EUROPEAN COMMISSION
Directorate-General for Research and Innovation

RTD.D – People
D.1 – Combatting Diseases

GRANT AGREEMENT

Project 101103089 — STOP2030

PREAMBLE

This **Agreement** ('the Agreement') is **between** the following parties:

on the one part,

the **European Union** ('EU'), represented by the European Commission ('European Commission' or 'granting authority'),

and

on the other part,

1. 'the coordinator':

LABORATORIOS LICONSA SA (Liconsa), PIC 990555950, established in MANUEL POMBO ANGULO 28, Madrid 28050, Spain,

and the following other beneficiaries, if they sign their 'accession form' (see Annex 3 and Article 40):

2. **FUNDACION PRIVADA INSTITUTO DE SALUD GLOBAL BARCELONA (ISGLOBAL)**, PIC 951414122, established in C ROSSELLO 132 PLANTA 05, BARCELONA 08036, Spain,

3. **FUNDACION MUNDO SANO ESPANA (FMS ESPANA)**, PIC 885624551, established in GRAN VIA CARLOS III, 98, BARCELONA 08028, Spain,

4. **KENYA MEDICAL RESEARCH INSTITUTE (KEMRI)**, PIC 997741225, established in Off Mbagathi Way, Nairobi 00200, Kenya,

5. **GHANA HEALTH SERVICE (GHS)**, PIC 894057343, established in PRIVATE MAIL BAG MINISTRIES ACCRA, Accra, Ghana,

6. **GENOME RESEARCH LIMITED (GRL)**, PIC 999981343, established in THE GIBBS BUILDING, EUSTON ROAD 215, LONDON NW1 2BE, United Kingdom,

Unless otherwise specified, references to 'beneficiary' or 'beneficiaries' include the coordinator and affiliated entities (if any).

If only one beneficiary signs the grant agreement ('mono-beneficiary grant'), all provisions referring to the 'coordinator' or the 'beneficiaries' will be considered — mutatis mutandis — as referring to the beneficiary.

The parties referred to above have agreed to enter into the Agreement.

By signing the Agreement and the accession forms, the beneficiaries accept the grant and agree to implement the action under their own responsibility and in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

The Agreement is composed of:

Preamble

Terms and Conditions (including Data Sheet)

Annex 1 Description of the action[1]

Annex 2 Estimated budget for the action

Annex 2a Additional information on unit costs and contributions (if applicable)

Annex 3 Accession forms (if applicable)[2]

Annex 3a Declaration on joint and several liability of affiliated entities (if applicable)[3]

Annex 4 Model for the financial statements

Annex 5 Specific rules (if applicable)

[1] Template published on Portal Reference Documents.
[2] Template published on Portal Reference Documents.
[3] Template published on Portal Reference Documents.

TERMS AND CONDITIONS

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DATA SHEET

1. General data

Project summary:

Project summary
Soil-Transmitted Helminths (STH) remain a significant public health problem with recognized obstacles for control and elimination with the current benzimidazole regimens in Mass Drug Administration (MDA) campaigns. Renewed targets from WHO for 2030 include elimination of STH morbidity in pre-school and school age children (PSAC & SAC), increased country governance and financial support and a strongyloidiasis control program; 2030 has also been targeted by WHO for controlling NTDs to attain the Sustainable Development Goals. The current proposal aims at accelerating the implementation of an innovative health technology, a fixed-dose combination (FDC) tablet of co-formulated albendazole and ivermectin, with adequate safety and significantly superior efficacy against T. trichiura in a registrational randomized clinical trial. This trial is being conducted in Ethiopia, Kenya and Mozambique with the guidance of EMA and sponsored by EDCTP (STOP projects) with a Phase II trial completed and a Phase III currently recruiting. This project, STOP2030, seeks to complement the results of the safety and efficacy trial with a field-based safety and effectiveness clinical study, acceptability studies in Ghana and Kenya, modelling and cost-effectiveness exercises. The resulting information will be consolidated to build a multidisciplinary package for policy making and WHO guidance with the support of advocacy and communication activities to reach stakeholders and maximize the exploitation and impact of the FDC for STH control and elimination. The Consortium assembled to execute the STOP2030 proposal combines expertise in complementary fields from program assessment and implementation through Ministries of Health in sub-Saharan African countries, advocacy, state of the art technology, leadership in clinical research and a pharma that has shown commitment for generating access to drugs against NTDs and has recently obtained WHO prequalification for generic ivermectin.

Keywords:

- Global health
- Health inequalities
- Health policies
- Infectious diseases
- Soil-transmitted helminthiases, ivermectin, albendazole

Project number: 101103089

Project name: STOP 2030: TOWARDS THE INTERRUPTION OF TRANSMISSION OF SOIL-TRANSMITTED HELMINTHS: PROMOTING IMPLEMENTATION OF RESEARCH RESULTS OF A FIXED-DOSE COMBINATION OF CO-FORMULATED IVERMECTIN AND ALBENDAZOLE

Project acronym: STOP2030

Call: HORIZON-JU-GH-EDCTP3-2022-01

Topic: HORIZON-JU-GH-EDCTP3-2022-CALL1-01-01

Type of action: HORIZON JU Research and Innovation Actions

Granting authority: European Commission-EU

Grant managed through EU Funding & Tenders Portal: Yes (eGrants)

Project starting date: fixed date: 1 July 2023

Project end date: 30 June 2026

Project duration: 36 months

Consortium agreement: No

2. Participants

List of participants:

N°	Role	Short name	Legal name	Ctry	PIC	Total eligible costs (BEN and AE)	Max grant amount
1	COO	Liconsa	LABORATORIOS LICONSA SA	ES	990555950	483 815.25	483 815.25
2	BEN	ISGLOBAL	FUNDACION PRIVADA INSTITUTO DE SALUD GLOBAL BARCELONA	ES	951414122	742 892.50	742 892.50
3	BEN	FMS ESPANA	FUNDACION MUNDO SANO ESPANA	ES	885624551	248 750.00	248 750.00
4	BEN	KEMRI	KENYA MEDICAL RESEARCH INSTITUTE	KE	997741225	821 393.75	821 393.75
5	BEN	GHS	GHANA HEALTH SERVICE	GH	894057343	887 500.00	887 500.00
6	BEN	GRL	GENOME RESEARCH LIMITED	UK	999981343	369 150.75	369 150.75
7	AP	Bridges	BRIDGES TO DEVELOPMENT	CH	896766941	0.00	0.00
Total						3 553 502.25	3 553 502.25

Coordinator:

– LABORATORIOS LICONSA SA (Liconsa)

3. Grant

Maximum grant amount, total estimated eligible costs and contributions and funding rate:

Total eligible costs (BEN and AE)	Funding rate (%)	Maximum grant amount (Annex 2)	Maximum grant amount (award decision)
3 553 502.25	100	3 553 502.25	3 553 502.25

Grant form: Budget-based

Grant mode: Action grant

Budget categories/activity types:

- A. Personnel costs
  - A.1 Employees, A.2 Natural persons under direct contract, A.3 Seconded persons
  - A.4 SME owners and natural person beneficiaries
- B. Subcontracting costs
- C. Purchase costs
  - C.1 Travel and subsistence
  - C.2 Equipment
  - C.3 Other goods, works and services
- D. Other cost categories
  - D.2 Internally invoiced goods and services
  - D.3 Transnational access to research infrastructure unit costs
  - D.4 Virtual access to research infrastructure unit costs
- E. Indirect costs

Cost eligibility options:

- In-kind contributions eligible costs
- Parental leave
- Project-based supplementary payments

- Average personnel costs (unit cost according to usual cost accounting practices)
- Limitation for subcontracting
- Travel and subsistence:
  - Travel: Actual costs
  - Accommodation: Actual costs
  - Subsistence: Actual costs
- Equipment: depreciation only
- Indirect cost flat-rate: 25% of the eligible direct costs (categories A-D, except volunteers costs, subcontracting costs, financial support to third parties and exempted specific cost categories, if any)
- VAT: Yes
- Other ineligible costs

Budget flexibility: Yes (no flexibility cap)

4. Reporting, payments and recoveries

4.1 Continuous reporting (art 21)

Deliverables: see Funding & Tenders Portal Continuous Reporting tool

4.2 Periodic reporting and payments

Reporting and payment schedule (art 21, 22):

Reporting					Payments	
Reporting periods			Type	Deadline	Type	Deadline (time to pay)
RP No	Month from	Month to				
					Initial prefinancing	30 days from entry into force/10 days before starting date – whichever is the latest
1	1	18	Periodic report	60 days after end of reporting period	Interim payment	90 days from receiving periodic report
2	19	36	Periodic report	60 days after end of reporting period	Final payment	90 days from receiving periodic report

Prefinancing payments and guarantees:

Prefinancing payment	
Type	Amount
Prefinancing 1 (initial)	2 309 776.00

Reporting and payment modalities (art 21, 22):

Mutual Insurance Mechanism (MIM): Yes

MIM contribution: 5% of the maximum grant amount (177 675.11), retained from the initial prefinancing

Restrictions on distribution of initial prefinancing: The prefinancing may be distributed only if the minimum number of beneficiaries set out in the call condititions (if any) have acceded to the Agreement and only to beneficiaries that have acceded.

Interim payment ceiling (if any): 90% of the maximum grant amount

Exception for revenues: Yes

No-profit rule: Yes

Late payment interest: ECB + 3.5%

Bank account for payments:

ES3801822325030204019796

Conversion into euros: Double conversion

Reporting language: Language of the Agreement

4.3 Certificates (art 24):

Certificates on the financial statements (CFS):

Conditions:

Schedule: only at final payment, if threshold is reached

Standard threshold (beneficiary-level):

- financial statement: requested EU contribution to costs ≥ EUR 430 000.00

Special threshold for beneficiaries with a systems and process audit(see Article 24): financial statement: requested EU contribution to costs ≥ EUR 725 000.00

4.4 Recoveries (art 22)

First-line liability for recoveries:

Beneficiary termination: Beneficiary concerned

Final payment: Each beneficiary for their own debt

After final payment: Beneficiary concerned

Joint and several liability for enforced recoveries (in case of non-payment):

Individual financial responsibility: Each beneficiary is liable only for its own debts (and those of its affiliated entities, if any)

5. Consequences of non-compliance, applicable law & dispute settlement forum

Suspension and termination:

Additional suspension grounds (art 31)

Additional termination grounds (art 32)

Applicable law (art 43):

Standard applicable law regime: EU law + law of Belgium

Dispute settlement forum (art 43):

Standard dispute settlement forum:

EU beneficiaries: EU General Court + EU Court of Justice (on appeal)

Non-EU beneficiaries: Courts of Brussels, Belgium (unless an international agreement provides for the enforceability of EU court judgements)

6. Other

Specific rules (Annex 5): Yes

Standard time-limits after project end:

Confidentiality (for X years after final payment): 5

Record-keeping (for X years after final payment): 5 (or 3 for grants of not more than EUR 60 000)

Reviews (up to X years after final payment): 2

Audits (up to X years after final payment): 2

Extension of findings from other grants to this grant (no later than X years after final payment): 2

Impact evaluation (up to X years after final payment): 5 (or 3 for grants of not more than EUR 60 000)

CHAPTER 1 GENERAL

ARTICLE 1 — SUBJECT OF THE AGREEMENT

This Agreement sets out the rights and obligations and terms and conditions applicable to the grant awarded for the implementation of the action set out in Chapter 2.

ARTICLE 2 — DEFINITIONS

For the purpose of this Agreement, the following definitions apply:

Actions — The project which is being funded in the context of this Agreement.

Grant — The grant awarded in the context of this Agreement.

EU grants — Grants awarded by EU institutions, bodies, offices or agencies (including EU executive agencies, EU regulatory agencies, EDA, joint undertakings, etc.).

Participants — Entities participating in the action as beneficiaries, affiliated entities, associated partners, third parties giving in-kind contributions, subcontractors or recipients of financial support to third parties.

Beneficiaries (BEN) — The signatories of this Agreement (either directly or through an accession form).

Affiliated entities (AE) — Entities affiliated to a beneficiary within the meaning of Article 187 of EU Financial Regulation 2018/1046[4] which participate in the action with similar rights and obligations as the beneficiaries (obligation to implement action tasks and right to charge costs and claim contributions).

Associated partners (AP) — Entities which participate in the action, but without the right to charge costs or claim contributions.

Purchases — Contracts for goods, works or services needed to carry out the action (e.g. equipment, consumables and supplies) but which are not part of the action tasks (see Annex 1).

Subcontracting — Contracts for goods, works or services that are part of the action tasks (see Annex 1).

