is to develop and evaluate an advanced oscillometric signal generator (aOSG) able to accurately reproduce pre-recorded real-life oscillometric signals. The intention is that this aOSG will substitute human subjects when testing the accuracy of automated sphygmomanometers by replaying pre-recorded human oscillometric signals stored in a data base. Since a considerable database containing a large variety of human oscillometric signals is needed, a pre-existing database will be used for tests using the aOSG. The consortium was authorised to use an already existing database containing real-life oscillometric signals collected by Newcastle University prior to the project.

To test the performance of the aOSG, a recording unit (RU) is necessary and will be developed to record the signals generated by the aOSG and compare these with the database (input) signals.

In Task 1.1 specifications for the hardware and software of the aOSG will be defined and a forward model for the technical measurement uncertainty of systolic, diastolic and mean blood pressure will be proposed.

In Task 1.2 a thorough market research will be performed, appropriate commercial devices will be identified, their performance investigated and necessary improvements recommended.

In Task 1.3 a recording unit able to record oscillometric signals will be designed, produced, and subsequently tested.

In Task 1.4 an oscillometric signal generator, including hardware and software, will be developed. The performance of the aOSG will be tested.

C1.a Task 1.1: Defining the specifications

The aim of this task is to define the requirements for the hardware and software components of the aOSG. Besides the definition of software and hardware requirements of the aOSG, a model will be proposed for the estimation of the technical measurement uncertainty of the systolic, diastolic and mean blood pressure.

Activity number	Activity description	Partners (Lead in bold)
A1.1.1 M4	A series of hardware requirements concerning the aOSG will be established by PTB, CMI, UL, IMBiH and SMU upon revision of existing literature and commercially available hardware. One important aspect which will be addressed is the dependence of the signals on the volume of the pneumatic system. The aOSG will be required to withstand constant pressures up to 300 mmHg and to generate pulses of 0.5-10 mmHg for frequency up to 10 Hz. It is expected that the aOSG will be capable to determine the pneumatic frequency response in the frequency range 1-20 Hz. It is important that the oscillometric signal generated by the aOSG will be as close as possible in shape and amplitude to the real-life oscillometric signal.	PTB, CMI, UL, IMBiH, SMU
A1.1.2 M4	Software requirements for the aOSG will be defined by PTB, CMI, IMBiH, SMU and GUM. To allow the aOSG to work as intended, the software should i) allow corrections of potential deviations from ideal shapes of the pressure pulses; ii) have a user interface for selection of oscillometric test signal and other test parameters, as well as for saving the results of the tests; and iii) allow loading of the oscillometric signal databases (in appropriate form).	PTB, CMI, IMBiH, SMU, GUM
A1.1.3 M12	Based on information and analysis from A1.1.1 and A1.1.2, a forward model for the estimation of the technical measurement uncertainty (i.e. estimate of the uncertainty associated with results of the measurement of sphygmomanometer using the aOSG as a standard) will be proposed by IMBiH with support from UL. The model will cover the measurements of the aOSG and will be further used in A1.4.4. The model will be reviewed by PTB, CMI and SMU. These partners will provide IMBiH and UL with their inputs for the deliverable D1 in A1.4.4.	**IMBiH**, PTB, CMI, UL, SMU

C1.b Task 1.2: Investigation of hardware and software of commercially available devices

The aim of this task is to perform a market research on existing commercial oscillometric signal generators. A series of commercial devices will be selected and analysed with respect to their hardware and software, their shortcomings will be identified and suggestions for improvement will be formulated.

Activity number	Activity description	Partners (Lead in bold)
A1.2.1 M4	To get an overview of the state of the art, a literature review will be conducted and a list of exiting oscillometric signal generators will be created by PTB with support of CMI, UL and SMU. For the selected devices, their hardware and software will be carefully analysed.	PTB, CMI, UL, SMU
A1.2.2 M5	A document containing suggestions for the improvement of the existing commercial devices selected in A1.2.1 will be drafted by PTB with support of CMI, SMU and UL. Suggestions for the improvement will aim at upgrading the performance of the commercially available devices to the level of advanced oscillometric generators, either by their manufacturers, or users. The document will be made available to the stakeholders, either by email and/or upload on the project website.	PTB, CMI, UL, SMU
A1.2.3 M6	The analysis of the commercially available devices from A1.2.1 will be compared against results of activities A1.1.1 and A1.1.2 (software and hardware requirements for the aOSG) by IPQ with support of SMU, to identify weak points of proven technical solution and to simplify the development of the aOSG. The input of this activity will be used for designing mechanical and electrical components of the aOSG in A1.4.1.	IPQ, SMU

C1.c Task 1.3 Development of the recording unit

The aim of this task is to build a recording unit (RU) that allows to record the oscillometric signal superimposed to the cuff pressure. The RU is needed to assess the performance of the aOSG by allowing a quantitative comparison between the oscillometric input data from the test database created in A2.1.4 and the dynamic pressure signal generated by the aOSG. The RU will aid the development of the aOSG and it will generate crucial input data for its performance assessment, in Task 1.4.

The RU will consist of a pressure pump, a pressure sensor with a range of 0-400 mmHg, a potentiometer that allows the selection of the maximum pressure and a software controlled piezo-electric valve controlling the deflation of the cuff at a rate of 2-3 mmHg/s.

Activity number	Activity description	Partners (Lead in bold)
A1.3.1 M12	PTB will perform a literature and market surveillance, define technical and metrological specifications, analyse and select the appropriate components for the recording unit. The main hardware components of the recording unit will be: small pressure pump; pressure sensor with the range of 0-400 mmHg; software controlled (piezo)-electric valve allowing the deflation of the cuff at a rate of 2-3 mmHg/s independent of the attached volume (cuff and tubing); additional independent pressure control and relieve valve for safety reasons (to avoid too high cuff pressure); digital interface for computer control as well as data output and storage.	PTB
A1.3.2 M14	PTB will build the recording unit with the components selected in A1.3.1 and subsequently characterise the device (including calibration and performance tests), which will be used in A1.4.3.	PTB
A1.3.3 M16	PTB will develop the software associated to the recording unit. The electronic format of the output data should be compatible with the input data from the test database created in A2.1.4.	PTB
A1.3.4 M18	The performance of the RU will be evaluated by PTB. It is considered satisfactory if the contribution of the RU to the total uncertainty budget of the aOSG, assessed utilising the RU, is negligible. The RU will allow to record the oscillometric signal superimposed to the cuff pressure. The device is needed to assess the performance of the aOSG by allowing a quantitative comparison between the oscillometric input data from the database and the dynamic pressure signal generated by the aOSG. The RU will aid the development of the aOSG but will also generate crucial input data for its performance assessment, for the testing in A1.4.3 – A1.4.5.	PTB

C1.d Task 1.4: Development of the advanced oscillometric signal generator

The aim of this task is to develop an oscillometric signal generator (aOSG) capable to generate oscillometric signals, which were pre-recorded and stored in an existing database i.e. the Newcastle database. The

database includes files containing the pressure information: the arterial BP information superimposed on the slowly decreasing cuff pressure. The developed aOSG will be able to generate oscillations with desired amplitude, independent on the cuff pressure and the attached volume.

For a more thorough testing of the aOSG, an evaluation using the pre-existing database will be performed. The pre-recorded signals were collected in the past –as part of another EU funded project– by the Newcastle University from approximately 600 patients attending Freeman Hospital in Newcastle, a large specialist regional hospital with patient referrals for cardiac disease, cardiac surgery and hypertension. The data were collected in accordance with the clinical investigation method described in ISO 81060-2; only data fulfilling the criteria of these international standards are included in the database. The consortium was authorised by the Newcastle University (through a letter of authorisation) to use this database for this project.

Activity number	Activity description	Partners (Lead in bold)
A1.4.1 M14	Based on inputs from A1.1.1, A1.1.2, A1.1.3 and A1.2.3, PTB will design the mechanical and electrical components of the aOSG. The commercially available components will be purchased while the commercially non-available ones will be manufactured. The main hardware components of the aOSG will be: motor with lever; pressure chamber; pressure sensor with the range of 0–400 mmHg with uncertainty of measurement ≤ 1 mmHg; component to generate the oscillometric signal (membrane or piston) and independent pressure control for safety reasons to avoid damaging the device.	**PTB**
A1.4.2 M18	PTB will develop the software associated to the aOSG taking into account the requirements from A1.1.2. It is required that the software will be able to choose the right signal from a data base without artefacts (remains of data processing, errors; e.g. in the case of appended generated segments) and will have a user-friendly interface. In order to use the recordings from the databse for simulations, in a first step, the arterial pressure oscillations will be separated from the baseline pressure and these oscillations will be displayed as a function of the baseline pressure. The second step will involve the segmentation of the oscillations into single oscillation periods and the corresponding cuff pressure range. The individual segments are then stored in a new dataset which will be used for the testing of sphygmomanometers by means of the aOSG. During the testing of a sphygmomanometer, the software of the developed aOSG will select the segment corresponding to the measured baseline pressure of the sphygmomanometer.	**PTB**
A1.4.3 M24	PTB will assemble and characterise the aOSG utilising the recording unit built in A1.3.2. The stability and reproducibility of the aOSG will be evaluated against the requirements specified in A1.1.1, A1.1.2 and A1.1.3. The aOSG will be able to generate oscillations with desired amplitude, independent on the cuff pressure and the attached volume. It must withstand constant pressures up to 300 mmHg and to generate pulses of 0.5 mmHg to 10 mmHg for frequency up to 10 Hz. It is expected that the aOSG will be capable to determine the pneumatic frequency response in the frequency range 1-20 Hz. Shape of pressure oscillations generated by the aOSG will be of key importance - they must be as close as possible in shape and amplitude to the real-life oscillometric signals.	**PTB**
A1.4.4 M27	Based on results of activities A1.1.1 to A1.4.3, PTB with support of GUM, CMI, IMBiH, IPQ, SMU and UL will prepare a document containing technical details on the development of an aOSG and send this to the coordinator. Once agreed by the consortium, the coordinator on behalf of PTB, GUM, CMI, IMBiH, IPQ, SMU and UL will submit the document to EURAMET as **D1**: '*Technical document on the development of the advanced oscillometric signal generator, able to withstand constant pressures up to 300 mmHg, generate pulses of 0.5-10 mmHg for frequency up to 10 Hz and determine the pneumatic frequency response in the frequency range 1-20 Hz*'.	**PTB, GUM, CMI, IMBiH, IPQ, SMU, UL**
A1.4.5 M36	PTB, CMI, and UL will evaluate the aOSG from A1.4.3 with respect to applicability in market surveillance and/or clinical trials. Evaluation will be conducted by comparison of expected values (set in A1.1.1 to A1.1.3) and actual values obtained from the aOSG that will be generated within this activity. Evaluation of the aOSG will be focused on interchangeability of the generated (artificial) oscillometric pressure signals with real-life oscillometric during clinical trials and market surveillance.	**PTB, CMI, UL**

A1.4.6 M36	Based on the input from A1.4.5, PTB with support of CMI, and UL will write a validation report on applicability of the aOSG and send this to the coordinator. Once agreed by the consortium, the coordinator on behalf of PTB, CMI and UL will submit the report to EURAMET as deliverable D2: '*Validation report on applicability of the advanced oscillometric generator in market surveillance and/or clinical trials*'.	PTB, CMI, UL

C2 *WP2: Development of procedures for testing sphygmomanometers with an aOSG*

The aim of this work package is to elaborate procedures for the dynamic testing of automated oscillometric sphygmomanometers using the advanced oscillometric signal generator (aOSG) developed in WP1, Task 1.4. These procedures will allow the aOSG to be used as an absolute reference device for the metrological verification and reverification of sphygmomanometers.

The test procedures for the aOSG are the crucial step in assessing the suitability and performance of the aOSG and hence shall at least satisfy the requirements of the ISO standard ISO 81060-2. That requires detail knowledge of the standard ISO 81060-2, extensive database of accurate (validated) real-life oscillometric signals, development and testing of the procedure itself and finally drafting a guide for testing sphygmomanometers using an aOSG.

The consortium was authorised to use an already existing database containing real-life oscillometric signals collected by Newcastle University prior the project.

In Task 2.1, a procedure will be proposed for collecting and processing real-life oscillometric data. Although it is not intended within this project to collect additional oscillometric data, the expertise in the consortium should be used to propose an adequate procedure for future purposes. This procedure will be made available on the project's website.

In Task 2.2, a set of procedures for the testing of automated sphygmomanometers using the aOSG developed in Task 1.4 will be defined.

In Task 2.3, the procedure proposed in Task 2.2 will be practically validated. If required, the procedure will be adjusted and optimised.

C2.a Task 2.1: Real-life oscillometric data

The aim of this task is to set up procedures for the collection of real-life oscillometric data during clinical campaigns. This will involve carrying out a literature review of the requirements for the aOSG to be used in clinical tests and for market surveillance. Additionally, the oscillometric blood pressure signals data from the Newcastle University database will be converted into an easy-to-use digital database of real-life oscillometric signals.

Activity number	Activity description	Partners (Lead in bold)
A2.1.1 M15	CMI, UL, SMU and PTB will perform a literature review, which will include relevant standards, to get an overview of the requirements for the aOSG to be used to substitute clinical tests and for market surveillance. This will identify specific requirements for blood pressure ranges, heart rates, patient groups etc., that are needed to establish a database of real-life oscillometric signals in A2.1.2. As the aOSG will be suitable for substituting clinical tests (to verify the CE marking as well as to support the testing of new metrological software for the sphygmomanometer by the manufacturer) and for market surveillance, these procedures will take into account the stipulations in relevant standardisation documents such as EN 1060-4 and ISO 81060-2.	**CMI**, UL, PTB, SMU
A2.1.2 M18	GUM with support from CMI, UL, PTB and SMU will convert the oscillometric blood pressure signals data from the Newcastle University database into an easy-to-use digital database of real-life oscillometric signals. The converted database will be located at PTB. If significant problems with the oscillometric signal database arise, the consortium will seek an alternative database within European NMIs and stakeholders and/or the consortium will subcontract (through NSAI) the essential clinical expertise in collecting real-life data in order to obtain database of real-life oscillometric signals.	**GUM**, CMI, UL, PTB, SMU, NSAI

A2.1.3 M21	Based on inputs from A2.1.1 and A2.1.2, CMI and SMU with support of UL, PTB and GUM will investigate which signals that fulfil the criteria and parameters identified in activity A2.1.1 are available in the database of real-life oscillometric signals created in A2.1.2.	**CMI**, UL, PTB, SMU, GUM
A2.1.4 M23	CMI with support of SMU, UL, PTB and GUM will use the output of A2.1.1 and A2.1.3 and select appropriate signals available from the database of real-life oscillometric signals created in A2.1.2 and create a test database at CMI for the aOSG. This test database will be located at PTB and will be subsequently used in A2.3.1.	**CMI**, SMU, UL, PTB, GUM

C2.b Task 2.2: Development of test procedures for automated sphygmomanometers

The aim of this task is to develop test procedures for automated oscillometric sphygmomanometers using the aOSG developed in Task 1.4. In addition, a draft procedure for collecting real-life oscillometric data will be developed, which will include general guidance on ethical aspects with regards to collecting data from human subjects.

Activity number	Activity description	Partners (Lead in bold)
A2.2.1 M24	Using inputs from activity A2.1.1, SMU with support from CMI, NSAI, UL and PTB will define technical and metrological requirements (such as maximal permissible error) the sphygmomanometers shall fulfil during the testing with the aOSG.	**SMU**, CMI, NSAI, UL, PTB
A2.2.2 M26	Using outputs of activities in A2.1.1, A2.1.4 and A2.2.1, CMI with support from SMU, NSAI, UL, and PTB will develop a draft of test procedures containing test procedures for testing the stability and repeatability of sphygmomanometers with the aOSG. As the aOSG is intended to be used in in-depth testing of sphygmomanometers, the draft of test procedures will take into account the stipulations in relevant standardisation documents such as EN 1060-4 and ISO 81060-2 (e.g. number of test points, simulated blood pressure ranges).	**CMI**, SMU, NSAI, UL, PTB
A2.2.3 M27	To allow future expansion of the real-life oscillometric signal database created in A2.1.2, CMI with support from SMU, UL, NSAI and PTB will develop a draft procedure for collecting real-life oscillometric data. This will also include general guidance on ethical aspects with regards to collecting data from human subjects. This guidance will be made available to stakeholders, either by email or by being posted on project website.	**CMI**, UL, NSAI, PTB, SMU

C2.c Task 2.3: Evaluation of test procedures for automated sphygmomanometers

The aim of this task is to perform the evaluation of test procedures defined in Task 2.2, and their optimisation, if necessary. Guidelines will be written on sphygmomanometer testing with an aOSG.

Activity number	Activity description	Partners (Lead in bold)
A2.3.1 M31	The applicability of the test procedures drafted in A2.2.2 will be evaluated with the test signals selected in A2.1.4. CMI with support of PTB, UL and SMU will perform practical tests with automated sphygmomanometer to show the feasibility of the test procedures such as their ease of use, ability to test all crucial parameters etc.	**CMI**, UL, SMU PTB
A2.3.2 M33	CMI and SMU with support of PTB and UL will review the results of A2.3.1 and if necessary, optimisation of the procedures will be undertaken by CMI, UL, SMU and PTB.	**CMI**, UL, SMU, PTB
A2.3.3 M36	Using outputs from A2.3.1 and A2.3.2, CMI with support of GUM, NSAI, PTB, SMU and UL will write the guidelines for sphygmomanometer evaluation using an aOSG and oscillometric data and send these to the coordinator. Once agreed by the consortium, the coordinator on behalf of CMI, GUM, NSAI, PTB, SMU and UL will submit the guidelines to EURAMET as D3: *'Guidelines for the evaluation of automated sphygmomanometers using an aOSG and oscillometric data'*.	**CMI**, GUM, NSAI, PTB, SMU, UL

C3 *WP3: Procedure for calibration and recalibration of the aOSG*

The aim of this work package is to define procedures and select appropriate methods for calibration of the oscillometric signal generator.

In order to serve as an absolute standard for oscillometric blood pressure signals, dynamic traceability of the aOSG must be ensured. This has to be done at static and at dynamic pressures and a maximum uncertainty of ± 1.5 mmHg must be achieved. New means and methods have to be selected and evaluated, model for uncertainty budget has to be formulated and guidelines how to perform such calibrations have to be written.

Therefore, this work-package will focus on specific aspects of establishing the dynamic pressure traceability of the aOSG:

In Task 3.1, a survey on possible solutions of dynamic pressure traceability will be undertaken, technical and metrological requirements for the test equipment will be stated and appropriate calibration equipment will be selected.

In Task 3.2, the routes to traceability of the aOSG will be established based on findings of Task 3.1. That will require extensive research on all aspects of the aOSG calibration, e.g. selection of appropriate test signals, formulation of model for uncertainty, drafting the procedure for calibration, etc.

In Task 3.3, results of Task 3.2 will be evaluated. Sample calibration of the aOSG will be performed to prove the suitability of the selected tools and methods, final version of the calibration guide will be created and the outcome of this task will be published as a paper on dynamic pressure calibration.

C3.a Task 3.1: Test equipment for traceable dynamic pressure measurements

The aim of this task is to select test equipment which will be a first step to establish dynamic pressure traceability for the aOSG. This means establishing a new traceability chain in area of pressure metrology, which is not fully covered by most NMIs.

To select appropriate and optimal tools and equipment for traceable dynamic pressure measurements, there will be an extensive literature survey on available dynamic pressure solutions (techniques, methods, standards). Based on the survey, the requirements for the calibration equipment will be determined. The requirements will take into account the target uncertainty of the calibration (± 1.5 mmHg). Finally, software for performing the calibration will be created.