In-kind contributions — In-kind contributions within the meaning of Article 2(36) of EU Financial

[4] For the definition, see Article 187 Regulation (EU, Euratom) 2018/1046 of the European Parliament and of the Council of 18 July 2018 on the financial rules applicable to the general budget of the Union, amending Regulations (EU) No 1296/2013, (EU) No 1301/2013, (EU) No 1303/2013, (EU) No 1304/2013, (EU) No 1309/2013, (EU) No 1316/2013, (EU) No 223/2014, (EU) No 283/2014, and Decision No 541/2014/EU and repealing Regulation (EU, Euratom) No 966/2012 ('EU Financial Regulation') (OJ L 193, 30.7.2018, p. 1): "**affiliated entities** [are]:
(a) entities that form a sole beneficiary [(i.e. where an entity is formed of several entities that satisfy the criteria for being awarded a grant, including where the entity is specifically established for the purpose of implementing an action to be financed by a grant)];
(b) entities that satisfy the eligibility criteria and that do not fall within one of the situations referred to in Article 136(1) and 141(1) and that have a link with the beneficiary, in particular a legal or capital link, which is neither limited to the action nor established for the sole purpose of its implementation".

Regulation 2018/1046, i.e. non-financial resources made available free of charge by third parties.

Fraud — Fraud within the meaning of Article 3 of EU Directive 2017/1371[5] and Article 1 of the Convention on the protection of the European Communities' financial interests, drawn up by the Council Act of 26 July 1995[6], as well as any other wrongful or criminal deception intended to result in financial or personal gain.

Irregularities — Any type of breach (regulatory or contractual) which could impact the EU financial interests, including irregularities within the meaning of Article 1(2) of EU Regulation 2988/95[7].

Grave professional misconduct — Any type of unacceptable or improper behaviour in exercising one's profession, especially by employees, including grave professional misconduct within the meaning of Article 136(1)(c) of EU Financial Regulation 2018/1046.

Applicable EU, international and national law — Any legal acts or other (binding or non-binding) rules and guidance in the area concerned.

Portal — EU Funding & Tenders Portal; electronic portal and exchange system managed by the European Commission and used by itself and other EU institutions, bodies, offices or agencies for the management of their funding programmes (grants, procurements, prizes, etc.).

CHAPTER 2 ACTION

ARTICLE 3 — ACTION

The grant is awarded for the action **101103089 — STOP2030** ('action'), as described in Annex 1.

ARTICLE 4 — DURATION AND STARTING DATE

The duration and the starting date of the action are set out in the Data Sheet (see Point 1).

CHAPTER 3 GRANT

ARTICLE 5 — GRANT

5.1 Form of grant

The grant is an action grant[8] which takes the form of a budget-based mixed actual cost grant (i.e. a

[5] Directive (EU) 2017/1371 of the European Parliament and of the Council of 5 July 2017 on the fight against fraud to the Union's financial interests by means of criminal law (OJ L 198, 28.7.2017, p. 29).

[6] OJ C 316, 27.11.1995, p. 48.

[7] Council Regulation (EC, Euratom) No 2988/95 of 18 December 1995 on the protection of the European Communities financial interests (OJ L 312, 23.12.1995, p. 1).

[8] For the definition, see Article 180(2)(a) EU Financial Regulation 2018/1046: '**action grant**' means an EU grant to finance "an action intended to help achieve a Union policy objective".

grant based on actual costs incurred, but which may also include other forms of funding, such as unit costs or contributions, flat-rate costs or contributions, lump sum costs or contributions or financing not linked to costs).

5.2 Maximum grant amount

The maximum grant amount is set out in the Data Sheet (see Point 3) and in the estimated budget (Annex 2).

5.3 Funding rate

The funding rate for costs is 100% of the action's eligible costs.

Contributions are not subject to any funding rate.

5.4 Estimated budget, budget categories and forms of funding

The estimated budget for the action is set out in Annex 2.

It contains the estimated eligible costs and contributions for the action, broken down by participant and budget category.

Annex 2 also shows the types of costs and contributions (forms of funding)[9] to be used for each budget category.

If unit costs or contributions are used, the details on the calculation will be explained in Annex 2a.

5.5 Budget flexibility

The budget breakdown may be adjusted — without an amendment (see Article 39) — by transfers (between participants and budget categories), as long as this does not imply any substantive or important change to the description of the action in Annex 1.

However:

- changes to the budget category for volunteers (if used) always require an amendment
- changes to budget categories with lump sums costs or contributions (if used; including financing not linked to costs) always require an amendment
- changes to budget categories with higher funding rates or budget ceilings (if used) always require an amendment
- addition of amounts for subcontracts not provided for in Annex 1 either require an amendment or simplified approval in accordance with Article 6.2
- other changes require an amendment or simplified approval, if specifically provided for in Article 6.2
- flexibility caps: not applicable.

[9] See Article 125 EU Financial Regulation 2018/1046.

ARTICLE 6 — ELIGIBLE AND INELIGIBLE COSTS AND CONTRIBUTIONS

In order to be eligible, costs and contributions must meet the **eligibility** conditions set out in this Article.

6.1 General eligibility conditions

The **general eligibility conditions** are the following:

(a) for actual costs:

(i) they must be actually incurred by the beneficiary

(ii) they must be incurred in the period set out in Article 4 (with the exception of costs relating to the submission of the final periodic report, which may be incurred afterwards; see Article 21)

(iii) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(iv) they must be incurred in connection with the action as described in Annex 1 and necessary for its implementation

(v) they must be identifiable and verifiable, in particular recorded in the beneficiary's accounts in accordance with the accounting standards applicable in the country where the beneficiary is established and with the beneficiary's usual cost accounting practices

(vi) they must comply with the applicable national law on taxes, labour and social security and

(vii) they must be reasonable, justified and must comply with the principle of sound financial management, in particular regarding economy and efficiency

(b) for unit costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the units must:

- be actually used or produced by the beneficiary in the period set out in Article 4 (with the exception of units relating to the submission of the final periodic report, which may be used or produced afterwards; see Article 21)

- be necessary for the implementation of the action and

(iii) the number of units must be identifiable and verifiable, in particular supported by records and documentation (see Article 20)

(c) for flat-rate costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the costs or contributions to which the flat-rate is applied must:

- be eligible
- relate to the period set out in Article 4 (with the exception of costs or contributions relating to the submission of the final periodic report, which may be incurred afterwards; see Article 21)

(d) for lump sum costs or contributions (if any):

(i) they must be declared under one of the budget categories set out in Article 6.2 and Annex 2

(ii) the work must be properly implemented by the beneficiary in accordance with Annex 1

(iii) the deliverables/outputs must be achieved in the period set out in Article 4 (with the exception of deliverables/outputs relating to the submission of the final periodic report, which may be achieved afterwards; see Article 21)

(e) for unit, flat-rate or lump sum costs or contributions according to usual cost accounting practices (if any):

(i) they must fulfil the general eligibility conditions for the type of cost concerned

(ii) the cost accounting practices must be applied in a consistent manner, based on objective criteria, regardless of the source of funding

(f) for financing not linked to costs (if any): the results must be achieved or the conditions must be fulfilled as described in Annex 1.

In addition, for direct cost categories (e.g. personnel, travel & subsistence, subcontracting and other direct costs) only costs that are directly linked to the action implementation and can therefore be attributed to it directly are eligible. They must not include any indirect costs (i.e. costs that are only indirectly linked to the action, e.g. via cost drivers).

In-kind contributions provided by third parties free of charge may be declared as eligible direct costs by the beneficiaries which use them (under the same conditions as if they were their own, provided that they concern only direct costs and that the third parties and their in-kind contributions are set out in Annex 1 (or approved ex post in the periodic report, if their use does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants; 'simplified approval procedure').

6.2 Specific eligibility conditions for each budget category

For each budget category, the **specific eligibility conditions** are as follows:

Direct costs

A. Personnel costs

A.1 Costs for employees (or equivalent) are eligible as personnel costs if they fulfil the general eligibility conditions and are related to personnel working for the beneficiary under an employment contract (or equivalent appointing act) and assigned to the action.

They must be limited to salaries (including net payments during parental leave), social security contributions, taxes and other costs linked to the remuneration, if they arise from national law or the employment contract (or equivalent appointing act) and be calculated on the basis of the costs actually incurred, in accordance with the following method:

{daily rate for the person

multiplied by

number of day-equivalents worked on the action (rounded up or down to the nearest half-day)}.

The daily rate must be calculated as:

{annual personnel costs for the person

divided by

215}.

The number of day-equivalents declared for a person must be identifiable and verifiable (see Article 20).

The actual time spent on parental leave by a person assigned to the action may be deducted from the 215 days indicated in the above formula.

The total number of day-equivalents declared in EU grants, for a person for a year, cannot be higher than 215, minus time spent on parental leave (if any).

For personnel which receives supplementary payments for work in projects (project-based remuneration), the personnel costs must be calculated at a rate which:

- corresponds to the actual remuneration costs paid by the beneficiary for the time worked by the person in the action over the reporting period
- does not exceed the remuneration costs paid by the beneficiary for work in similar projects funded by national schemes (‘national projects reference’)
- is defined based on objective criteria allowing to determine the amount to which the person is entitled

and

- reflects the usual practice of the beneficiary to pay consistently bonuses or supplementary payments for work in projects funded by national schemes.

The national projects reference is the remuneration defined in national law, collective labour agreement or written internal rules of the beneficiary applicable to work in projects funded by national schemes.

If there is no such national law, collective labour agreement or written internal rules or if the project-based remuneration is not based on objective criteria, the national project reference will be the average

remuneration of the person in the last full calendar year covered by the reporting period, excluding remuneration paid for work in EU actions.

If the beneficiary uses average personnel costs (unit cost according to usual cost accounting practices), the personnel costs must fulfil the general eligibility conditions for such unit costs and the daily rate must be calculated:

- using the actual personnel costs recorded in the beneficiary's accounts and excluding any costs which are ineligible or already included in other budget categories; the actual personnel costs may be adjusted on the basis of budgeted or estimated elements, if they are relevant for calculating the personnel costs, reasonable and correspond to objective and verifiable information

and

- according to usual cost accounting practices which are applied in a consistent manner, based on objective criteria, regardless of the source of funding.

A.2 and **A.3 Costs for natural persons working under a direct contract** other than an employment contract and costs for **seconded persons by a third party against payment** are also eligible as personnel costs, if they are assigned to the action, fulfil the general eligibility conditions and:

(a) work under conditions similar to those of an employee (in particular regarding the way the work is organised, the tasks that are performed and the premises where they are performed) and

(b) the result of the work belongs to the beneficiary (unless agreed otherwise).

They must be calculated on the basis of a rate which corresponds to the costs actually incurred for the direct contract or secondment and must not be significantly different from those for personnel performing similar tasks under an employment contract with the beneficiary.

A.4 The work of **SME owners** for the action (i.e. owners of beneficiaries that are small and medium-sized enterprises[10] not receiving a salary) or **natural person beneficiaries** (i.e. beneficiaries that are natural persons not receiving a salary) may be declared as personnel costs, if they fulfil the general eligibility conditions and are calculated as unit costs in accordance with the method set out in Annex 2a.

B. Subcontracting costs

Subcontracting costs for the action (including related duties, taxes and charges, such as non-deductible or non-refundable value added tax (VAT)) are eligible, if they are calculated on the basis of the costs actually incurred, fulfil the general eligibility conditions and are awarded using the

[10] For the definition, see Commission Recommendation 2003/361/EC: micro, small or medium-sized enterprise (SME) are enterprises

- engaged in an economic activity, irrespective of their legal form (including, in particular, self- employed persons and family businesses engaged in craft or other activities, and partnerships or associations regularly engaged in an economic activity) and

- employing fewer than 250 persons (expressed in 'annual working units' as defined in Article 5 of the Recommendation) and which have an annual turnover not exceeding EUR 50 million, and/or an annual balance sheet total not exceeding EUR 43 million.

beneficiary's usual purchasing practices — provided these ensure subcontracts with best value for money (or if appropriate the lowest price) and that there is no conflict of interests (see Article 12).

Beneficiaries that are 'contracting authorities/entities' within the meaning of the EU Directives on public procurement must also comply with the applicable national law on public procurement.

Subcontracting may cover only a limited part of the action.

The tasks to be subcontracted and the estimated cost for each subcontract must be set out in Annex 1 and the total estimated costs of subcontracting per beneficiary must be set out in Annex 2 (or may be approved ex post in the periodic report, if the use of subcontracting does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants; 'simplified approval procedure').

C. Purchase costs

Purchase costs for the action (including related duties, taxes and charges, such as non-deductible or non-refundable value added tax (VAT)) are eligible if they fulfil the general eligibility conditions and are bought using the beneficiary's usual purchasing practices — provided these ensure purchases with best value for money (or if appropriate the lowest price) and that there is no conflict of interests (see Article 12).