Activity number	Activity description	Partners (Lead in bold)
A3.1.1 M6	CMI, IMBiH, PTB, SMU, UL and GUM will perform a literature survey on available solutions (techniques, methods, standards) for dynamic pressure traceability. Emphasis will be given to specific dynamic pressure ranges required for the oscillometric signal generator (e.g. static pressure up to 300 mmHg, deflation rate at 2-3 mmHg/s, dynamic pressure variations up to ± 10 mmHg and frequencies up to 10 Hz).	**CMI**, IMBiH, PTB, SMU, UL, GUM
A3.1.2 M10	Based on the results of A3.1.1, UL with support of CMI, PTB, SMU and GUM will define the technical and metrological requirements (such as response time) for the test equipment to be used for the calibration of the aOSG developed in A1.4.3 to reach the target uncertainty of ± 1.5 mmHg.	**UL**, CMI, PTB, SMU, GUM
A3.1.3 M14	Based on the outputs of A3.1.1 and A3.1.2, UL with support of CMI, PTB, SMU and GUM will select the appropriate test equipment (dynamic pressure standard) for the aOSG calibrations.	**UL**, CMI, PTB, SMU, GUM
A3.1.4 M18	Based on the outputs of activities A3.1.1, A3.1.2 and A3.1.3, UL with support of GUM, CMI, SMU and PTB will create a first draft of the procedure for calibration of the aOSG with the methods and test equipment selected in A3.1.1 and A3.1.3.	**UL**, GUM, CMI, PTB, SMU
A3.1.5 M18	A software will be developed by GUM with support of UL, CMI, SMU and PTB to support the draft of the calibration procedure created in A3.1.4. The purpose of the software is to enable calibration of the aOSG using the test equipment selected in A3.1.3.	**GUM**, UL, CMI, PTB, SMU

C3.b Task 3.2: Establishing the routes of traceability for the aOSG

The aim of this task is to establish the traceability for the aOSG developed at PTB. This will require knowledge of the dynamic properties of the devices to be calibrated, creation of the analytical model for uncertainty budget,

knowledge of the influences of external disturbances, selection of appropriate calibration signals and finally, drafting of the calibration procedure.

Activity number	Activity description	Partners (Lead in bold)
A3.2.1 M24	In order to establish dynamic pressure traceability of the aOSG developed in A1.4.3, its dynamic properties will be evaluated (by selecting appropriate test signal and testing the device's response using the test signal) by UL with support from CMI, IMBiH, PTB, SMU and GUM. For this purpose, the equipment selected in activity A3.1.3 and the first draft of the procedure developed in A3.1.4 and/or software developed in A3.1.5 will be used.	**UL**, CMI, IMBiH, PTB, SMU, GUM
A3.2.2 M26	IMBiH with support from CMI, UL, PTB, SMU and GUM will formulate the model for the uncertainty budget for aOSG calibrations with the target uncertainty ± 1.5 mmHg. The model will use findings from the evaluation of the dynamic properties in A3.2.1 and output of A3.1.1 and take into account test equipment selected in activity A3.1.3 and requirements defined in activity A3.1.2.	**IMBiH**, CMI, PTB, SMU, UL GUM
A3.2.3 M26	IMBiH with support from CMI, UL, PTB, SMU and GUM will write a report on the model for the uncertainty budget for aOSG calibrations formulated in A3.2.2 and send this to the coordinator. Once agreed by the consortium, the coordinator on behalf of IMBiH, CMI, PTB, SMU, UL and GUM will submit the report on the uncertainty model to EURAMET as D4: *'Report on the development of an uncertainty model for the aOSG calibration with a target uncertainty ± 1.5 mmHg'*.	**IMBiH**, CMI, PTB, SMU, UL, GUM
A3.2.4 M30	UL, CMI, IMBiH, PTB, SMU and GUM will verify and discuss the maximum permissible errors for aOSG calibrations after practical experience is available (iterative process; A3.3.1 and A3.3.2). The target uncertainty of ± 1.5 mmHg and parameters of test equipment proposed in A3.1.2 will be discussed by all involved partners with respect to the overall performance of the aOSG, the optimal recalibration interval and the aim to use the aOSG as absolute reference for sphygmomanometer testing.	**UL**, CMI, IMBiH, PTB, SMU, GUM
A3.2.5 M28	UL, CMI, PTB, SMU and GUM will perform an investigation of external disturbances during aOSG calibrations (e.g. attached volume, length, diameter and volume of tubing, temperature, inflation or deflation rate, etc.). External disturbances will be evaluated in order to reach lower uncertainties during calibration, lower signal distortion, etc.	**UL**, CMI, PTB, SMU, GUM
A3.2.6 M28	Based on the results of the evaluation of dynamic properties of the aOSG (A3.2.1), UL, CMI, PTB, SMU and GUM will define and select appropriate test signals for dynamic pressure calibration of these devices. The selected signals will allow in-depth evaluation of the aOSG.	**UL**, CMI, PTB, SMU, GUM
A3.2.7 M28	Using the available inputs from activities A3.1.4 and A3.2.1 to A3.2.6, UL, CMI, PTB and IMBiH will draft a calibration procedure for the aOSG. GUM and SMU will review the draft. The input of this activity will be incorporated in the final version of calibration procedure produced in A3.3.3.	**UL**, CMI, PTB, SMU, GUM, IMBiH

C3.c Task 3.3: Analysis of results towards the establishment of a traceability route

The aim of this task is to evaluate the results of Task 3.2 and define a calibration procedure to implement a new traceability route. Calibration of the aOSG will be performed to confirm the suitability of the selected tools and methods. If necessary, these will be optimised. Once the calibration procedure is verified, the final calibration procedure will be written.

Activity number	Activity description	Partners (Lead in bold)
A3.3.1 M30	PTB with support of CMI, SMU, UL, NSAI and GUM will calibrate the aOSG to verify the applicability of the calibration procedure drafted in A3.2.7 and applicability of test signals selected in A3.2.6.	**PTB**, CMI, SMU, UL, NSAI, GUM
A3.3.2 M30	CMI with support of PTB, SMU, UL, NSAI and GUM will review the results of A3.3.1 and, if there are issues with stability or if the target uncertainty (± 1.5 mmHg) is not reached, the procedure (A3.2.7) or test signals selection (A3.2.6) will be optimised, e.g. by using another equipment or by adjusting the software developed in A3.1.5.	**CMI**, PTB, SMU, UL, NSAI, GUM

A3.3.3 M32	Based on A3.3.2 and with the input from A3.2.7, CMI with support of PTB, SMU, UL, NSAI and GUM will create a final version of the calibration procedure for the aOSG, demonstrating the new traceability route.	CMI, PTB, SMU, UL, NSAI, GUM
A3.3.4 M34	UL with support from PTB, SMU, GUM, NSAI, IMBiH and CMI will write a report on the calibration procedure of the aOSG and send this to the coordinator. Once agreed by the consortium, the coordinator on behalf of UL, CMI, GUM, IMBiH, PTB, SMU and NSAI will submit the report to EURAMET as **D5**: *'Report on the aOSG calibration procedure enabling to obtain an uncertainty of ± 1.5 mmHg or better'.*	UL, CMI, GUM, IMBiH, NSAI, PTB, SMU

C4 WP4: Smart specialisation concept

The aim of this work package is to develop and implement a smart specialisation concept for traceable oscillometric blood pressure measurements and research in Europe.

This concept will be suitable as a foundation for a long-term partnership, i.e. beyond the end of this project, in advanced blood pressure metrology in Europe. The specialisation will be coordinated to optimally utilise the limited national capacities in a smart division of labour and resources. Stakeholder involvement will be crucial to achieve the goal of this work package. The implementation of the smart specialisation concept will be essential to ensure that the main aim of the whole project will persist beyond the end of the project. The perpetuation of this concept is another important objective of this work package.

Since there are other, already running, projects utilising and developing the smart specialisation concept for medical measuring instruments, e.g. 16RPT03 inTENSE, the consortium will actively investigate for possible cooperation, knowledge, infrastructure sharing and synergy with such projects. The long-term goal of such collaboration and synergy would be creation of European centre for medical device metrology.

Besides implementing the smart specialisation concept, this work package aims to take all the necessary steps to allow the use of the aOSG as intended, i.e. as market surveillance tool and tool for in-depth sphygmomanometer performance checks during pre-market and subsequent examination. This will require detailed assessment of important findings from WP1, WP2 and WP3. The aim of this WP will be achieved through the combination of the technical findings of all previous WPs, knowledge of needs of the stakeholders and eventual legal requirements.

In Task 4.1, a network of organisations interested in advanced blood pressure measurements and a competence centre will be established.

In Task 4.2, conformity of the project aims with legal requirements in each partner's country will be checked.

In Task 4.3, a laboratory which will be able to provide dynamic traceability to the aOSG will be set up.

In Task 4.4, the smart specialisation concept will be further expanded and a White Paper on smart specialisation concept will be created.

In Task 4.5, individual strategies for the use of the joint research capacity (i.e competence centre) will be prepared by the internal partners.

C4.a Task 4.1: Creating a network of organisations and a competence centre

The aim of this task is to create and maintain a network of NMIs/DIs, academic and other research institutions, governmental, surveillance and non-governmental regulatory bodies, manufacturers/distributors of BP measuring devices and BP simulators, medical professional bodies and associations which will benefit from the use of the aOSG and which are able to give feedback to the project. This network will need to reach a critical mass (at least 6-8 organisations) in order to be sustained beyond the project's duration. A centre of excellence for blood pressure metrology (competence centre) will be established at CMI which will be designed for the needs of Czech Republic and all European NMIs/DIs in this field who cannot or do not want to build and maintain this capacity for themselves.

Activity number	Activity description	Partners (Lead in bold)
A4.1.1 M4	BEV-PTP with support of the consortium will identify at least 30 relevant stakeholders from the national and international medical and research community and from European NMIs/DIs, as well as industry and state or private calibration and verification offices. A database of stakeholders will be created by CMI.	BEV-PTP, CMI, GUM, IMBiH, NSAI, PTB, SMU, UL, IPQ

A4.1.2 M6	BEV-PTP with support of the consortium will create a network of organisations that will benefit from the use of the aOSG. These will be NMIs/DIs, academic and other research institutions, governmental, surveillance and non-governmental regulatory bodies, manufacturers/distributors of BP measuring devices and BP simulators, medical professional bodies and associations. The stakeholders identified in A4.1.1 and the members of the stakeholder committee (A5.1.1) will be invited to join this network and to attend the workshops being organised within A5.2.1.	**BEV-PTP**, CMI, GUM, IMBiH, NSAI, PTB, SMU, UL, IPQ
A4.1.3 M36	Following the stakeholders' participation at the workshops organised in A5.2.1, the consortium will sustain the network throughout the project by keeping in contact with the stakeholders via email. These stakeholders will be invited to attend the project meetings. CMI will maintain the contacts' database created from the inputs of the consortium members.	**CMI**, GUM, IMBiH, NSAI, PTB, SMU, UL, BEV-PTP, IPQ
A4.1.4 M36	Using the network created in A4.1.2, CMI with the support of the consortium will establish a competence centre for advanced blood pressure metrology, which will be able to serve the whole European region. The centre will provide calibration services for aOSGs and similar devices (A4.3.2) and provide support for the whole chain of BP measurements. The competence centre will have a metrological infrastructure with advanced calibration services and will provide the end-users with clear guidance, metrological expertise and calibration services for all aspects of use of the automated sphygmomanometers.	**CMI**, GUM, IMBiH, NSAI, PTB, SMU, UL, BEV-PTP, IPQ

C4.b Task 4.2: Checking conformity to legal framework

The aim of this task is to check the conformity of the use of the aOSG as market surveillance tool and establishment of the European centre for medical device metrology against legal framework of the consortium countries and the latest development of the Medical Device Regulation (MDR). Members of the consortium will contact their national metrology legislation authorities and market surveillance authorities to investigate the possible use of the aOSG as tool for market surveillance.

Activity number	Activity description	Partners (Lead in bold)
A4.2.1 M12	IPQ with support of all partners will investigate the regulatory situation in European countries and possible future changes of CE conformity assessments in the context of the MDR and other national and European legislature.	**IPQ**, CMI, GUM, IMBiH, NSAI, PTB, SMU, UL, BEV-PTP
A4.2.2 M27	Using the findings of A4.2.1, all partners will contact their national metrology regulatory authorities and propose the idea of the use of the aOSG as market surveillance tool. Conformity of the project aim with the MDR and national regulations will be checked. IPQ will collect the viewpoint of all national authorities and summarise the results.	**IPQ**, CMI, GUM, IMBiH, NSAI, PTB, SMU, UL, BEV-PTP
A4.2.3 M36	The consortium, led by CMI and based on A2.2.3 and D3 (A2.3.3), will prepare a set of recommendations that will help to use the aOSG as market surveillance tool by respective stakeholders and ensure uniformity and correctness of the measurements. This set of recommendations, will be subsequently published as an appendix to the White Paper (A4.4.3).	**CMI**, GUM, IMBiH, NSAI, PTB, SMU, UL, BEV-PTP, IPQ

C4.c Task 4.3: Setting-up a calibration laboratory

The aim of this task is to set-up a calibration laboratory to provide traceability of the aOSG and similar devices at CMI. The promotion of the use of the aOSG as market surveillance tool and as means of in-depth performance control tool of oscillometric sphygmomanometer brings the need to establish a valid traceability chain of dynamic pressure for these generators. In order to establish a continuous research and traceability base for a future medical device centre, a testing laboratory that will provide dynamic pressure traceability for the aOSG and similar devices will be set up at CMI. The laboratory will use and further develop the tools and methods developed within WP3 and will subsequently provide traceability for stakeholders, verification bodies and other NMIs and DIs all over Europe.

Activity number	Activity description	Partners (Lead in bold)
A4.3.1 M36	CMI, with support of UL, PTB, SMU and GUM and based on results of WP3, will select optimal tools for the calibration of the aOSG and similar devices, which will be used in the laboratory to be established at CMI in A4.3.2.	**CMI**, SMU, UL, PTB, GUM
A4.3.2 M36	A testing laboratory to provide the traceability of the aOSG and similar devices will be established at CMI using the outcomes of A4.3.1. This laboratory will form a part of the competence centre for advanced blood pressure metrology established in A4.1.4.	**CMI**
A4.3.3 M36	The laboratory established at CMI in A4.3.2 will perform the assessment of the measurement capabilities and validate the measurement methods. The output of this activity will be used in A4.3.4.	**CMI**
A4.3.4 M36	Based on A4.3.3, CMI will produce a document demonstrating that the measurements carried out in the laboratory established in A4.3.2 are traceable and send this to the coordinator. Once agreed by the consortium, the coordinator on behalf of CMI will submit the document to EURAMET as D7: *'Report demonstrating the qualified traceable measurement and extended calibration services for the aOSG and similar devices'*.	**CMI**

C4.d Task 4.4: Engaging in the framework of the smart specialisation concept

The aim of this task is to develop the framework of the smart specialisation concept. This will involve seeking collaboration with similar projects e.g. 16RPT03 inTENSE. The long-term goal of such collaboration and synergy would be the creation of a future European centre for medical device metrology.

Feedback from the stakeholder network will be used to consolidate the smart specialisation concept framework that will ensure a coordinated and optimised European approach towards the European centre for medical device metrology. This concept will be specified in an outline of a White Paper which will be presented and discussed at the M18 (November 2020) stakeholder workshop (A5.2.1). Based on feedback from the workshop a final version of the White Paper will be compiled.

A4.4.1 M36	The consortium, led by BEV-PTP, will contact participants of 16RPT03 inTENSE, to investigate and to negotiate the possibilitiy of sharing knowledge, resources and infrastructure. This activity will be active for the duration of the project. Progress will be reviewed and updated at least at each project meeting.	**BEV-PTP**, CMI, GUM, IMBiH, NSAI, PTB, SMU, UL, IPQ
A4.4.2 M18	An outline of a White Paper on the smart specialisation concept will be written by CMI and NSAI with assistance of all project partners. The outline of the White Paper will be provided to the participants of the stakeholder workshop (A5.2.1) for discussion and feedback will be sought.	**CMI**, NSAI, GUM, IMBiH, PTB, SMU, UL, BEV-PTP, IPQ
A4.4.3 M36	Based on feedback from A4.4.2 and A4.3.1, CMI with help from the consortium will correct and extend the outline of the White Paper produced in A4.4.2. Its appendix will contain the set of recommendations created in A4.2.3.	**CMI**, IPQ, GUM, IMBiH, NSAI, PTB, SMU, UL, BEV-PTP
A4.4.4 M36	CMI with assistance of the consortium will prepare the final version of the White Paper. Once the White Paper has been agreed within the consortium, the coordinator on behalf of all the partners will submit the White Paper to EURAMET as D6: *'White Paper on the smart specialisation concept developed to ensure a coordinated and optimised European approach towards European metrology centre'*.	**CMI**, IPQ, GUM, IMBiH, NSAI, PTB, SMU, UL, BEV-PTP

C4.e Task 4.5: Individual strategies for the use of the joint research capacity (competence centre)

The aim of this task is to develop individual strategies for the long-term operation and transnational use of the joint research capacity (competence centre) established in A4.1.4, and for granting access to the calibration and testing services to the end-users of the partners' countries. These documents will also include individual contributions of each partner towards the improvement of the competence centre and a plan for the implementation of the individual strategy.

A4.5.1 M36	CMI will write the strategic plan for CMI. The individual strategy for CMI will include: i) priorities for collaborations with the research community in Czech Republic or with neighbouring NMIs for the long-term operation and transnational use of the joint research capacity (competence centre); ii) sustainable strategy to facilitate the access to calibration and research services to national customers iii) expected individual contribution to the improvement of the competence centre for the next five years; iv) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	CMI
A4.5.2 M36	BEV-PTP will write the strategic plan for BEV-PTP. The individual strategy for BEV-PTP will include: i) priorities for collaborations with the research community in Austria or with neighbouring NMIs for the long-term operation and transnational use of the joint research capacity (competence centre); ii) sustainable strategy to facilitate the access to calibration and research services to national customers iii) expected individual contribution to the improvement of the competence centre for the next five years; iv) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	BEV-PTP
A4.5.3 M36	GUM will write the strategic plan for GUM. The individual strategy for GUM will include: i) priorities for collaborations with the research community in Poland or with neighbouring NMIs for the long-term operation and transnational use of the joint research capacity (competence centre); ii) sustainable strategy to facilitate the access to calibration and research services to national customers iii) expected individual contribution to the improvement of the competence centre for the next five years; iv) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	GUM
A4.5.4 M36	IMBiH will write the strategic plan for IMBiH. The national strategy will take into account requirements for international cooperation and smart specialisation, including priorities for collaborations with the research community in the partner's country. The individual strategy for IMBiH will include: i) priorities for collaborations with the research community in Bosnia and Herzegovina or with neighbouring NMIs for the long-term operation and transnational use of the joint research capacity (competence centre); ii) sustainable strategy to facilitate the access to calibration and research services to national customers iii) expected individual contribution to the improvement of the competence centre for the next five years; iv) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	IMBiH
A4.5.5 M36	IPQ will write the strategic plan for IPQ. The national strategy will take into account requirements for international cooperation and smart specialisation, including priorities for collaborations with the research community in the partner's country. The individual strategy for IPQ will include: i) establishing priorities and mechanisms to engage with the potential users and beneficiaries of the project and establishment of a national network of users in this field; ii) priorities for collaborations with the research community in Portugal or with neighbouring NMIs for the long-term operation and transnational use of the joint research capacity (competence centre); iii) sustainable strategy to facilitate the access to calibration and research services to national customers; iv) expected individual contribution to the improvement of the competence centre for the next five years; v) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	IPQ
A4.5.6 M36	NSAI will write the strategic plan for NSAI. The individual strategy for NSAI will include: i) establishing priorities and mechanisms to engage with the potential users and beneficiaries of the project and establishment of a national network of users in this field ii) priorities for collaborations with the research community in Ireland or with neighbouring NMIs for the long-term operation and transnational use of the joint research capacity (competence centre); iii) sustainable strategy to facilitate the access to calibration and research services to national customers iv) plan for the establishment of calibration capability in Ireland and for the development of the competence centre for the next five years; iv) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	NSAI
A4.5.7 M36	PTB will write the strategic plan for PTB. The individual strategy for PTB will include: i) priorities for collaborations with German legislators and test offices, international manufacturers and research community; ii) sustainable strategy to facilitate the access to calibration and research services to national customers iii) expected individual contribution to the improvement of the competence centre for the next five years; iv) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	PTB