Beneficiaries that are 'contracting authorities/entities' within the meaning of the EU Directives on public procurement must also comply with the applicable national law on public procurement.

C.1 Travel and subsistence

Purchases for **travel, accommodation** and **subsistence** must be calculated as follows:

- travel: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel
- accommodation: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel
- subsistence: on the basis of the costs actually incurred and in line with the beneficiary's usual practices on travel .

C.2 Equipment

Purchases of **equipment, infrastructure or other assets** used for the action must be declared as depreciation costs, calculated on the basis of the costs actually incurred and written off in accordance with international accounting standards and the beneficiary's usual accounting practices.

Only the portion of the costs that corresponds to the rate of actual use for the action during the action duration can be taken into account.

Costs for **renting or leasing** equipment, infrastructure or other assets are also eligible, if they do not exceed the depreciation costs of similar equipment, infrastructure or assets and do not include any financing fees.

C.3 Other goods, works and services

Purchases of **other goods, works and services** must be calculated on the basis of the costs actually incurred.

Such goods, works and services include, for instance, consumables and supplies, promotion, dissemination, protection of results, translations, publications, certificates and financial guarantees, if required under the Agreement.

D. Other cost categories

D.2 Internally invoiced goods and services

Costs for internally invoiced goods and services directly used for the action may be declared as unit cost according to usual cost accounting practices, if and as declared eligible in the call conditions, if they fulfil the general eligibility conditions for such unit costs and the amount per unit is calculated:

- using the actual costs for the good or service recorded in the beneficiary's accounts, attributed either by direct measurement or on the basis of cost drivers, and excluding any cost which are ineligible or already included in other budget categories; the actual costs may be adjusted on the basis of budgeted or estimated elements, if they are relevant for calculating the costs, reasonable and correspond to objective and verifiable information

and

- according to usual cost accounting practices which are applied in a consistent manner, based on objective criteria, regardless of the source of funding.

'Internally invoiced goods and services' means goods or services which are provided within the beneficiary's organisation directly for the action and which the beneficiary values on the basis of its usual cost accounting practices.

This cost will not be taken into account for the indirect cost flat-rate.

D.3 Transnational access to research infrastructure unit costs

Unit costs for providing transnational access to research infrastructure are eligible, if and as declared eligible in the call conditions, if they fulfil the general eligibility conditions, are calculated in accordance with the method set out in Annex 2a and exclude any cost which are ineligible or already included in other budget categories.

Beneficiaries that declare costs under this cost category cannot use other cost categories such as internally invoiced goods and services or equipment costs (for charging the capital costs of the infrastructure), unless explicitly allowed in the call conditions.

This cost will not be taken into account for the indirect cost flat-rate.

D.4 Virtual access to research infrastructure unit costs

Unit costs for providing virtual access to research infrastructure are eligible, if and as declared eligible in the call conditions, if they fulfil the general eligibility conditions, are calculated in accordance with the method set out in Annex 2a and exclude any cost which are ineligible or already included in other budget categories.

Beneficiaries that declare costs under this cost category cannot use other cost categories such as internally invoiced goods and services or equipment costs (for charging the capital costs of the infrastructure), unless explicitly allowed by the call conditions.

This cost will not be taken into account for the indirect cost flat-rate.

Indirect costs

E. Indirect costs

Indirect costs will be reimbursed at the flat-rate of 25% of the eligible direct costs (categories A-D, except volunteers costs, subcontracting costs, financial support to third parties and exempted specific cost categories, if any).

Contributions

Not applicable

6.3 Ineligible costs and contributions

The following costs or contributions are **ineligible**:

(a) costs or contributions that do not comply with the conditions set out above (Article 6.1 and 6.2), in particular:

(i) costs related to return on capital and dividends paid by a beneficiary

(ii) debt and debt service charges

(iii) provisions for future losses or debts

(iv) interest owed

(v) currency exchange losses

(vi) bank costs charged by the beneficiary's bank for transfers from the granting authority

(vii) excessive or reckless expenditure

(viii) deductible or refundable VAT (including VAT paid by public bodies acting as public authority)

(ix) costs incurred or contributions for activities implemented during grant agreement suspension (see Article 31)

(x) in-kind contributions by third parties: not applicable

(b) costs or contributions declared under other EU grants (or grants awarded by an EU Member State, non-EU country or other body implementing the EU budget), except for the following cases:

(i) Synergy actions: not applicable

(ii) if the action grant is combined with an operating grant[11] running during the same period and the beneficiary can demonstrate that the operating grant does not cover any (direct or indirect) costs of the action grant

(c) costs or contributions for staff of a national (or regional/local) administration, for activities that are part of the administration's normal activities (i.e. not undertaken only because of the grant)

(d) costs or contributions (especially travel and subsistence) for staff or representatives of EU institutions, bodies or agencies

(e) other :

(i) country restrictions for eligible costs: not applicable

(ii) costs or contributions declared specifically ineligible in the call conditions.

6.4 Consequences of non-compliance

If a beneficiary declares costs or contributions that are ineligible, they will be rejected (see Article 27).

This may also lead to other measures described in Chapter 5.

CHAPTER 4 GRANT IMPLEMENTATION

SECTION 1 CONSORTIUM: BENEFICIARIES, AFFILIATED ENTITIES AND OTHER PARTICIPANTS

ARTICLE 7 — BENEFICIARIES

The beneficiaries, as signatories of the Agreement, are fully responsible towards the granting authority for implementing it and for complying with all its obligations.

They must implement the Agreement to their best abilities, in good faith and in accordance with all the obligations and terms and conditions it sets out.

They must have the appropriate resources to implement the action and implement the action under their own responsibility and in accordance with Article 11. If they rely on affiliated entities or other participants (see Articles 8 and 9), they retain sole responsibility towards the granting authority and the other beneficiaries.

They are jointly responsible for the *technical* implementation of the action. If one of the beneficiaries fails to implement their part of the action, the other beneficiaries must ensure that this part is implemented by someone else (without being entitled to an increase of the maximum grant amount and subject to an amendment; see Article 39). The *financial* responsibility of each beneficiary in case of recoveries is governed by Article 22.

[11] For the definition, see Article 180(2)(b) of EU Financial Regulation 2018/1046: '**operating grant**' means an EU grant to finance "the functioning of a body which has an objective forming part of and supporting an EU policy".

The beneficiaries (and their action) must remain eligible under the EU programme funding the grant for the entire duration of the action. Costs and contributions will be eligible only as long as the beneficiary and the action are eligible.

The **internal roles and responsibilities** of the beneficiaries are divided as follows:

(a) Each beneficiary must:

(i) keep information stored in the Portal Participant Register up to date (see Article 19)

(ii) inform the granting authority (and the other beneficiaries) immediately of any events or circumstances likely to affect significantly or delay the implementation of the action (see Article 19)

(iii) submit to the coordinator in good time:

- the prefinancing guarantees (if required; see Article 23)
- the financial statements and certificates on the financial statements (CFS) (if required; see Articles 21 and 24.2 and Data Sheet, Point 4.3)
- the contribution to the deliverables and technical reports (see Article 21)
- any other documents or information required by the granting authority under the Agreement

(iv) submit via the Portal data and information related to the participation of their affiliated entities.

(b) The coordinator must:

(i) monitor that the action is implemented properly (see Article 11)

(ii) act as the intermediary for all communications between the consortium and the granting authority, unless the Agreement or granting authority specifies otherwise, and in particular:

- submit the prefinancing guarantees to the granting authority (if any)
- request and review any documents or information required and verify their quality and completeness before passing them on to the granting authority
- submit the deliverables and reports to the granting authority
- inform the granting authority about the payments made to the other beneficiaries (report on the distribution of payments; if required, see Articles 22 and 32)

(iii) distribute the payments received from the granting authority to the other beneficiaries without unjustified delay (see Article 22).

The coordinator may not delegate or subcontract the above-mentioned tasks to any other beneficiary or third party (including affiliated entities).

However, coordinators which are public bodies may delegate the tasks set out in Point (b)(ii) last indent and (iii) above to entities with 'authorisation to administer' which they have created or which are controlled by or affiliated to them. In this case, the coordinator retains sole responsibility for the payments and for compliance with the obligations under the Agreement.

Moreover, coordinators which are 'sole beneficiaries'[12] (or similar, such as European research infrastructure consortia (ERICs)) may delegate the tasks set out in Point (b)(i) to (iii) above to one of their members. The coordinator retains sole responsibility for compliance with the obligations under the Agreement.

The beneficiaries must have **internal arrangements** regarding their operation and co-ordination, to ensure that the action is implemented properly.

If required by the granting authority (see Data Sheet, Point 1), these arrangements must be set out in a written **consortium agreement** between the beneficiaries, covering for instance:

- the internal organisation of the consortium
- the management of access to the Portal
- different distribution keys for the payments and financial responsibilities in case of recoveries (if any)
- additional rules on rights and obligations related to background and results (see Article 16)
- settlement of internal disputes
- liability, indemnification and confidentiality arrangements between the beneficiaries.

The internal arrangements must not contain any provision contrary to this Agreement.

ARTICLE 8 — AFFILIATED ENTITIES

Not applicable

ARTICLE 9 — OTHER PARTICIPANTS INVOLVED IN THE ACTION

9.1 Associated partners

The following entities which cooperate with a beneficiary will participate in the action as 'associated partners':

- **BRIDGES TO DEVELOPMENT (Bridges)**, PIC 896766941

Associated partners must implement the action tasks attributed to them in Annex 1 in accordance with Article 11. They may not charge costs or contributions to the action and the costs for their tasks are not eligible.

[12] For the definition, see Article 187(2) EU Financial Regulation 2018/1046: "Where several entities satisfy the criteria for being awarded a grant and together form one entity, that entity may be treated as the **sole beneficiary**, including where it is specifically established for the purpose of implementing the action financed by the grant."

The tasks must be set out in Annex 1.

The beneficiaries must ensure that their contractual obligations under Articles 11 (proper implementation), 12 (conflict of interests), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping) also apply to the associated partners.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the associated partners.

9.2 Third parties giving in-kind contributions to the action

Other third parties may give in-kind contributions to the action (i.e. personnel, equipment, other goods, works and services, etc. which are free-of-charge) if necessary for the implementation.

Third parties giving in-kind contributions do not implement any action tasks. They may not charge costs or contributions to the action, but the costs for the in-kind contributions are eligible and may be charged by the beneficiaries which use them, under the conditions set out in Article 6. The costs will be included in Annex 2 as part of the beneficiaries' costs.

The third parties and their in-kind contributions should be set out in Annex 1.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the third parties giving in-kind contributions.

9.3 Subcontractors

Subcontractors may participate in the action, if necessary for the implementation.

Subcontractors must implement their action tasks in accordance with Article 11. The costs for the subcontracted tasks (invoiced price from the subcontractor) are eligible and may be charged by the beneficiaries, under the conditions set out in Article 6. The costs will be included in Annex 2 as part of the beneficiaries' costs.

The beneficiaries must ensure that their contractual obligations under Articles 11 (proper implementation), 12 (conflict of interest), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping) also apply to the subcontractors.

The beneficiaries must ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the subcontractors.

9.4 Recipients of financial support to third parties

If the action includes providing financial support to third parties (e.g. grants, prizes or similar forms of support), the beneficiaries must ensure that their contractual obligations under Articles 12 (conflict of interest), 13 (confidentiality and security), 14 (ethics), 17.2 (visibility), 18 (specific rules for carrying out action), 19 (information) and 20 (record-keeping)also apply to the third parties receiving the support (recipients).

The beneficiaries must also ensure that the bodies mentioned in Article 25 (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.) can exercise their rights also towards the recipients.

ARTICLE 10 — PARTICIPANTS WITH SPECIAL STATUS

10.1 Non-EU participants

Participants which are established in a non-EU country (if any) undertake to comply with their obligations under the Agreement and:

- to respect general principles (including fundamental rights, values and ethical principles, environmental and labour standards, rules on classified information, intellectual property rights, visibility of funding and protection of personal data)
- for the submission of certificates under Article 24: to use qualified external auditors which are independent and comply with comparable standards as those set out in EU Directive 2006/43/EC[13]
- for the controls under Article 25: to allow for checks, reviews, audits and investigations (including on-the-spot checks, visits and inspections) by the bodies mentioned in that Article (e.g. granting authority, OLAF, Court of Auditors (ECA), etc.).

Special rules on dispute settlement apply (see Data Sheet, Point 5).

10.2 Participants which are international organisations

Participants which are international organisations (IOs; if any) undertake to comply with their obligations under the Agreement and:

- to respect general principles (including fundamental rights, values and ethical principles, environmental and labour standards, rules on classified information, intellectual property rights, visibility of funding and protection of personal data)
- for the submission of certificates under Article 24: to use either independent public officers or external auditors which comply with comparable standards as those set out in EU Directive 2006/43/EC
- for the controls under Article 25: to allow for the checks, reviews, audits and investigations by the bodies mentioned in that Article, taking into account the specific agreements concluded by them and the EU (if any).