A4.5.8 M36	SMU will write the strategic plan for SMU. The individual strategy for SMU will include: i) priorities for collaborations with the research community in Slovakia or with neighbouring NMIs for the long-term operation and transnational use of the joint research capacity (competence centre); ii) sustainable strategy to facilitate the access to calibration and research services to national customers iii) expected individual contribution to the improvement of the competence centre for the next five years; iv) Gantt chart presenting the planning of the individual strategy implementation: access to the centre, usage, improvements, etc.	SMU
A4.5.9 M36	CMI will collect all the individual strategies and will ensure that all individual strategies are agreed within the consortium. The development of individual strategies will be discussed and agreed on project meetings in M18, M27 and M36. Once agreed by the consortium, the coordinator on behalf of CMI, BEV-PTP, GUM, IMBiH, IPQ, NSAI, PTB and SMU will submit the document to EURAMET as D8: '*Agreed individual strategies for internal partners for the long-term operation and transnational use of the joint research capacity (competence centre) and for the access to its calibration and testing services from their respective countries*'.	CMI, BEV-PTP, GUM, IMBiH, IPQ, NSAI, PTB, SMU

C5 *WP5: Creating impact*

C5.a Task 5.1 Knowledge transfer

Activity number	Activity description	Partners (Lead in bold)
A5.1.1 M12 M36	A stakeholder list will be created and maintained by CMI. Upon creation, this list will contain all relevant stakeholders known at the beginning of the project and it will grow throughout the project's duration. The network partners identified in A4.1.1 will be added to the stakeholder list. The consortium will engage closely with all major regional stakeholders. The stakeholders' needs will be considered by the consortium throughout the project and the stakeholders will at least every 9 months be informed about the project and use its results in their future work. The project will create a stakeholder committee in the first 12 months which will contain at least 5 representatives from state authorities, calibration services, manufacturers and clinicians representing at least three European countries. The aim of the stakeholder committee is to clarify the needs of the various interested parties and to feed these into the project. Interaction with the stakeholder committee will be achieved via a central website (A5.1.3) and ad-hoc meetings will be held at suitable events where the committee is in attendance. Additional meetings or virtual meetings will be organised when required.	CMI, all partners
A5.1.2 M36	The consortium will establish a working group on "advanced blood pressure metrology" coordinated by CMI. This working group will be part of the communication and knowledge transfer channel between the competence centre established in A4.1.4 and (medical metrology) end-users, and will provide a forum and communication channels for stakeholders in the field. It will be open to participants from NMIs/DIs, regulatory and market surveillance authorities, governmental (national or local) calibration authorities, private calibration offices, SM producers. The working group will persist beyond the lifetime of the project. CMI, with support of the consortium, will write a document containing the terms of reference for the working group whose objective is to establish the basis for cooperation and information exchange in the field of advanced metrology. The document will include the objectives and rules of the group, together with a proposal of its structure (e.g. periodical meetings, communication channels).	CMI, all partners
A5.1.3 M1 M36	A project website will be developed via a subcontract and hosted by CMI. The website will have public access and a part restricted for partners only. The website will be regularly updated with information such as project reports, papers published by the partners, project meetings. The part of the website with restricted access will be dedicated to exchange information and reports throughout the project. It will also include a digital archive of all presentations, reports and papers produced by the project.	CMI, all partners

<table>
<tr><td>A5.1.4
M36</td><td>The partners plan to present at least 4 papers at international conferences; e.g.:
19th International metrology congress, Paris 2019
IMEKO TC-16 – Pressure, 2020, date and location to be defined
European Society of Hypertension, Annual Meeting, 2020, Glasgow
International Conference on Medical and Biological Engineering 2021, date and location to be defined
Further relevant conferences may be identified during the project.</td><td>PTB, all partners</td></tr>
<tr><td>A5.1.5
M36</td><td>The project will submit at least two papers for publication in peer reviewed journals, in open access format. Target journals are e.g. "Metrologia" and "Blood pressure monitoring.
The authors of the peer reviewed papers will clearly acknowledge the financial support provided through the EMPIR as required by EURAMET. Effort will be made to ensure that these are joint publications between partners from different countries.</td><td>PTB, all partners</td></tr>
<tr><td>A5.1.6
M36</td><td>Information on the results of the project will be disseminated to a range of standards bodies and committees and feedback sought (see details below and in the table in Section B2.c).
<table>
<tr><th>Standards Committee / Technical Committee / Working Group</th><th>Partners involved</th><th>Likely area of impact / activities undertaken by partners related to standard / committee</th></tr>
<tr><td>ISO/TC 121/SC 3/J WG 7</td><td>PTB</td><td>PTB is convenor of JWG 7 - Non-Invasive sphygmomanometers.
This working group has developed several standards on non-automated non-invasive sphygmomanometers, automated non-invasive sphygmomanometers and on clinical investigation of automated sphygmomanometers. Simulators are required for several tests in the standard on automated non-invasive sphygmomanometers and will be the focus of a new technical specification. Due to technical advancements, these standards are revised regularly. This working group meets twice a year to discuss the revisions of published standards and the development of new technical specifications. In its convenor role, PTB will lead all these discussions and present this project and its results. Feedback will be sought on the results presented to this technical committee.</td></tr>
<tr><td>OIML TC18 / SC1</td><td>PTB, BEV-PTP, CMI, IPQ</td><td>PTB is secretary, BEV-PTP, IPQ are members and CMI is observer of the TC18 "Medical Measuring Instruments".
This committee communicates mostly by e-mail and ad-hoc meetings. PTB, with the assistance of BEV-PTP, CMI and IPQ, will update the committee on the project's targets and results, and seek feedback on those.
The recommendation R 16-2: Non-invasive automated sphygmomanometers, which requires the use of simulators for the testing of automated sphygmomanometers is under revision. PTB is actively taking part in this work.</td></tr>
<tr><td>IMEKO TC16</td><td>CMI, PTB, SMU</td><td>CMI is scientific secretary, and PTB and SMU are members of TC16 "Pressure". The area of dynamic BP measurement will be highlighted within this committee.
IMEKO TC16 meets every 2 – 3 years in connection with IMEKO events. The group will be updated on the project's targets and results by CMI, or PTB and SMU. Cooperation on the dissemination of these results will be requested from this committee and from IMEKO TC13 Medicine.</td></tr>
<tr><td>EURAMET TG Health</td><td>CMI, GUM, IMBiH, IPQ, SMU, UL, PTB, NSAI, BEV-PTP</td><td>The consortium will contact this task group to explore cooperation within the framework of the smart specialisation concept. The consortium will keep EURAMET regularly updated about the project's plans and progress whilst simultaneously learning about their views on the project's planned activities, their possible experience in this respect and their recommendations. The consortium will seek support and endorsement for</td></tr>
</table></td><td>PTB, all partners</td></tr>
</table>

			the European centre for medical device metrology from EURAMET whilst offering to take their recommendations and requests into account when building it.
	CCM WGPV	CMI, PTB	CMI and PTB are members of the "Comité consultatif pour la masse et les grandeurs apparentées" – "Groupe de travail pression-vide". The area of dynamic BP measurement will be highlighted within this committee. The WGPV meets every 3 years (May 2020). The group will be updated on the project's targets and results by CMI or PTB on its next meeting.
	The representatives on the corresponding committee or WG from the partners will jointly ask the chairperson to include a point in the agenda to briefly present the outputs of the project related to the WG activities and ask for comments. Where appropriate, a written report will be submitted for consideration by the committee or WG.		
A5.1.7 M36	PTB and CMI will make the document on development of the advanced oscillometric pressure generator (D1 in A1.4.4) available for download on the project website. The target audience for D1 will be NMIs, DIs and other authorised metrology service providers.		PTB, CMI
A5.1.8 M36	CMI will make the guidelines for testing sphygmomanometers using the aOSG (D3 in A2.3.3) available for download on the project website. The target audience for the guidelines for traceable BP metrology will be NMIs, DIs and other authorised metrology service providers.		CMI
A5.1.9 M36	UL will make the report on dynamic pressure calibration method for the aOSG and similar devices (D5 in A3.3.4) available for download on the project website. The target audience will be NMIs, DIs and other authorised metrology service providers.		UL
A5.1.10 M36	CMI will make the White Paper on the smart specialisation concept (D6 in A4.4.4) available to all relevant stakeholders in BP metrology and to relevant metrology organisations (OIML, BIPM, EURAMET, IMEKO) using the contacts database from A4.1.1. The White Paper will also be made available for download from the project website.		CMI
A5.1.11 M36	PTB and CMI will make the validation report on applicability of the advanced oscillometric pressure generator in market surveillance and/or clinical trials (D2 in A1.4.6) available for download on the project's website. The target audience will be manufacturers, authorities responsible for CE marking, market surveillance bodies, NMIs, DIs and other authorised metrology service providers.		CMI, PTB

C5.b Task 5.2 Training

Activity number	Activity description	Partners (Lead in bold)
A5.2.1 M27	Two workshops for stakeholders will be organised during the project. A first stakeholder workshop (1-2 days duration) will be organised by SMU around M18 (November 2020). Possible attendees will be identified from the stakeholder list (A5.1.1) and contacted directly by e-mail. The target number of delegates is 25. A second stakeholder workshop and dissemination symposium (1-2 days duration) will be organised by UL around M27 (August 2021). The workshop will be open to all NMIs, instrument manufacturers, accredited laboratories and standardisation organisations. The workshop will present the results achieved by the project and will include a discussion with all the participating stakeholders. Possible attendees will be identified from the stakeholder list and contacted directly by e-mail. The target number of delegates is 30.	SMU, UL
A5.2.2 M36	A webinar on the development of the aOSG and dynamical in-depth testing of SMs using an aOSG will take place and its recording will be posted on the project website.	PTB, all partners

A5.2.3 M36	A national stakeholder workshop will be held by NSAI in Ireland to disseminate the results and outputs of the research project and to discuss their utilisation by the stakeholders. The delegates will come from national standards bodies, medical device regulatory sector, and medical instrumentation calibration and service companies. The delegates could also be quality managers from major hospitals and practitioners in the field. The target number of delegates is 50. The workshop will be advertised on the project website, Twitter and LinkedIn as well as NSAI's comprehensive medical device contact listing and company database.	NSAI

C5.c Task 5.3 Uptake and exploitation

Activity number	Activity description	Partners (Lead in bold)
A5.3.1 M36	An exploitation plan will be created at the beginning of the project and reviewed and updated at least at each project meeting.	**CMI**, all partners
A5.3.2 M36	Based on the extended measurement capabilities acquired within WP3 and WP4, CMI will introduce extended calibration services for aOSGs and similar devices. The commercial measurement services will be provided to interested parties, such as test and calibration laboratories, NMIs, DIs, stakeholders and the working group on advanced blood pressure metrology. The information on the availability of measurement services will be advertised on the project website and sent by email to the interested parties.	**CMI**
A5.3.3 M36	CMI, with assistance of all partners, will be in regular contact with the working group on advanced blood pressure metrology (A5.1.2). As this group will provide a constant forum, where customers and stakeholders of advanced BP metrology meet, discuss and find solutions for the newest challenges in BP metrology, the consortium will promote the uptake of the outcomes of the project, e.g. the aOSG, within this group.	**CMI**, all partners
A5.3.4 M36	The consortium will identify measures that they will use to demonstrate that the project has narrowed the gap between the capabilities of their consortium and other NMIs/DIs in Europe. Summaries will be produced at months 18 (November 2020) and 36 (May 2022), demonstrating how the project helped emerging/smaller NMIs in the consortium to develop their capabilities closer to the wider European NMI/DI level. Where appropriate this improvement will be quantified. All partners will provide input to these summaries and the coordinator will provide this information demonstrating the narrowing of the capability gap at the mid-term review and at the end of the project.	**CMI**, all partners

All IP and potential licencing/exploitation will be handled in accordance with the Grant Agreement and the Consortium Agreement.

C6 WP6: Management and coordination

C6.a Task 6.1: Project management

Activity number	Activity description	Partners (Lead in bold)
A6.1.1 M36	The project will be managed by the coordinator from CMI, who will be supported by the project management board consisting of one representative from each partner. The members of the project management board will guide the project, attend the project meetings, organise the progress meetings and call additional meetings if needed to ensure the overall project's success.	**CMI**, all partners
A6.1.2 M36	The work package leaders will report on the on-going progress of the project to the coordinator by e-mail and telephone conferences.	**CMI**, all partners
A6.1.3 M36	The coordinator, with support from the partners, will manage the project's risks to ensure timely and effective delivery of the scientific and technical objectives and deliverables.	**CMI**, all partners

A6.1.4 M36	The consortium will ensure that any ethics issues identified (see Section D3) are addressed.	**CMI**, all partners

C6.b Task 6.2: Project meetings

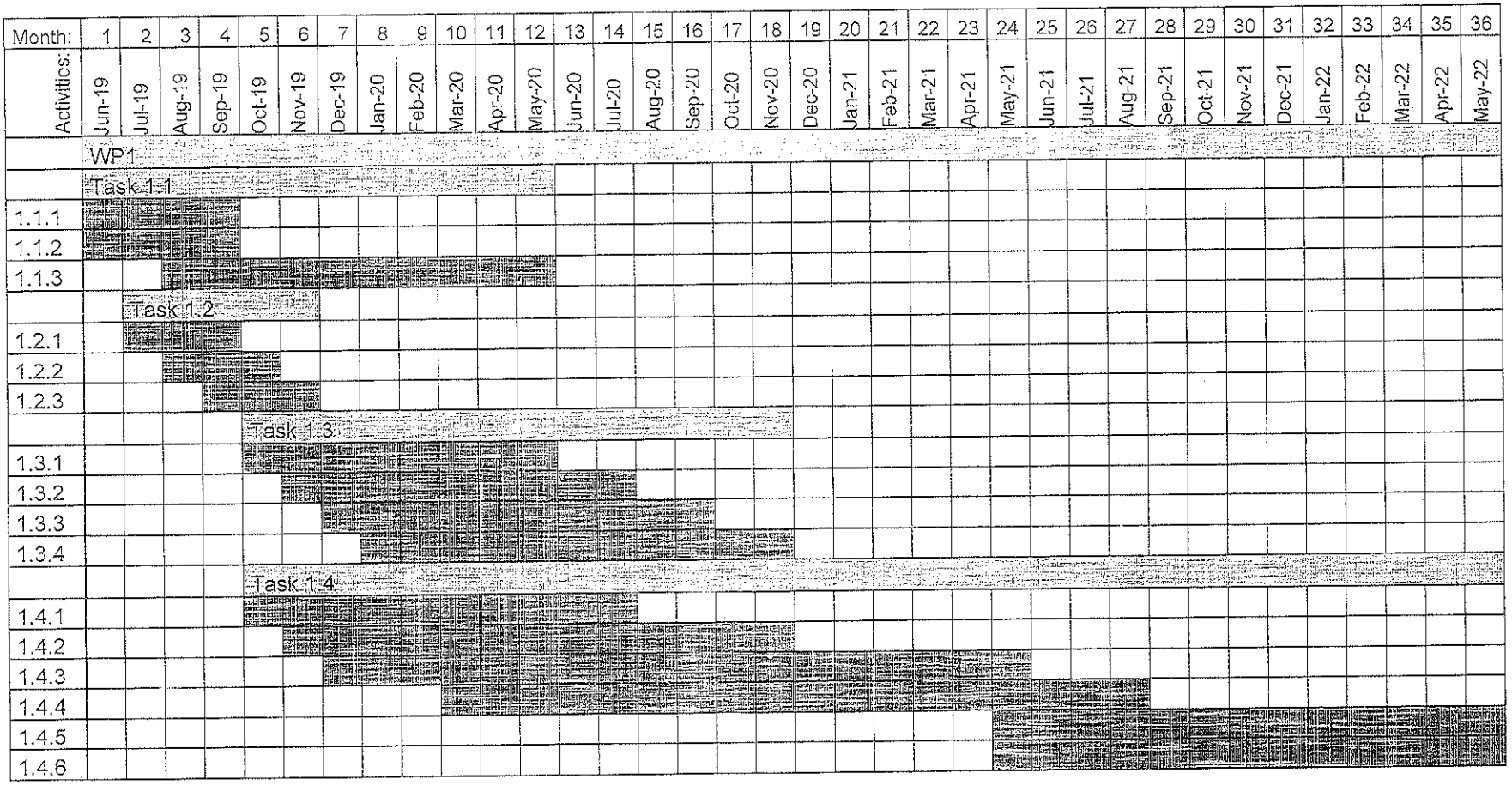
Activity number	Activity description	Partners (Lead in bold)
A6.2.1 M1	The kick-off meeting involving all partners will be held approximately one month after the start of the project, at CMI.	**CMI**, all partners
A6.2.2 M36	There will be five formal project meetings. These meetings, held approximately every 9 months, will include the kick-off, mid-term (around M18, November 2020) and final meeting (around M36, May 2022). The meetings will be held prior to reporting. The meetings will review progress and will be used to ensure partners are clear as to their role for the next period. The location of the meetings will rotate among the partners. Where possible, meetings may be held as satellite meetings to important conferences or committee meetings.	**CMI**, all partners
A6.2.3 M36	In addition, technical meetings of work package groups may be held whenever necessary, and will be arranged on an ad hoc basis.	**CMI**, all partners