For such participants, nothing in the Agreement will be interpreted as a waiver of their privileges or immunities, as accorded by their constituent documents or international law.

Special rules on applicable law and dispute settlement apply (see Article 43 and Data Sheet, Point 5).

10.3 Pillar-assessed participants

[13] Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts or similar national regulations (OJ L 157, 9.6.2006, p. 87).

Pillar-assessed participants (if any) may rely on their own systems, rules and procedures, in so far as they have been positively assessed and do not call into question the decision awarding the grant or breach the principle of equal treatment of applicants or beneficiaries.

'Pillar-assessment' means a review by the European Commission on the systems, rules and procedures which participants use for managing EU grants (in particular internal control system, accounting system, external audits, financing of third parties, rules on recovery and exclusion, information on recipients and protection of personal data; see Article 154 EU Financial Regulation 2018/1046).

Participants with a positive pillar assessment may rely on their own systems, rules and procedures, in particular for:

- record-keeping (Article 20): may be done in accordance with internal standards, rules and procedures
- currency conversion for financial statements (Article 21): may be done in accordance with usual accounting practices
- guarantees (Article 23): for public law bodies, prefinancing guarantees are not needed
- certificates (Article 24):
    - certificates on the financial statements (CFS): may be provided by their regular internal or external auditors and in accordance with their internal financial regulations and procedures
    - certificates on usual accounting practices (CoMUC): are not needed if those practices are covered by an ex-ante assessment

and use the following specific rules, for:

- recoveries (Article 22): in case of financial support to third parties, there will be no recovery if the participant has done everything possible to retrieve the undue amounts from the third party receiving the support (including legal proceedings) and non-recovery is not due to an error or negligence on its part
- checks, reviews, audits and investigations by the EU (Article 25): will be conducted taking into account the rules and procedures specifically agreed between them and the framework agreement (if any)
- impact evaluation (Article 26): will be conducted in accordance with the participant's internal rules and procedures and the framework agreement (if any)
- grant agreement suspension (Article 31): certain costs incurred during grant suspension are eligible (notably, minimum costs necessary for a possible resumption of the action and costs relating to contracts which were entered into before the pre-information letter was received and which could not reasonably be suspended, reallocated or terminated on legal grounds)
- grant agreement termination (Article 32): the final grant amount and final payment will be calculated taking into account also costs relating to contracts due for execution only after termination takes effect, if the contract was entered into before the pre-information letter was received and could not reasonably be terminated on legal grounds

- liability for damages (Article 33.2): the granting authority must be compensated for damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement only if the damage is due to an infringement of the participant's internal rules and procedures or due to a violation of third parties' rights by the participant or one of its employees or individual for whom the employees are responsible.

Participants whose pillar assessment covers procurement and granting procedures may also do purchases, subcontracting and financial support to third parties (Article 6.2) in accordance with their internal rules and procedures for purchases, subcontracting and financial support.

Participants whose pillar assessment covers data protection rules may rely on their internal standards, rules and procedures for data protection (Article 15).

The participants may however not rely on provisions which would breach the principle of equal treatment of applicants or beneficiaries or call into question the decision awarding the grant, such as in particular:

- eligibility (Article 6)
- consortium roles and set-up (Articles 7-9)
- security and ethics (Articles 13, 14)
- IPR (including background and results, access rights and rights of use), communication, dissemination and visibility (Articles 16 and 17)
- information obligation (Article 19)
- payment, reporting and amendments (Articles 21, 22 and 39)
- rejections, reductions, suspensions and terminations (Articles 27, 28, 29-32)

If the pillar assessment was subject to remedial measures, reliance on the internal systems, rules and procedures is subject to compliance with those remedial measures.

Participants whose assessment has not yet been updated to cover (the new rules on) data protection may rely on their internal systems, rules and procedures, provided that they ensure that personal data is:

- processed lawfully, fairly and in a transparent manner in relation to the data subject
- collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes
- adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed
- accurate and, where necessary, kept up to date
- kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the data is processed and
- processed in a manner that ensures appropriate security of the personal data.

Participants must inform the coordinator without delay of any changes to the systems, rules and procedures that were part of the pillar assessment. The coordinator must immediately inform the granting authority.

Pillar-assessed participants that have also concluded a framework agreement with the EU, may moreover — under the same conditions as those above (i.e. not call into question the decision awarding the grant or breach the principle of equal treatment of applicants or beneficiaries) — rely on the provisions set out in that framework agreement.

SECTION 2 RULES FOR CARRYING OUT THE ACTION

ARTICLE 11 — PROPER IMPLEMENTATION OF THE ACTION

11.1 Obligation to properly implement the action

The beneficiaries must implement the action as described in Annex 1 and in compliance with the provisions of the Agreement, the call conditions and all legal obligations under applicable EU, international and national law.

11.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 12 — CONFLICT OF INTERESTS

12.1 Conflict of interests

The beneficiaries must take all measures to prevent any situation where the impartial and objective implementation of the Agreement could be compromised for reasons involving family, emotional life, political or national affinity, economic interest or any other direct or indirect interest (‘conflict of interests’).

They must formally notify the granting authority without delay of any situation constituting or likely to lead to a conflict of interests and immediately take all the necessary steps to rectify this situation.

The granting authority may verify that the measures taken are appropriate and may require additional measures to be taken by a specified deadline.

12.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28) and the grant or the beneficiary may be terminated (see Article 32).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 13 — CONFIDENTIALITY AND SECURITY

13.1 Sensitive information

The parties must keep confidential any data, documents or other material (in any form) that is identified as sensitive in writing ('sensitive information') — during the implementation of the action and for at least until the time-limit set out in the Data Sheet (see Point 6).

If a beneficiary requests, the granting authority may agree to keep such information confidential for a longer period.

Unless otherwise agreed between the parties, they may use sensitive information only to implement the Agreement.

The beneficiaries may disclose sensitive information to their personnel or other participants involved in the action only if they:

(a) need to know it in order to implement the Agreement and

(b) are bound by an obligation of confidentiality.

The granting authority may disclose sensitive information to its staff and to other EU institutions and bodies.

It may moreover disclose sensitive information to third parties, if:

(a) this is necessary to implement the Agreement or safeguard the EU financial interests and

(b) the recipients of the information are bound by an obligation of confidentiality.

The confidentiality obligations no longer apply if:

(a) the disclosing party agrees to release the other party

(b) the information becomes publicly available, without breaching any confidentiality obligation

(c) the disclosure of the sensitive information is required by EU, international or national law.

Specific confidentiality rules (if any) are set out in Annex 5.

13.2 Classified information

The parties must handle classified information in accordance with the applicable EU, international or national law on classified information (in particular, Decision 2015/444[14] and its implementing rules).

Deliverables which contain classified information must be submitted according to special procedures agreed with the granting authority.

Action tasks involving classified information may be subcontracted only after explicit approval (in writing) from the granting authority.

[14] Commission Decision 2015/444/EC, Euratom of 13 March 2015 on the security rules for protecting EU classified information (OJ L 72, 17.3.2015, p. 53).

Classified information may not be disclosed to any third party (including participants involved in the action implementation) without prior explicit written approval from the granting authority.

Specific security rules (if any) are set out in Annex 5.

13.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 14 — ETHICS AND VALUES

14.1 Ethics

The action must be carried out in line with the highest ethical standards and the applicable EU, international and national law on ethical principles.

Specific ethics rules (if any) are set out in Annex 5.

14.2 Values

The beneficiaries must commit to and ensure the respect of basic EU values (such as respect for human dignity, freedom, democracy, equality, the rule of law and human rights, including the rights of minorities).

Specific rules on values (if any) are set out in Annex 5.

14.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 15 — DATA PROTECTION

15.1 Data processing by the granting authority

Any personal data under the Agreement will be processed under the responsibility of the data controller of the granting authority in accordance with and for the purposes set out in the Portal Privacy Statement.

For grants where the granting authority is the European Commission, an EU regulatory or executive agency, joint undertaking or other EU body, the processing will be subject to Regulation 2018/1725[15].

[15] Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC (OJ L 295, 21.11.2018, p. 39).

15.2 Data processing by the beneficiaries

The beneficiaries must process personal data under the Agreement in compliance with the applicable EU, international and national law on data protection (in particular, Regulation 2016/679[16]).

They must ensure that personal data is:

- processed lawfully, fairly and in a transparent manner in relation to the data subjects
- collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes
- adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed
- accurate and, where necessary, kept up to date
- kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the data is processed and
- processed in a manner that ensures appropriate security of the data.

The beneficiaries may grant their personnel access to personal data only if it is strictly necessary for implementing, managing and monitoring the Agreement. The beneficiaries must ensure that the personnel is under a confidentiality obligation.

The beneficiaries must inform the persons whose data are transferred to the granting authority and provide them with the Portal Privacy Statement.

15.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 16 — INTELLECTUAL PROPERTY RIGHTS (IPR) — BACKGROUND AND RESULTS —ACCESS RIGHTS AND RIGHTS OF USE

16.1 Background and access rights to background

The beneficiaries must give each other and the other participants access to the background identified as needed for implementing the action, subject to any specific rules in Annex 5.

'Background' means any data, know-how or information — whatever its form or nature (tangible or intangible), including any rights such as intellectual property rights — that is:

(a) held by the beneficiaries before they acceded to the Agreement and

[16] Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC ('GDPR') (OJ L 119, 4.5.2016, p. 1).

(b) needed to implement the action or exploit the results.

If background is subject to rights of a third party, the beneficiary concerned must ensure that it is able to comply with its obligations under the Agreement.

16.2 Ownership of results

The granting authority does not obtain ownership of the results produced under the action.

'Results' means any tangible or intangible effect of the action, such as data, know-how or information, whatever its form or nature, whether or not it can be protected, as well as any rights attached to it, including intellectual property rights.

16.3 Rights of use of the granting authority on materials, documents and information received for policy, information, communication, dissemination and publicity purposes

The granting authority has the right to use non-sensitive information relating to the action and materials and documents received from the beneficiaries (notably summaries for publication, deliverables, as well as any other material, such as pictures or audio-visual material, in paper or electronic form) for policy, information, communication, dissemination and publicity purposes — during the action or afterwards.

The right to use the beneficiaries' materials, documents and information is granted in the form of a royalty-free, non-exclusive and irrevocable licence, which includes the following rights:

(a) **use for its own purposes** (in particular, making them available to persons working for the granting authority or any other EU service (including institutions, bodies, offices, agencies, etc.) or EU Member State institution or body; copying or reproducing them in whole or in part, in unlimited numbers; and communication through press information services)

(b) **distribution to the public** (in particular, publication as hard copies and in electronic or digital format, publication on the internet, as a downloadable or non-downloadable file, broadcasting by any channel, public display or presentation, communicating through press information services, or inclusion in widely accessible databases or indexes)

(c) **editing or redrafting** (including shortening, summarising, inserting other elements (e.g. meta-data, legends, other graphic, visual, audio or text elements), extracting parts (e.g. audio or video files), dividing into parts, use in a compilation)

(d) **translation**

(e) **storage** in paper, electronic or other form

(f) **archiving**, in line with applicable document-management rules

(g) the right to authorise **third parties** to act on its behalf or sub-license to third parties the modes of use set out in Points (b), (c), (d) and (f), if needed for the information, communication and publicity activity of the granting authority

(h) **processing**, analysing, aggregating the materials, documents and information received and **producing derivative works**.

The rights of use are granted for the whole duration of the industrial or intellectual property rights concerned.

If materials or documents are subject to moral rights or third party rights (including intellectual property rights or rights of natural persons on their image and voice), the beneficiaries must ensure that they comply with their obligations under this Agreement (in particular, by obtaining the necessary licences and authorisations from the rights holders concerned).

Where applicable, the granting authority will insert the following information:

> "© – [year] – [name of the copyright owner]. All rights reserved. Licensed to the [name of granting authority] under conditions."

16.4 Specific rules on IPR, results and background

Specific rules regarding intellectual property rights, results and background (if any) are set out in Annex 5.

16.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such a breach may also lead to other measures described in Chapter 5.

ARTICLE 17 — COMMUNICATION, DISSEMINATION AND VISIBILITY

17.1 Communication — Dissemination — Promoting the action

Unless otherwise agreed with the granting authority, the beneficiaries must promote the action and its results by providing targeted information to multiple audiences (including the media and the public), in accordance with Annex 1 and in a strategic, coherent and effective manner.

Before engaging in a communication or dissemination activity expected to have a major media impact, the beneficiaries must inform the granting authority.