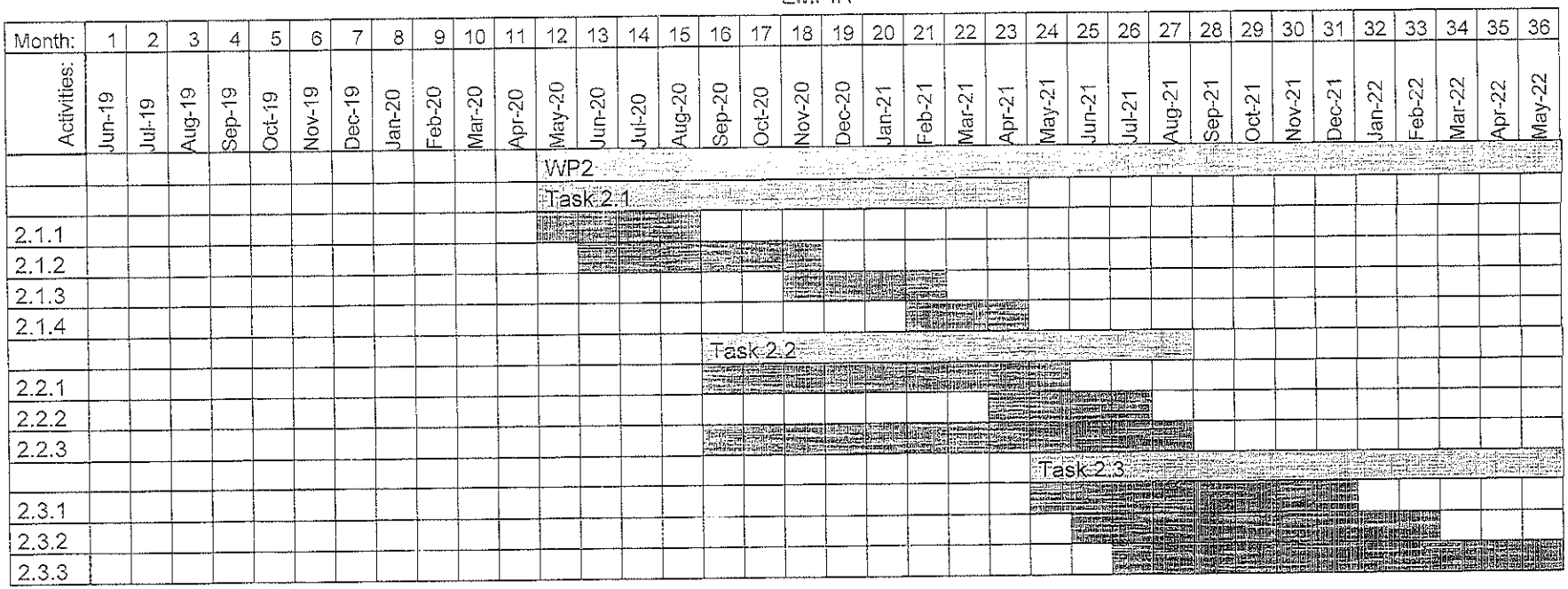
C6.c Task 6.3: Project reporting

Activity number	Activity description	Partners (Lead in bold)
A6.3.1 M1	One month after the start of the project a publishable summary and data management plan (DMP) will be produced and submitted to EURAMET.	**CMI**, all partners
A6.3.2 M36 +60 days	Following Articles 17 and 20 of the grant agreement, information will be submitted to EURAMET, in accordance with the procedures issued by them to enable EURAMET to comply with its obligations to report on the programme to the European Commission. • Progress reports will be submitted at months 9, 27 (February 2020 + 45 days, August 2021 + 45 days), 18, 36 (November 2020+ 60 days, May 2022 + 60 days). • Impact/Output reports will be submitted at the same times. All partners will provide input to these reports and the coordinator will provide these and updated publishable summaries to EURAMET.	**CMI**, all partners
A6.3.3 M36 +60 days	Periodic Reports (including updated data management plan, financial reports and questionnaires) will be delivered at months 18 and 36 (November 2020, May 2022 + 60 days) in accordance with Article 20 of the grant agreement. All partners will provide input to these reports and the coordinator will provide these to EURAMET.	**CMI**, all partners
A6.3.4 M36 +60 days	Final Reports will be delivered at month 36 (May 2022 + 60 days) in accordance with Article 20 of the grant agreement. All partners will provide input to these reports and the coordinator will provide these to EURAMET.	**CMI**, all partners
A6.3.5 M23	The project will be subject to a midterm review in Spring 2021. Reports (project self-assessment, updated publishable summary and presentation) will be delivered prior to the midterm reviews for Call 2018, following the schedule detailed by EURAMET for the specific review. All partners will provide input to these reporting documents and the coordinator will provide the documents to EURAMET.	**CMI**, all partners

Formal reporting will be in line with EURAMET's requirements and will be submitted in accordance with the Reporting Guidelines.

C7 Gantt chart

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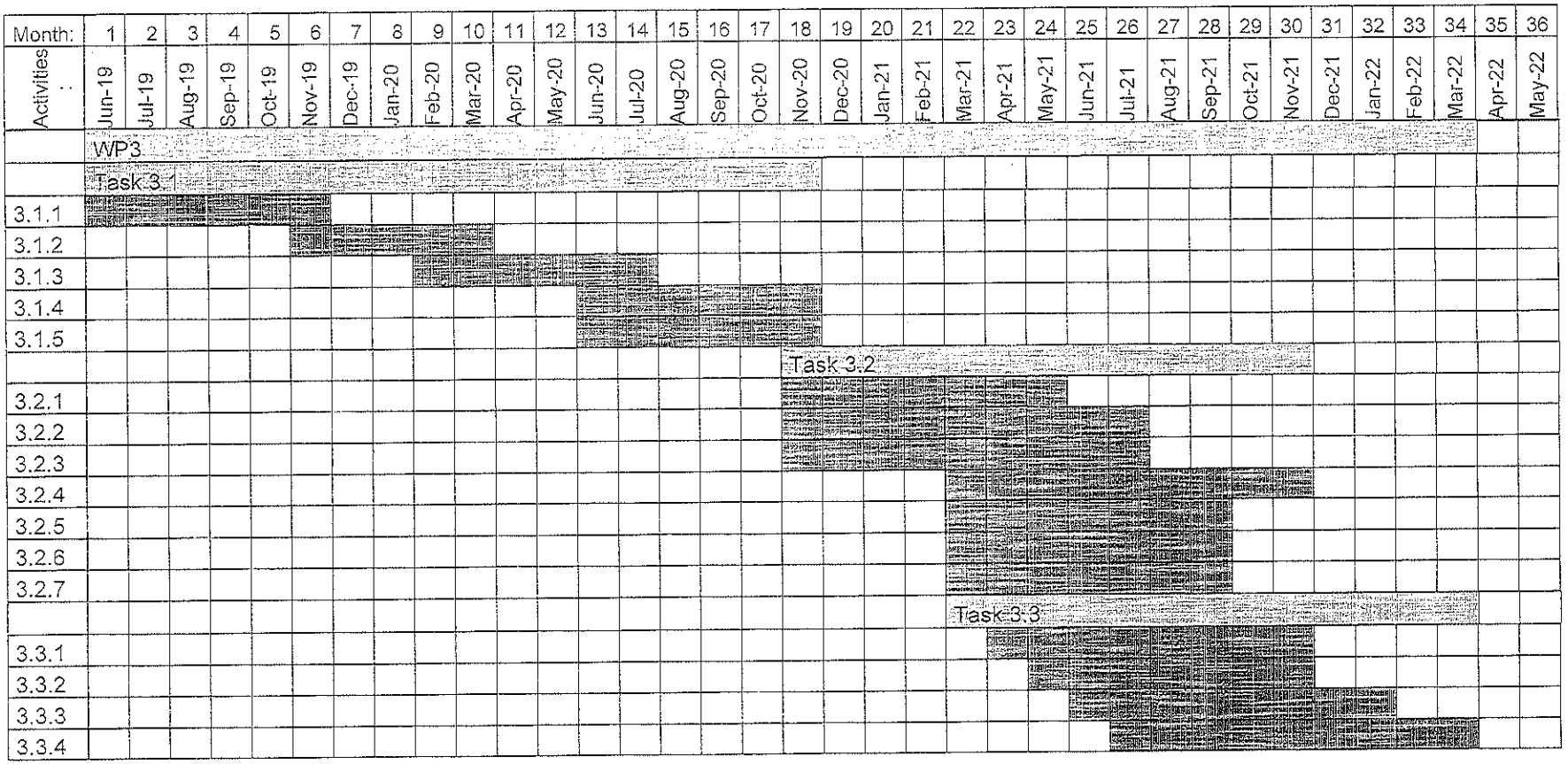
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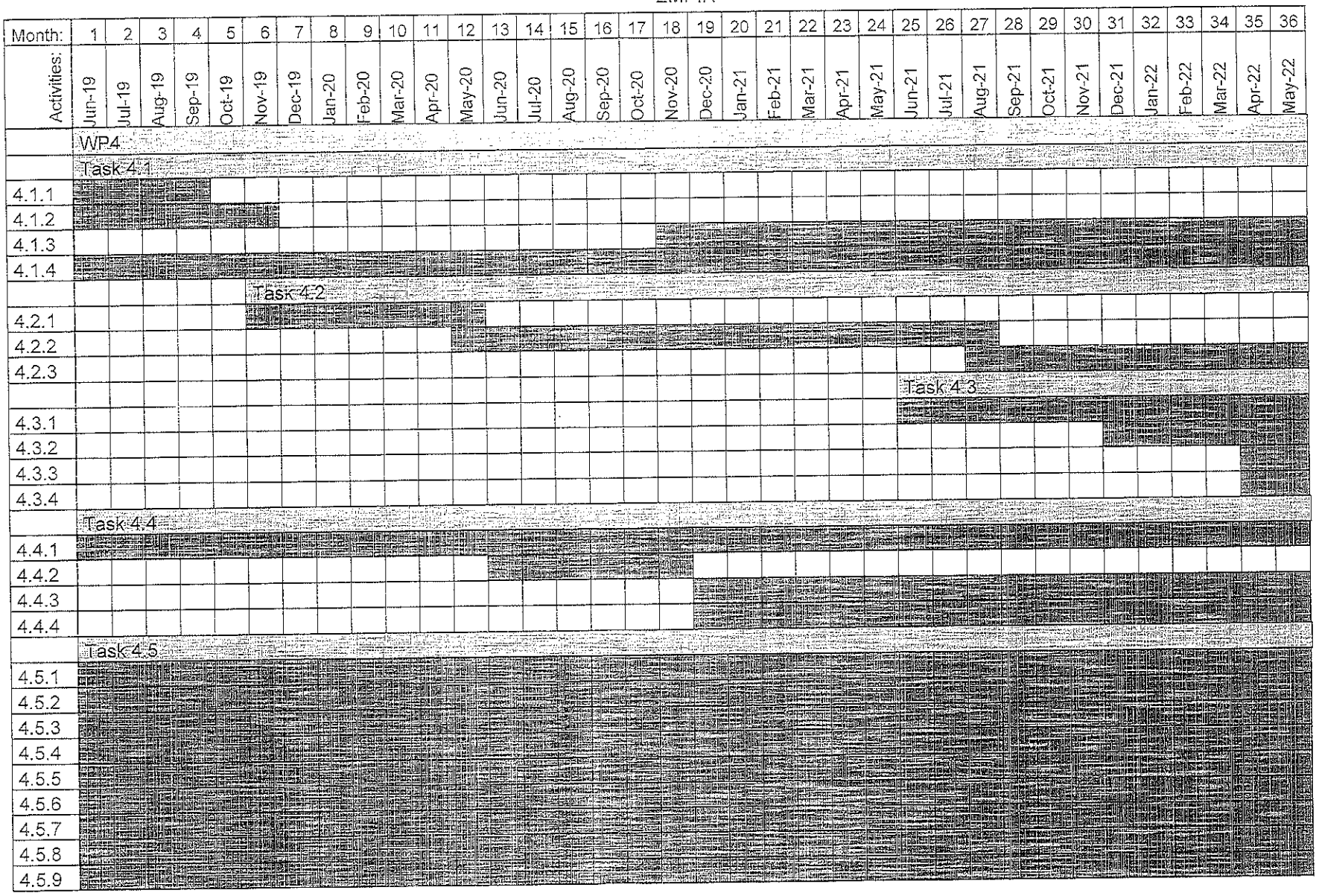
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Activities:
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Activities:	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19	Jan-20	Feb-20	Mar-20	Apr-20	May-20	Jun-20	Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20	Jan-21	Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21	Oct-21	Nov-21	Dec-21	Jan-22	Feb-22	Mar-22	Apr-22	May-22
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Activities:	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19	Jan-20	Feb-20	Mar-20	Apr-20	May-20	Jun-20	Jul-20	Aug-20	Sep-20	Oct-20	Nov-20	Dec-20	Jan-21	Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21	Oct-21	Nov-21	Dec-21	Jan-22	Feb-22	Mar-22	Apr-22	May-22
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Section D: Risk and risk mitigation