17.2 Visibility — European flag and funding statement

Unless otherwise agreed with the granting authority, communication activities of the beneficiaries related to the action (including media relations, conferences, seminars, information material, such as brochures, leaflets, posters, presentations, etc., in electronic form, via traditional or social media, etc.), dissemination activities and any infrastructure, equipment, vehicles, supplies or major result funded by the grant must acknowledge EU support and display the European flag (emblem) and funding statement (translated into local languages, where appropriate):

The emblem must remain distinct and separate and cannot be modified by adding other visual marks, brands or text.

Apart from the emblem, no other visual identity or logo may be used to highlight the EU support.

When displayed in association with other logos (e.g. of beneficiaries or sponsors), the emblem must be displayed at least as prominently and visibly as the other logos.

For the purposes of their obligations under this Article, the beneficiaries may use the emblem without first obtaining approval from the granting authority. This does not, however, give them the right to exclusive use. Moreover, they may not appropriate the emblem or any similar trademark or logo, either by registration or by any other means.

17.3 Quality of information — Disclaimer

Any communication or dissemination activity related to the action must use factually accurate information.

Moreover, it must indicate the following disclaimer (translated into local languages where appropriate):

> "Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or [name of the granting authority]. Neither the European Union nor the granting authority can be held responsible for them."

17.4 Specific communication, dissemination and visibility rules

Specific communication, dissemination and visibility rules (if any) are set out in Annex 5.

17.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 18 — SPECIFIC RULES FOR CARRYING OUT THE ACTION

18.1 Specific rules for carrying out the action

Specific rules for implementing the action (if any) are set out in Annex 5.

18.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such a breach may also lead to other measures described in Chapter 5.

SECTION 3 GRANT ADMINISTRATION

ARTICLE 19 — GENERAL INFORMATION OBLIGATIONS

19.1 Information requests

The beneficiaries must provide — during the action or afterwards and in accordance with Article 7 — any information requested in order to verify eligibility of the costs or contributions declared, proper implementation of the action and compliance with the other obligations under the Agreement.

The information provided must be accurate, precise and complete and in the format requested, including electronic format.

19.2 Participant Register data updates

The beneficiaries must keep — at all times, during the action or afterwards — their information stored in the Portal Participant Register up to date, in particular, their name, address, legal representatives, legal form and organisation type.

19.3 Information about events and circumstances which impact the action

The beneficiaries must immediately inform the granting authority (and the other beneficiaries) of any of the following:

(a) **events** which are likely to affect or delay the implementation of the action or affect the EU's financial interests, in particular:

(i) changes in their legal, financial, technical, organisational or ownership situation (including changes linked to one of the exclusion grounds listed in the declaration of honour signed before grant signature)

(ii) linked action information: not applicable

(b) **circumstances** affecting:

(i) the decision to award the grant or

(ii) compliance with requirements under the Agreement.

19.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 20 — RECORD-KEEPING

20.1 Keeping records and supporting documents

The beneficiaries must — at least until the time-limit set out in the Data Sheet (see Point 6) — keep records and other supporting documents to prove the proper implementation of the action in line with the accepted standards in the respective field (if any).

In addition, the beneficiaries must — for the same period — keep the following to justify the amounts declared:

(a) for actual costs: adequate records and supporting documents to prove the costs declared (such as contracts, subcontracts, invoices and accounting records); in addition, the beneficiaries' usual accounting and internal control procedures must enable direct reconciliation between the amounts declared, the amounts recorded in their accounts and the amounts stated in the supporting documents

(b) for flat-rate costs and contributions (if any): adequate records and supporting documents to prove the eligibility of the costs or contributions to which the flat-rate is applied

(c) for the following simplified costs and contributions: the beneficiaries do not need to keep specific records on the actual costs incurred, but must keep:

  (i) for unit costs and contributions (if any): adequate records and supporting documents to prove the number of units declared

  (ii) for lump sum costs and contributions (if any): adequate records and supporting documents to prove proper implementation of the work as described in Annex 1

  (iii) for financing not linked to costs (if any): adequate records and supporting documents to prove the achievement of the results or the fulfilment of the conditions as described in Annex 1

(d) for unit, flat-rate and lump sum costs and contributions according to usual cost accounting practices (if any): the beneficiaries must keep any adequate records and supporting documents to prove that their cost accounting practices have been applied in a consistent manner, based on objective criteria, regardless of the source of funding, and that they comply with the eligibility conditions set out in Articles 6.1 and 6.2.

Moreover, the following is needed for specific budget categories:

(e) for personnel costs: time worked for the beneficiary under the action must be supported by declarations signed monthly by the person and their supervisor, unless another reliable time-record system is in place; the granting authority may accept alternative evidence supporting the time worked for the action declared, if it considers that it offers an adequate level of assurance

(f) additional record-keeping rules: not applicable

The records and supporting documents must be made available upon request (see Article 19) or in the context of checks, reviews, audits or investigations (see Article 25).

If there are on-going checks, reviews, audits, investigations, litigation or other pursuits of claims under the Agreement (including the extension of findings; see Article 25), the beneficiaries must keep these records and other supporting documentation until the end of these procedures.

The beneficiaries must keep the original documents. Digital and digitalised documents are considered originals if they are authorised by the applicable national law. The granting authority may accept non-original documents if they offer a comparable level of assurance.

20.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs or contributions insufficiently substantiated will be ineligible (see Article 6) and will be rejected (see Article 27), and the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 21 — REPORTING

21.1 Continuous reporting

The beneficiaries must continuously report on the progress of the action (e.g. **deliverables, milestones, outputs/outcomes, critical risks, indicators,** etc; if any), in the Portal Continuous Reporting tool and in accordance with the timing and conditions it sets out (as agreed with the granting authority).

Standardised deliverables (e.g. progress reports not linked to payments, reports on cumulative expenditure, special reports, etc; if any) must be submitted using the templates published on the Portal.

21.2 Periodic reporting: Technical reports and financial statements

In addition, the beneficiaries must provide reports to request payments, in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2):

- for additional prefinancings (if any): an **additional prefinancing report**
- for interim payments (if any) and the final payment: a **periodic report**.

The prefinancing and periodic reports include a technical and financial part.

The technical part includes an overview of the action implementation. It must be prepared using the template available in the Portal Periodic Reporting tool.

The financial part of the additional prefinancing report includes a statement on the use of the previous prefinancing payment.

The financial part of the periodic report includes:

- the financial statements (individual and consolidated; for all beneficiaries/affiliated entities)
- the explanation on the use of resources (or detailed cost reporting table, if required)
- the certificates on the financial statements (CFS) (if required; see Article 24.2 and Data Sheet, Point 4.3).

The **financial statements** must detail the eligible costs and contributions for each budget category and, for the final payment, also the revenues for the action (see Articles 6 and 22).

All eligible costs and contributions incurred should be declared, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Amounts that are not declared in the individual financial statements will not be taken into account by the granting authority.

By signing the financial statements (directly in the Portal Periodic Reporting tool), the beneficiaries confirm that:

- the information provided is complete, reliable and true
- the costs and contributions declared are eligible (see Article 6)
- the costs and contributions can be substantiated by adequate records and supporting documents (see Article 20) that will be produced upon request (see Article 19) or in the context of checks, reviews, audits and investigations (see Article 25)
- for the final periodic report: all the revenues have been declared (if required; see Article 22).

Beneficiaries will have to submit also the financial statements of their affiliated entities (if any). In case of recoveries (see Article 22), beneficiaries will be held responsible also for the financial statements of their affiliated entities.

21.3 Currency for financial statements and conversion into euros

The financial statements must be drafted in euro.

Beneficiaries with general accounts established in a currency other than the euro must convert the costs recorded in their accounts into euro, at the average of the daily exchange rates published in the C series of the *Official Journal of the European Union* (ECB website), calculated over the corresponding reporting period.

If no daily euro exchange rate is published in the *Official Journal* for the currency in question, they must be converted at the average of the monthly accounting exchange rates published on the European Commission website (InforEuro), calculated over the corresponding reporting period.

Beneficiaries with general accounts in euro must convert costs incurred in another currency into euro according to their usual accounting practices.

21.4 Reporting language

The reporting must be in the language of the Agreement, unless otherwise agreed with the granting authority (see Data Sheet, Point 4.2).

21.5 Consequences of non-compliance

If a report submitted does not comply with this Article, the granting authority may suspend the payment deadline (see Article 29) and apply other measures described in Chapter 5.

If the coordinator breaches its reporting obligations, the granting authority may terminate the grant or the coordinator's participation (see Article 32) or apply other measures described in Chapter 5.

ARTICLE 22 — PAYMENTS AND RECOVERIES — CALCULATION OF AMOUNTS DUE

22.1 Payments and payment arrangements

Payments will be made in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2).

They will be made in euro to the bank account indicated by the coordinator (see Data Sheet, Point 4.2) and must be distributed without unjustified delay (restrictions may apply to distribution of the initial prefinancing payment; see Data Sheet, Point 4.2).

Payments to this bank account will discharge the granting authority from its payment obligation.

The cost of payment transfers will be borne as follows:

- the granting authority bears the cost of transfers charged by its bank
- the beneficiary bears the cost of transfers charged by its bank
- the party causing a repetition of a transfer bears all costs of the repeated transfer.

Payments by the granting authority will be considered to have been carried out on the date when they are debited to its account.

22.2 Recoveries

Recoveries will be made, if — at beneficiary termination, final payment or afterwards — it turns out that the granting authority has paid too much and needs to recover the amounts undue.

Each beneficiary's financial responsibility in case of recovery is in principle limited to their own debt and undue amounts of their affiliated entities.

In case of enforced recoveries (see Article 22.4), affiliated entities will be held liable for repaying debts of their beneficiaries, if required by the granting authority (see Data Sheet, Point 4.4).

22.3 Amounts due

22.3.1 Prefinancing payments

The aim of the prefinancing is to provide the beneficiaries with a float.

It remains the property of the EU until the final payment.

For **initial prefinancings** (if any), the amount due, schedule and modalities are set out in the Data Sheet (see Point 4.2).

For **additional prefinancings** (if any), the amount due, schedule and modalities are also set out in the Data Sheet (see Point 4.2). However, if the statement on the use of the previous prefinancing payment shows that less than 70% was used, the amount set out in the Data Sheet will be reduced by the difference between the 70% threshold and the amount used.

The contribution to the Mutual Insurance Mechanism will be retained from the prefinancing payments (at the rate and in accordance with the modalities set out in the Data Sheet, see Point 4.2) and transferred to the Mechanism.

Prefinancing payments (or parts of them) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

22.3.2 Amount due at beneficiary termination — Recovery

In case of beneficiary termination, the granting authority will determine the provisional amount due for the beneficiary concerned. Payments (if any) will be made with the next interim or final payment.

The **amount due** will be calculated in the following step:

Step 1 — Calculation of the total accepted EU contribution

Step 1 — Calculation of the total accepted EU contribution

The granting authority will first calculate the 'accepted EU contribution' for the beneficiary for all reporting periods, by calculating the 'maximum EU contribution to costs' (applying the funding rate to the accepted costs of the beneficiary), taking into account requests for a lower contribution to costs and CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions (if any). The resulting amount is the 'total accepted EU contribution' for the beneficiary.

The **balance** is then calculated by deducting the payments received (if any; see report on the distribution of payments in Article 32), from the total accepted EU contribution:

{total accepted EU contribution for the beneficiary

minus

{prefinancing and interim payments received (if any)}}.

If the balance is **positive**, the amount will be included in the next interim or final payment to the consortium.

If the balance is **negative**, it will be **recovered** in accordance with the following procedure:

The granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to recover, the amount due, the amount to be recovered and the reasons why and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received), it will confirm the amount to be recovered and ask this amount to be paid to the coordinator (**confirmation letter**).

If payment is not made to the coordinator by the date specified in the confirmation letter, the granting authority may call on the Mutual Insurance Mechanism to intervene, if continuation of the action is guaranteed and the conditions set out in the rules governing the Mechanism are met.

In this case, it will send a **beneficiary recovery letter**, together with a **debit note** with the terms and date for payment.

The debit note for the beneficiary will include the amount calculated for the affiliated entities which also had to end their participation (if any).

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

The amounts will later on also be taken into account for the next interim or final payment.

22.3.3 Interim payments

Interim payments reimburse the eligible costs and contributions claimed for the implementation of the action during the reporting periods (if any).

Interim payments (if any) will be made in accordance with the schedule and modalities set out the Data Sheet (see Point 4.2).

Payment is subject to the approval of the periodic report. Its approval does not imply recognition of compliance, authenticity, completeness or correctness of its content.

The **interim payment** will be calculated by the granting authority in the following steps:

Step 1 — Calculation of the total accepted EU contribution

Step 2 — Limit to the interim payment ceiling

Step 1 — Calculation of the total accepted EU contribution

The granting authority will calculate the ‘accepted EU contribution’ for the action for the reporting period, by first calculating the ‘maximum EU contribution to costs’ (applying the funding rate to the accepted costs of each beneficiary), taking into account requests for a lower contribution to costs, and CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions from beneficiary termination (if any). The resulting amount is the 'total accepted EU contribution'.

Step 2 — Limit to the interim payment ceiling

The resulting amount is then capped to ensure that the total amount of prefinancing and interim payments (if any) does not exceed the interim payment ceiling set out in the Data Sheet (see Point 4.2).

Interim payments (or parts of them) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

22.3.4 Final payment — Final grant amount — Revenues and Profit — Recovery

The final payment (payment of the balance) reimburses the remaining part of the eligible costs and contributions claimed for the implementation of the action (if any).

The final payment will be made in accordance with the schedule and modalities set out in the Data Sheet (see Point 4.2).

Payment is subject to the approval of the final periodic report. Its approval does not imply recognition of compliance, authenticity, completeness or correctness of its content.

The **final grant amount for the action** will be calculated in the following steps:

Step 1 — Calculation of the total accepted EU contribution

Step 2 — Limit to the maximum grant amount

Step 3 — Reduction due to the no-profit rule

Step 1 — Calculation of the total accepted EU contribution

The granting authority will first calculate the 'accepted EU contribution' for the action for all reporting periods, by calculating the 'maximum EU contribution to costs' (applying the funding rate to the total accepted costs of each beneficiary), taking into account requests for a lower contribution to costs, CFS threshold cappings (if any; see Article 24.5) and adding the contributions (accepted unit, flat-rate or lump sum contributions and financing not linked to costs, if any).

After that, the granting authority will take into account grant reductions (if any). The resulting amount is the 'total accepted EU contribution'.

Step 2 — Limit to the maximum grant amount

If the resulting amount is higher than the maximum grant amount set out in Article 5.2, it will be limited to the latter.

Step 3 — Reduction due to the no-profit rule

If the no-profit rule is provided for in the Data Sheet (see Point 4.2), the grant must not produce a profit (i.e. surplus of the amount obtained following Step 2 plus the action's revenues, over the eligible costs and contributions approved by the granting authority).

'Revenue' is all income generated by the action, during its duration (see Article 4), for beneficiaries that are profit legal entities (— with the exception of income generated by the exploitation of results, which are not considered as revenues).

If there is a profit, it will be deducted in proportion to the final rate of reimbursement of the eligible costs approved by the granting authority (as compared to the amount calculated following Steps 1 and 2 minus the contributions).

The **balance** (final payment) is then calculated by deducting the total amount of prefinancing and interim payments already made (if any), from the final grant amount:

{final grant amount

minus

{prefinancing and interim payments made (if any)}}.

If the balance is **positive**, it will be **paid** to the coordinator.

The amount retained for the Mutual Insurance Mechanism (see above) will be released and **paid** to the coordinator (in accordance with the rules governing the Mechanism).

The final payment (or part of it) may be offset (without the beneficiaries' consent) against amounts owed by a beneficiary to the granting authority — up to the amount due to that beneficiary.

For grants where the granting authority is the European Commission or an EU executive agency, offsetting may also be done against amounts owed to other Commission services or executive agencies.

Payments will not be made if the payment deadline or payments are suspended (see Articles 29 and 30).

If — despite the release of the Mutual Insurance Mechanism contribution — the balance is **negative**, it will be **recovered** in accordance with the following procedure:

The granting authority will send a **pre-information letter** to the coordinator:

- formally notifying the intention to recover, the final grant amount, the amount to be recovered and the reasons why
- requesting a report on the distribution of payments to the beneficiaries within 30 days of receiving notification and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received) and the coordinator has submitted the report on the distribution of payments, it will calculate the **share of the debt per beneficiary**, by:

(a) identifying the beneficiaries for which the amount calculated as follows is negative:

{{{total accepted EU contribution for the beneficiary

divided by

total accepted EU contribution for the action}

multiplied by

final grant amount for the action}},

minus

{prefinancing and interim payments received by the beneficiary (if any)}}

and

(b) dividing the debt:

{{amount calculated according to point (a) for the beneficiary concerned

divided by

the sum of the amounts calculated according to point (a) for all the beneficiaries identified according to point (a)}

multiplied by

the amount to be recovered}.

and confirm the amount to be recovered from each beneficiary concerned (**confirmation letter**), together with **debit notes** with the terms and date for payment.

The debit notes for beneficiaries will include the amounts calculated for their affiliated entities (if any).

If the coordinator has not submitted the report on the distribution of payments, the granting authority will **recover** the full amount from the coordinator (**confirmation letter** and **debit note** with the terms and date for payment).

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

22.3.5 Audit implementation after final payment — Revised final grant amount — Recovery

If — after the final payment (in particular, after checks, reviews, audits or investigations; see Article 25) — the granting authority rejects costs or contributions (see Article 27) or reduces the grant (see Article 28), it will calculate the **revised final grant amount** for the beneficiary concerned.

The **beneficiary revised final grant amount** will be calculated in the following step:

Step 1 — Calculation of the revised total accepted EU contribution

Step 1 — Calculation of the revised total accepted EU contribution

The granting authority will first calculate the ‘revised accepted EU contribution’ for the beneficiary, by calculating the ‘revised accepted costs’ and ‘revised accepted contributions’.

After that, it will take into account grant reductions (if any). The resulting 'revised total accepted EU contribution' is the beneficiary revised final grant amount.

If the revised final grant amount is lower than the beneficiary's final grant amount (i.e. its share in the final grant amount for the action), it will be **recovered** in accordance with the following procedure:

The **beneficiary final grant amount** (i.e. share in the final grant amount for the action) is calculated as follows:

{{total accepted EU contribution for the beneficiary

divided by

total accepted EU contribution for the action}

multiplied by

final grant amount for the action}.

The granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to recover, the amount to be recovered and the reasons why and
- requesting observations within 30 days of receiving notification.

If no observations are submitted (or the granting authority decides to pursue recovery despite the observations it has received), it will confirm the amount to be recovered (**confirmation letter**), together with a **debit note** with the terms and the date for payment.

Recoveries against affiliated entities (if any) will be handled through their beneficiaries.

If payment is not made by the date specified in the debit note, the granting authority will **enforce recovery** in accordance with Article 22.4.

22.4 Enforced recovery

If payment is not made by the date specified in the debit note, the amount due will be recovered:

(a) by offsetting the amount — without the coordinator or beneficiary's consent — against any amounts owed to the coordinator or beneficiary by the granting authority.

In exceptional circumstances, to safeguard the EU financial interests, the amount may be offset before the payment date specified in the debit note.

For grants where the granting authority is the European Commission or an EU executive agency, debts may also be offset against amounts owed by other Commission services or executive agencies.

(b) financial guarantee(s): not applicable

(c) joint and several liability of beneficiaries: not applicable

(d) by holding affiliated entities jointly and severally liable (if any, see Data Sheet, Point 4.4)

(e) by taking legal action (see Article 43) or, provided that the granting authority is the European

Commission or an EU executive agency, by adopting an enforceable decision under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 100(2) of EU Financial Regulation 2018/1046.

If the Mutual Insurance Mechanism was called on by the granting authority to intervene, recovery will be continued in the name of the Mutual Insurance Mechanism. If two debit notes were sent, the second one (in the name of the Mutual Insurance Mechanism) will be considered to replace the first one (in the name of the granting authority). Where the MIM intervened, offsetting, enforceable decisions or any other of the above-mentioned forms of enforced recovery may be used mutatis mutandis.

The amount to be recovered will be increased by **late-payment interest** at the rate set out in Article 22.5, from the day following the payment date in the debit note, up to and including the date the full payment is received.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2015/2366[17] applies.

For grants where the granting authority is an EU executive agency, enforced recovery by offsetting or enforceable decision will be done by the services of the European Commission (see also Article 43).

22.5 Consequences of non-compliance

22.5.1 If the granting authority does not pay within the payment deadlines (see above), the beneficiaries are entitled to **late-payment interest** at the rate applied by the European Central Bank (ECB) for its main refinancing operations in euros ('reference rate'), plus the rate specified in the Data Sheet (Point 4.2). The reference rate is the rate in force on the first day of the month in which the payment deadline expires, as published in the C series of the *Official Journal of the European Union*.

If the late-payment interest is lower than or equal to EUR 200, it will be paid to the coordinator only on request submitted within two months of receiving the late payment.

Late-payment interest is not due if all beneficiaries are EU Member States (including regional and local government authorities or other public bodies acting on behalf of a Member State for the purpose of this Agreement).

If payments or the payment deadline are suspended (see Articles 29 and 30), payment will not be considered as late.

Late-payment interest covers the period running from the day following the due date for payment (see above), up to and including the date of payment.

Late-payment interest is not considered for the purposes of calculating the final grant amount.

22.5.2 If the coordinator breaches any of its obligations under this Article, the grant may be reduced (see Article 28) and the grant or the coordinator may be terminated (see Article 32).

[17] Directive (EU) 2015/2366 of the European Parliament and of the Council of 25 November 2015 on payment services in the internal market, amending Directives 2002/65/EC, 2009/110/EC and 2013/36/EU and Regulation (EU) No 1093/2010, and repealing Directive 2007/64/EC (OJ L 337, 23.12.2015, p. 35).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 23 — GUARANTEES

Not applicable

ARTICLE 24 — CERTIFICATES

24.1 Operational verification report (OVR)

Not applicable

24.2 Certificate on the financial statements (CFS)

If required by the granting authority (see Data Sheet, Point 4.3), the beneficiaries must provide certificates on their financial statements (CFS), in accordance with the schedule, threshold and conditions set out in the Data Sheet.

The coordinator must submit them as part of the periodic report (see Article 21).

The certificates must be drawn up using the template published on the Portal, cover the costs declared on the basis of actual costs and costs according to usual cost accounting practices (if any), and fulfil the following conditions:

(a) be provided by a qualified approved external auditor which is independent and complies with Directive 2006/43/EC[18] (or for public bodies: by a competent independent public officer)

(b) the verification must be carried out according to the highest professional standards to ensure that the financial statements comply with the provisions under the Agreement and that the costs declared are eligible.

The certificates will not affect the granting authority's right to carry out its own checks, reviews or audits, nor preclude the European Court of Auditors (ECA), the European Public Prosecutor's Office (EPPO) or the European Anti-Fraud Office (OLAF) from using their prerogatives for audits and investigations under the Agreement (see Article 25).

If the costs (or a part of them) were already audited by the granting authority, these costs do not need to be covered by the certificate and will not be counted for calculating the threshold (if any).

24.3 Certificate on the compliance of usual cost accounting practices (CoMUC)

Not applicable

24.4 Systems and process audit (SPA)

Beneficiaries which:

[18] Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts or similar national regulations (OJ L 157, 9.6.2006, p. 87).

- use unit, flat rate or lump sum costs or contributions according to documented (i.e. formally approved and in writing) usual costs accounting practices (if any) or

- have formalised documentation on the systems and processes for calculating their costs and contributions (i.e. formally approved and in writing), have participated in at least 150 actions under Horizon 2020 or the Euratom Research and Training Programme (2014-2018 or 2019-2020) and participate in at least 3 ongoing actions under Horizon Europe or the Euratom Research and Training Programme (2021-2025 or 2026-2027)

may apply to the granting authority for a systems and process audit (SPA).

This audit will be carried out as follows:

Step 1 – Application by the beneficiary.

Step 2 – If the application is accepted, the granting authority will carry out the systems and process audit, complemented by an audit of transactions (on a sample of the beneficiary's Horizon Europe or the Euratom Research and Training Programme financial statements).

Step 3 – The audit result will take the form of a risk assessment classification for the beneficiary: low, medium or high.

Low-risk beneficiaries will benefit from less (or less in-depth) ex-post audits (see Article 25) and a higher threshold for submitting certificates on the financial statements (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3).

24.5 Consequences of non-compliance

If a beneficiary does not submit a certificate on the financial statements (CFS) or the certificate is rejected, the accepted EU contribution to costs will be capped to reflect the CFS threshold.

If a beneficiary breaches any of its other obligations under this Article, the granting authority may apply the measures described in Chapter 5.

ARTICLE 25 — CHECKS, REVIEWS, AUDITS AND INVESTIGATIONS — EXTENSION OF FINDINGS

25.1 Granting authority checks, reviews and audits

25.1.1 Internal checks

The granting authority may — during the action or afterwards — check the proper implementation of the action and compliance with the obligations under the Agreement, including assessing costs and contributions, deliverables and reports.