D1 Scientific/technical risks

Risk (description)	Likelihood and impact of occurrence	Mitigation i.e. what the consortium will do to decrease the likelihood of the risk occurring	Contingency i.e. what the consortium will do if despite the mitigation the risk still occurs
Tasks 1.1 – 1.4 Advanced oscillometric signal generator development is significantly delayed due to the complexity of the device	Likelihood without mitigation: Medium Impact: Deliverables D1, D2 are significantly delayed; activities in Task 2.3 and D3 will be delayed, as well activities connected to D5. Likelihood after mitigation: Low	The WP leader responsible for the aOSG development has experience in similar work. Further to the distribution of the workload among partners involved, the consortium will address any eventual problems. Time will be spent on the aOSG design to significantly reduce the risk.	Additional time will be allocated to minimise the delays in deliverables D1, D2, D3. The sample calibration within WP3 will be performed on commercial NIBP simulator.
Tasks 1.1 – 1.4 The consortium fails to design or build the aOSG	Likelihood without mitigation: Low Impact: Deliverables D1, D3, D2 cannot be produced; significant obstacle for D4, D5 and D6. Likelihood after mitigation: Very low	The WP leader responsible for the aOSG development has experience in similar work. The development will be preceded by an extensive survey on available solutions, similar and previous designs, which will identify possible weak points and ease the actual development.	Additional time will be allocated to minimise the delays in deliverables D1, D2, D3. An existing prototype of an aOSG, even though technically outdated, will be re-activated and used to perform the calibration and recalibration procedures proposed in WP3.
Task 1.4. Evaluation of the aOSG does not prove its potential applicability in market surveillance or clinical trials	Likelihood without mitigation: Medium Impact: Significant delay to D2. Likelihood after mitigation: Low	The aOSG will be designed with great emphasis on its applicability in market surveillance or clinical trials and test results during the development will be used as the feedback to reach the intended goal, i.e. applicability in market surveillance.	Validation report D2, with negative results will be issued.
Tasks 2.1 – 2.3. Development and evaluation of the procedure for sphygmomanometer testing is significantly delayed due to the complexity of the task	Likelihood without mitigation: Medium Impact: Deliverables D3, D6 are significantly delayed. Early impact of the aOSG (i.e. in-depth performance checks of automated sphygmomanometers) might be delayed. Likelihood after mitigation: Low	Time will be spent on the development of the procedure to significantly reduce the risk. Workload will be shared among the partners and with effective communication channels, the potential problems will be solved immediately.	Additional time will be allocated to minimise the delays in deliverables D3, D6 and workload of Tasks T2.1 – T2.3 will be redistributed.
Tasks 2.1 – 2.3 The University of Newcastle does not provide access to their database of real-life oscillometric signals	Likelihood without mitigation: Low Impact: The testing of the aOSG with real-life oscillometric signals cannot be completed; significant obstacle for D2 and D3. Likelihood after mitigation: Very low	The consortium was already authorised by the Newcastle University (through a letter of authorisation) to use the database of real-life oscillometric signals.	The consortium will seek for an alternative database within European NMIs and stakeholders and/or the consortium will subcontract the essential clinical expertise in collecting real-life data to obtain database of real-life oscillometric signals.

Tasks 3.1 – 3.3 Establishment of the routes of traceability for the aOSG face unpredicted complications related to dynamic pressure measurements	Likelihood without mitigation: Medium Impact: Calibration laboratory (Task 4.3) will not be established on time. Likelihood after mitigation: Low	The consortium members are very experienced in field of pressure traceability. The consortium will seek advice from NMIs experienced with dynamic traceability as soon as issues that cannot be solved by the consortium are identified, e.g. participants of EMRP IND09 Dynamic.	Additional time and resources will be re-allocated to minimise the delays in establishment of the test laboratory and development of the calibration methods.
Tasks 3.1 – 3.3 The target uncertainty ± 1.5 mmHg for the aOSG calibrations cannot be reached	Likelihood without mitigation: Medium Impact: Issues in D5, in setting-up a test laboratory in Task 4.3 and D7. Likelihood after mitigation: Low	The development of the calibration methods will be accompanied by a literature survey on available solutions. The partners are very experienced in the field of pressure traceability. The consortium will seek advice from NMIs experienced with dynamic traceability, e.g. participants of IND09 Dynamic.	If the target uncertainty cannot be reached, emphasis will be given on reaching an uncertainty of ±2,5 mmHg).
Task 4.1: Too few participants join the network of organisations who are interested in the traceability of dynamic BP measurements for it to be sustainable	Likelihood without mitigation: Medium Impact: Significant delay to the general transition to the dynamic testing of sphygmomanometers. Likelihood after mitigation: Low	The partners will widely advertise this project to suitable organisations: seek contact to manufacturers of sphygmomanometers, testing offices and standard developing organisations.	A small network will be created during the project. Nevertheless, as the project intends to create a long-lasting network for blood pressure devices, interested organisations will be able to join it after the end of the project.
Task 4.2 Legal framework shows the use of the aOSG for planned purposes (market surveillance tool) is not possible	Likelihood without mitigation: Medium Impact: Applicability of the aOSG will be reduced. Likelihood after mitigation: Low	The aOSG will be designed with great emphasis on its applicability in market surveillance or clinical trials and test results during the development will be used as the feedback to reach the intended goal, i.e. applicability in market surveillance. To increase the likelihood of success, the consortium will be in contact with manufacturers, clinicians and testing offices during the development of the aOSG.	The use of the aOSG will be limited to in-depth performance checks of sphygmomanometers outside the conformity (re-) assessment.
Task 4.3: Establishing of the testing laboratory at CMI to provide the traceability for the aOSG fails due to unpredicted complications related to dynamic pressure measurements and traceability	Likelihood without mitigation: Medium Impact: Dynamic traceability of the aOSG will not be ensured. Likelihood after mitigation: Low	Close collaboration among the consortium will precede the fulfilment of task 4.3, eventual risks and problems will be immediately addressed with appropriate means.	The established laboratory will work to a lower capacity than proposed in this project.
Tasks 4.4: The consortium of advanced blood pressure metrology fails to collaborate with similar projects or network	Likelihood without mitigation: Low Impact: The exploitation of the project's results will be slower, the project and its results will have low visibility, the results will only be partially recognised and adopted and the intended expanding of the network to other European regions will be delayed. Likelihood after mitigation: Very low	The partners will actively seek support and collaboration possibilities with similar projects (e.g. IND09 Dynamic, 16RPT03 inTENSE) and networks. The consortium will ensure a productive communication with its collaborators and be in permanent contact to relevant stakeholders: manufacturers of sphygmomanometers, medical professionals, national legislators.	The consortium will have difficulties expanding the smart specialisation concept to other medical devices and expansion of the network to other European regions will be delayed.

D2 Management risks

Risk (description)	Likelihood and impact of occurrence	Mitigation i.e. what the consortium will do to decrease the likelihood of the risk occurring	Contingency i.e. what the consortium will do if despite the mitigation the risk still occurs
Key personnel are lost to the project	Likelihood without mitigation: Low Impact: The loss of key team members would create difficulties in delivering the project, or specific tasks or deliverables. Likelihood after mitigation: Very low	None of the team members are planning to leave or retire within the project. The grouping of experts within the consortium should minimise the areas where knowledge is held by a single person. All the partners will identify backups for key workers wherever possible to reduce the overall risk to the project. Project plans will be shared within the consortium and results and methodology will be documented.	If a key member leaves the project, then the partner concerned will be responsible for appointing a replacement. However, this may still lead to a delay in delivery.
Complexity of managing a large consortium	Likelihood without mitigation: Medium Impact: Failure to fully cooperate or communicate effectively within the consortium could endanger efficient delivery of the project. Likelihood after mitigation: Low	The partners are all experienced with complex multinational projects. Many have previously developed close relationships through collaborating within other European consortia. Regular communication and feedback will ensure that potential problems are identified early and that all partners are clear on their roles.	WP leaders will play an important role in flagging up potential problems to the coordinator and the project management board, who will then decide on the best course of action to take. If necessary, work will be reassigned to an alternative partner, or parts of the work re-scoped in agreement with EURAMET.
Inter-dependencies between technical activities and tasks are too complex	Likelihood without mitigation: Medium Impact: Tasks are delayed or it is not possible to deliver them. Likelihood after mitigation: Low	Technical meetings run by WP leaders have been scheduled to ensure proper sharing of knowledge. The interdependencies between tasks will be considered at meetings to ensure that this is addressed properly in the planning of the work. The technical WPs will be closely managed by their WP leaders to ensure that they deliver their own outputs.	In most cases, activities on the critical path have some overlap in time and thus a delay in the output of one deliverable does not necessarily cause an immediate delay in another.
Problems dealing with Intellectual Property (IP) ownership and/or exploitation might occur and could be a source of potential conflict	Likelihood without mitigation: Medium Impact: Disagreement between the partners could delay the progress of the project (in implementing the work and publishing results). Likelihood after mitigation: Low	All partners will sign the grant agreement and consortium agreement, which includes IP clauses.	Independent arbitrators will be used in the event of disagreement between partners.

D3 Ethics

The EMPIR Ethics Review 2018 has given JRP 18PRT02 adOSSIG "Conditional ethics clearance".

Data protection

By signing or acceding to this grant agreement each beneficiary asserts that the requirements of the General Data Protection Regulation (GDPR) 2016/679 which entered into force on 25 May 2018 will be met. Under the regulation, the data controllers and processors are fully accountable for the data processing operations. Any violation of the data subject rights may lead to sanctions as described in Chapter VIII, art.77-84 of the GDPR.

Third countries

The consortium will ensure that any partners or collaborators from Third Countries fully adhere to H2020 ethics standards, no matter where the research or activities are carried out and that research or activities performed outside the EU are compatible with European Union, national and international legislation and can be legally conducted in one of the EU Member States. If applicable, details on the material and/or software which will be imported to/exported from EU must be provided and the adequate authorisations granted by the relevant authorities are or will be obtained and kept on file. The consortium will also, in the case of dual use applications, clarify whether any export licence is required for the transfer of knowledge or material.

Ethical integrity

The consortium will ensure that the ethical policy to be followed in the project complies with the highest standards of research integrity (as set out in the European Code of Conduct for Research Integrity).

Section E: References

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