25.1.2 Project reviews

The granting authority may carry out reviews on the proper implementation of the action and compliance with the obligations under the Agreement (general project reviews or specific issues reviews).

Such project reviews may be started during the implementation of the action and until the time-limit

set out in the Data Sheet (see Point 6). They will be formally notified to the coordinator or beneficiary concerned and will be considered to start on the date of the notification.

If needed, the granting authority may be assisted by independent, outside experts. If it uses outside experts, the coordinator or beneficiary concerned will be informed and have the right to object on grounds of commercial confidentiality or conflict of interest.

The coordinator or beneficiary concerned must cooperate diligently and provide — within the deadline requested — any information and data in addition to deliverables and reports already submitted (including information on the use of resources). The granting authority may request beneficiaries to provide such information to it directly. Sensitive information and documents will be treated in accordance with Article 13.

The coordinator or beneficiary concerned may be requested to participate in meetings, including with the outside experts.

For **on-the-spot visits**, the beneficiary concerned must allow access to sites and premises (including to the outside experts) and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the review findings, a **project review report** will be drawn up.

The granting authority will formally notify the project review report to the coordinator or beneficiary concerned, which has 30 days from receiving notification to make observations.

Project reviews (including project review reports) will be in the language of the Agreement.

25.1.3 Audits

The granting authority may carry out audits on the proper implementation of the action and compliance with the obligations under the Agreement.

Such audits may be started during the implementation of the action and until the time-limit set out in the Data Sheet (see Point 6). They will be formally notified to the beneficiary concerned and will be considered to start on the date of the notification.

The granting authority may use its own audit service, delegate audits to a centralised service or use external audit firms. If it uses an external firm, the beneficiary concerned will be informed and have the right to object on grounds of commercial confidentiality or conflict of interest.

The beneficiary concerned must cooperate diligently and provide — within the deadline requested — any information (including complete accounts, individual salary statements or other personal data) to verify compliance with the Agreement. Sensitive information and documents will be treated in accordance with Article 13.

For **on-the-spot** visits, the beneficiary concerned must allow access to sites and premises (including for the external audit firm) and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the audit findings, a **draft audit report** will be drawn up.

The auditors will formally notify the draft audit report to the beneficiary concerned, which has 30 days from receiving notification to make observations (contradictory audit procedure).

The **final audit report** will take into account observations by the beneficiary concerned and will be formally notified to them.

Audits (including audit reports) will be in the language of the Agreement.

25.2 European Commission checks, reviews and audits in grants of other granting authorities

Where the granting authority is not the European Commission, the latter has the same rights of checks, reviews and audits as the granting authority.

25.3 Access to records for assessing simplified forms of funding

The beneficiaries must give the European Commission access to their statutory records for the periodic assessment of simplified forms of funding which are used in EU programmes.

25.4 OLAF, EPPO and ECA audits and investigations

The following bodies may also carry out checks, reviews, audits and investigations — during the action or afterwards:

- the European Anti-Fraud Office (OLAF) under Regulations No 883/2013[19] and No 2185/96[20]
- the European Public Prosecutor's Office (EPPO) under Regulation 2017/1939
- the European Court of Auditors (ECA) under Article 287 of the Treaty on the Functioning of the EU (TFEU) and Article 257 of EU Financial Regulation 2018/1046.

If requested by these bodies, the beneficiary concerned must provide full, accurate and complete information in the format requested (including complete accounts, individual salary statements or other personal data, including in electronic format) and allow access to sites and premises for on-the-spot visits or inspections — as provided for under these Regulations.

To this end, the beneficiary concerned must keep all relevant information relating to the action, at least until the time-limit set out in the Data Sheet (Point 6) and, in any case, until any ongoing checks, reviews, audits, investigations, litigation or other pursuits of claims have been concluded.

25.5 Consequences of checks, reviews, audits and investigations — Extension of results of reviews, audits or investigations

[19] Regulation (EU, Euratom) No 883/2013 of the European Parliament and of the Council of 11 September 2013 concerning investigations conducted by the European Anti-Fraud Office (OLAF) and repealing Regulation (EC) No 1073/1999 of the European Parliament and of the Council and Council Regulation (Euratom) No 1074/1999 (OJ L 248, 18/09/2013, p. 1).

[20] Council Regulation (Euratom, EC) No 2185/96 of 11 November 1996 concerning on-the-spot checks and inspections carried out by the Commission in order to protect the European Communities' financial interests against fraud and other irregularities (OJ L 292, 15/11/1996, p. 2).

25.5.1 Consequences of checks, reviews, audits and investigations in this grant

Findings in checks, reviews, audits or investigations carried out in the context of this grant may lead to rejections (see Article 27), grant reduction (see Article 28) or other measures described in Chapter 5.

Rejections or grant reductions after the final payment will lead to a revised final grant amount (see Article 22).

Findings in checks, reviews, audits or investigations during the action implementation may lead to a request for amendment (see Article 39), to change the description of the action set out in Annex 1.

Checks, reviews, audits or investigations that find systemic or recurrent errors, irregularities, fraud or breach of obligations in any EU grant may also lead to consequences in other EU grants awarded under similar conditions ('extension to other grants').

Moreover, findings arising from an OLAF or EPPO investigation may lead to criminal prosecution under national law.

25.5.2 Extension from other grants

Results of checks, reviews, audits or investigations in other grants may be extended to this grant, if:

(a) the beneficiary concerned is found, in other EU grants awarded under similar conditions, to have committed systemic or recurrent errors, irregularities, fraud or breach of obligations that have a material impact on this grant and

(b) those findings are formally notified to the beneficiary concerned — together with the list of grants affected by the findings — within the time-limit for audits set out in the Data Sheet (see Point 6).

The granting authority will formally notify the beneficiary concerned of the intention to extend the findings and the list of grants affected.

If the extension concerns **rejections of costs or contributions**: the notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings

(b) the request to submit revised financial statements for all grants affected

(c) the correction rate for extrapolation, established on the basis of the systemic or recurrent errors, to calculate the amounts to be rejected, if the beneficiary concerned:

  (i) considers that the submission of revised financial statements is not possible or practicable or

  (ii) does not submit revised financial statements.

If the extension concerns **grant reductions**: the notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings and

(b) the **correction rate for extrapolation**, established on the basis of the systemic or recurrent errors and the principle of proportionality.

The beneficiary concerned has **60 days** from receiving notification to submit observations, revised financial statements or to propose a duly substantiated **alternative correction method/rate**.

On the basis of this, the granting authority will analyse the impact and decide on the implementation (i.e. start rejection or grant reduction procedures, either on the basis of the revised financial statements or the announced/alternative method/rate or a mix of those; see Articles 27 and 28).

25.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs or contributions insufficiently substantiated will be ineligible (see Article 6) and will be rejected (see Article 27), and the grant may be reduced (see Article 28).

Such breaches may also lead to other measures described in Chapter 5.

ARTICLE 26 — IMPACT EVALUATIONS

26.1 Impact evaluation

The granting authority may carry out impact evaluations of the action, measured against the objectives and indicators of the EU programme funding the grant.

Such evaluations may be started during implementation of the action and until the time-limit set out in the Data Sheet (see Point 6). They will be formally notified to the coordinator or beneficiaries and will be considered to start on the date of the notification.

If needed, the granting authority may be assisted by independent outside experts.

The coordinator or beneficiaries must provide any information relevant to evaluate the impact of the action, including information in electronic format.

26.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the granting authority may apply the measures described in Chapter 5.

CHAPTER 5 CONSEQUENCES OF NON-COMPLIANCE

SECTION 1 REJECTIONS AND GRANT REDUCTION

ARTICLE 27 — REJECTION OF COSTS AND CONTRIBUTIONS

27.1 Conditions

The granting authority will — at beneficiary termination, interim payment, final payment or afterwards — reject any costs or contributions which are ineligible (see Article 6), in particular following checks, reviews, audits or investigations (see Article 25).

The rejection may also be based on the extension of findings from other grants to this grant (see Article 25).

Ineligible costs or contributions will be rejected.

27.2 Procedure

If the rejection does not lead to a recovery, the granting authority will formally notify the coordinator or beneficiary concerned of the rejection, the amounts and the reasons why. The coordinator or beneficiary concerned may — within 30 days of receiving notification — submit observations if it disagrees with the rejection (payment review procedure).

If the rejection leads to a recovery, the granting authority will follow the contradictory procedure with pre-information letter set out in Article 22.

27.3 Effects

If the granting authority rejects costs or contributions, it will deduct them from the costs or contributions declared and then calculate the amount due (and, if needed, make a recovery; see Article 22).

ARTICLE 28 — GRANT REDUCTION

28.1 Conditions

The granting authority may — at beneficiary termination, final payment or afterwards — reduce the grant for a beneficiary, if:

(a) the beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) the beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (see Article 25).

The amount of the reduction will be calculated for each beneficiary concerned and proportionate to the seriousness and the duration of the errors, irregularities or fraud or breach of obligations, by applying an individual reduction rate to their accepted EU contribution.

28.2 Procedure

If the grant reduction does not lead to a recovery, the granting authority will formally notify the coordinator or beneficiary concerned of the reduction, the amount to be reduced and the reasons why.

The coordinator or beneficiary concerned may — within 30 days of receiving notification — submit observations if it disagrees with the reduction (payment review procedure).

If the grant reduction leads to a recovery, the granting authority will follow the contradictory procedure with pre-information letter set out in Article 22.

28.3 Effects

If the granting authority reduces the grant, it will deduct the reduction and then calculate the amount due (and, if needed, make a recovery; see Article 22).

SECTION 2 SUSPENSION AND TERMINATION

ARTICLE 29 — PAYMENT DEADLINE SUSPENSION

29.1 Conditions

The granting authority may — at any moment — suspend the payment deadline if a payment cannot be processed because:

(a) the required report (see Article 21) has not been submitted or is not complete or additional information is needed

(b) there are doubts about the amount to be paid (e.g. ongoing audit extension procedure, queries about eligibility, need for a grant reduction, etc.) and additional checks, reviews, audits or investigations are necessary, or

(c) there are other issues affecting the EU financial interests.

29.2 Procedure

The granting authority will formally notify the coordinator of the suspension and the reasons why.

The suspension will **take effect** the day the notification is sent.

If the conditions for suspending the payment deadline are no longer met, the suspension will be **lifted** — and the remaining time to pay (see Data Sheet, Point 4.2) will resume.

If the suspension exceeds two months, the coordinator may request the granting authority to confirm if the suspension will continue.

If the payment deadline has been suspended due to the non-compliance of the report and the revised report is not submitted (or was submitted but is also rejected), the granting authority may also terminate the grant or the participation of the coordinator (see Article 32).

ARTICLE 30 — PAYMENT SUSPENSION

30.1 Conditions

The granting authority may — at any moment — suspend payments, in whole or in part for one or more beneficiaries, if:

(a) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed or is suspected of having committed:

(i) substantial errors, irregularities or fraud or

(ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant.

If payments are suspended for one or more beneficiaries, the granting authority will make partial payment(s) for the part(s) not suspended. If suspension concerns the final payment, the payment (or recovery) of the remaining amount after suspension is lifted will be considered to be the payment that closes the action.

30.2 Procedure

Before suspending payments, the granting authority will send a **pre-information letter** to the beneficiary concerned:

- formally notifying the intention to suspend payments and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the suspension (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

At the end of the suspension procedure, the granting authority will also inform the coordinator.

The suspension will **take effect** the day after the confirmation notification is sent.

If the conditions for resuming payments are met, the suspension will be **lifted**. The granting authority will formally notify the beneficiary concerned (and the coordinator) and set the suspension end date.

During the suspension, no prefinancing will be paid to the beneficiaries concerned. For interim payments, the periodic reports for all reporting periods except the last one (see Article 21) must not contain any financial statements from the beneficiary concerned (or its affiliated entities). The coordinator must include them in the next periodic report after the suspension is lifted or — if suspension is not lifted before the end of the action — in the last periodic report.

ARTICLE 31 — GRANT AGREEMENT SUSPENSION

31.1 Consortium-requested GA suspension

31.1.1 Conditions and procedure

The beneficiaries may request the suspension of the grant or any part of it, if exceptional circumstances — in particular *force majeure* (see Article 35) — make implementation impossible or excessively difficult.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the date the suspension takes effect; this date may be before the date of the submission of the amendment request and
- the expected date of resumption.

The suspension will **take effect** on the day specified in the amendment.

Once circumstances allow for implementation to resume, the coordinator must immediately request another **amendment** of the Agreement to set the suspension end date, the resumption date (one day after suspension end date), extend the duration and make other changes necessary to adapt the action to the new situation (see Article 39) — unless the grant has been terminated (see Article 32). The suspension will be **lifted** with effect from the suspension end date set out in the amendment. This date may be before the date of the submission of the amendment request.

During the suspension, no prefinancing will be paid. Costs incurred or contributions for activities implemented during grant suspension are not eligible (see Article 6.3).

31.2 EU-initiated GA suspension

31.2.1 Conditions

The granting authority may suspend the grant or any part of it, if:

(a) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed or is suspected of having committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.), or

(b) a beneficiary (or a person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant

(c) other:

  (i) linked action issues: not applicable

  (ii) the action has lost its scientific or technological relevance, for EIC Accelerator actions: the action has lost its economic relevance, for challenge-based EIC Pathfinder actions

and Horizon Europe Missions: the action has lost its relevance as part of the Portfolio for which it has been initially selected

31.2.2 Procedure

Before suspending the grant, the granting authority will send a **pre-information letter** to the coordinator:

- formally notifying the intention to suspend the grant and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the suspension (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

The suspension will **take effect** the day after the confirmation notification is sent (or on a later date specified in the notification).

Once the conditions for resuming implementation of the action are met, the granting authority will formally notify the coordinator a **lifting of suspension letter**, in which it will set the suspension end date and invite the coordinator to request an amendment of the Agreement to set the resumption date (one day after suspension end date), extend the duration and make other changes necessary to adapt the action to the new situation (see Article 39) — unless the grant has been terminated (see Article 32). The suspension will be **lifted** with effect from the suspension end date set out in the lifting of suspension letter. This date may be before the date on which the letter is sent.

During the suspension, no prefinancing will be paid. Costs incurred or contributions for activities implemented during suspension are not eligible (see Article 6.3).

The beneficiaries may not claim damages due to suspension by the granting authority (see Article 33).

Grant suspension does not affect the granting authority's right to terminate the grant or a beneficiary (see Article 32) or reduce the grant (see Article 28).

ARTICLE 32 — GRANT AGREEMENT OR BENEFICIARY TERMINATION

32.1 Consortium-requested GA termination

32.1.1 Conditions and procedure

The beneficiaries may request the termination of the grant.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the date the consortium ends work on the action ('end of work date') and
- the date the termination takes effect ('termination date'); this date must be after the date of the submission of the amendment request.

The termination will **take effect** on the termination date specified in the amendment.

If no reasons are given or if the granting authority considers the reasons do not justify termination, it may consider the grant terminated improperly.

32.1.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit a **periodic report** (for the open reporting period until termination).

The granting authority will calculate the final grant amount and final payment on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before the end of work date (see Article 22). Costs relating to contracts due for execution only after the end of work are not eligible.

If the granting authority does not receive the report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/contributions if no periodic report was ever approved).

Improper termination may lead to a grant reduction (see Article 28).

After termination, the beneficiaries' obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

32.2 Consortium-requested beneficiary termination

32.2.1 Conditions and procedure

The coordinator may request the termination of the participation of one or more beneficiaries, on request of the beneficiary concerned or on behalf of the other beneficiaries.

The coordinator must submit a request for **amendment** (see Article 39), with:

- the reasons why
- the opinion of the beneficiary concerned (or proof that this opinion has been requested in writing)
- the date the beneficiary ends work on the action ('end of work date')
- the date the termination takes effect ('termination date'); this date must be after the date of the submission of the amendment request.

If the termination concerns the coordinator and is done without its agreement, the amendment request must be submitted by another beneficiary (acting on behalf of the consortium).

The termination will **take effect** on the termination date specified in the amendment.

If no information is given or if the granting authority considers that the reasons do not justify termination, it may consider the beneficiary to have been terminated improperly.

32.2.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a **report on the distribution of payments** to the beneficiary concerned

(ii) a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, the financial statement, the explanation on the use of resources, and, if applicable, the certificate on the financial statement (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3)

(iii) a second **request for amendment** (see Article 39) with other amendments needed (e.g. reallocation of the tasks and the estimated budget of the terminated beneficiary; addition of a new beneficiary to replace the terminated beneficiary; change of coordinator, etc.).

The granting authority will calculate the amount due to the beneficiary on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before the end of work date (see Article 22). Costs relating to contracts due for execution only after the end of work are not eligible.

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 21).

If the granting authority does not receive the termination report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/ contributions if no periodic report was ever approved).

If the granting authority does not receive the report on the distribution of payments within the deadline, it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that
- the beneficiary concerned must not repay any amount to the coordinator.

If the second request for amendment is accepted by the granting authority, the Agreement is **amended** to introduce the necessary changes (see Article 39).

If the second request for amendment is rejected by the granting authority (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the grant may be terminated (see Article 32).

Improper termination may lead to a reduction of the grant (see Article 31) or grant termination (see Article 32).

After termination, the concerned beneficiary's obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

32.3 EU-initiated GA or beneficiary termination

32.3.1 Conditions

The granting authority may terminate the grant or the participation of one or more beneficiaries, if:

(a) one or more beneficiaries do not accede to the Agreement (see Article 40)

(b) a change to the action or the legal, financial, technical, organisational or ownership situation of a beneficiary is likely to substantially affect the implementation of the action or calls into question the decision to award the grant (including changes linked to one of the exclusion grounds listed in the declaration of honour)

(c) following termination of one or more beneficiaries, the necessary changes to the Agreement (and their impact on the action) would call into question the decision awarding the grant or breach the principle of equal treatment of applicants

(d) implementation of the action has become impossible or the changes necessary for its continuation would call into question the decision awarding the grant or breach the principle of equal treatment of applicants

(e) a beneficiary (or person with unlimited liability for its debts) is subject to bankruptcy proceedings or similar (including insolvency, winding-up, administration by a liquidator or court, arrangement with creditors, suspension of business activities, etc.)

(f) a beneficiary (or person with unlimited liability for its debts) is in breach of social security or tax obligations

(g) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has been found guilty of grave professional misconduct

(h) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed fraud, corruption, or is involved in a criminal organisation, money laundering, terrorism-related crimes (including terrorism financing), child labour or human trafficking

(i) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) was created under a different jurisdiction with the intent to circumvent fiscal, social or other legal obligations in the country of origin (or created another entity with this purpose)

(j) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed:

  (i) substantial errors, irregularities or fraud or

  (ii) serious breach of obligations under this Agreement or during its award (including improper implementation of the action, non-compliance with the call conditions, submission of false information, failure to provide required information, breach of ethics or security rules (if applicable), etc.)

(k) a beneficiary (or person having powers of representation, decision-making or control, or person essential for the award/implementation of the grant) has committed — in other EU grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (extension of findings from other grants to this grant; see Article 25)

(l) despite a specific request by the granting authority, a beneficiary does not request — through the coordinator — an amendment to the Agreement to end the participation of one of its affiliated entities or associated partners that is in one of the situations under points (d), (f), (e), (g), (h), (i) or (j) and to reallocate its tasks, or

(m) other:

(i) linked action issues: not applicable

(ii) the action has lost its scientific or technological relevance, for EIC Accelerator actions: the action has lost its economic relevance, for challenge-based EIC Pathfinder actions and Horizon Europe Missions: the action has lost its relevance as part of the Portfolio for which it has been initially selected

32.3.2 Procedure

Before terminating the grant or participation of one or more beneficiaries, the granting authority will send **a pre-information letter** to the coordinator or beneficiary concerned:

- formally notifying the intention to terminate and the reasons why and
- requesting observations within 30 days of receiving notification.

If the granting authority does not receive observations or decides to pursue the procedure despite the observations it has received, it will confirm the termination and the date it will take effect (**confirmation letter**). Otherwise, it will formally notify that the procedure is discontinued.

For beneficiary terminations, the granting authority will — at the end of the procedure — also inform the coordinator.

The termination will **take effect** the day after the confirmation notification is sent (or on a later date specified in the notification; 'termination date').

32.3.3 Effects

(a) for **GA termination**:

The coordinator must — within 60 days from when termination takes effect — submit a **periodic report** (for the last open reporting period until termination).

The granting authority will calculate the final grant amount and final payment on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before termination takes effect (see Article 22). Costs relating to contracts due for execution only after termination are not eligible.

If the grant is terminated for breach of the obligation to submit reports, the coordinator may not submit any report after termination.

If the granting authority does not receive the report within the deadline, only costs and contributions which are included in an approved periodic report will be taken into account (no costs/contributions if no periodic report was ever approved).

Termination does not affect the granting authority's right to reduce the grant (see Article 28) or to impose administrative sanctions (see Article 34).

The beneficiaries may not claim damages due to termination by the granting authority (see Article 33).

After termination, the beneficiaries' obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

(b) for **beneficiary termination**:

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a **report on the distribution of payments** to the beneficiary concerned

(ii) a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, the financial statement, the explanation on the use of resources, and, if applicable, the certificate on the financial statement (CFS; see Articles 21 and 24.2 and Data Sheet, Point 4.3)

(iii) a **request for amendment** (see Article 39) with any amendments needed (e.g. reallocation of the tasks and the estimated budget of the terminated beneficiary; addition of a new beneficiary to replace the terminated beneficiary; change of coordinator, etc.).

The granting authority will calculate the amount due to the beneficiary on the basis of the report submitted and taking into account the costs incurred and contributions for activities implemented before termination takes effect (see Article 22). Costs relating to contracts due for execution only after termination are not eligible.

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 21).

If the granting authority does not receive the termination report within the deadline, only costs and contributions included in an approved periodic report will be taken into account (no costs/ contributions if no periodic report was ever approved).

If the granting authority does not receive the report on the distribution of payments within the deadline, it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that
- the beneficiary concerned must not repay any amount to the coordinator.

If the request for amendment is accepted by the granting authority, the Agreement is **amended** to introduce the necessary changes (see Article 39).

If the request for amendment is rejected by the granting authority (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the grant may be terminated (see Article 32).

After termination, the concerned beneficiary's obligations (in particular Articles 13 (confidentiality and security), 16 (IPR), 17 (communication, dissemination and visibility), 21 (reporting), 25 (checks, reviews, audits and investigations), 26 (impact evaluation), 27 (rejections), 28 (grant reduction) and 42 (assignment of claims)) continue to apply.

SECTION 3 OTHER CONSEQUENCES: DAMAGES AND ADMINISTRATIVE SANCTIONS

ARTICLE 33 — DAMAGES

33.1 Liability of the granting authority

The granting authority cannot be held liable for any damage caused to the beneficiaries or to third parties as a consequence of the implementation of the Agreement, including for gross negligence.

The granting authority cannot be held liable for any damage caused by any of the beneficiaries or other participants involved in the action, as a consequence of the implementation of the Agreement.

33.2 Liability of the beneficiaries

The beneficiaries must compensate the granting authority for any damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement, provided that it was caused by gross negligence or wilful act.

The liability does not extend to indirect or consequential losses or similar damage (such as loss of profit, loss of revenue or loss of contracts), provided such damage was not caused by wilful act or by a breach of confidentiality.

ARTICLE 34 — ADMINISTRATIVE SANCTIONS AND OTHER MEASURES

Nothing in this Agreement may be construed as preventing the adoption of administrative sanctions (i.e. exclusion from EU award procedures and/or financial penalties) or other public law measures, in addition or as an alternative to the contractual measures provided under this Agreement (see, for instance, Articles 135 to 145 EU Financial Regulation 2018/1046 and Articles 4 and 7 of Regulation 2988/95[21]).

SECTION 4 FORCE MAJEURE

ARTICLE 35 — FORCE MAJEURE

A party prevented by force majeure from fulfilling its obligations under the Agreement cannot be considered in breach of them.

'Force majeure' means any situation or event that:

- prevents either party from fulfilling their obligations under the Agreement,

[21] Council Regulation (EC, Euratom) No 2988/95 of 18 December 1995 on the protection of the European Communities financial interests (OJ L 312, 23.12.1995, p. 1).

- was unforeseeable, exceptional situation and beyond the parties' control,
- was not due to error or negligence on their part (or on the part of other participants involved in the action), and
- proves to be inevitable in spite of exercising all due diligence.

Any situation constituting force majeure must be formally notified to the other party without delay, stating the nature, likely duration and foreseeable effects.

The parties must immediately take all the necessary steps to limit any damage due to force majeure and do their best to resume implementation of the action as soon as possible.

CHAPTER 6 FINAL PROVISIONS

ARTICLE 36 — COMMUNICATION BETWEEN THE PARTIES

36.1 Forms and means of communication — Electronic management

EU grants are managed fully electronically through the EU Funding & Tenders Portal ('Portal').

All communications must be made electronically through the Portal, in accordance with the Portal Terms and Conditions and using the forms and templates provided there (except if explicitly instructed otherwise by the granting authority).

Communications must be made in writing and clearly identify the grant agreement (project number and acronym).

Communications must be made by persons authorised according to the Portal Terms and Conditions. For naming the authorised persons, each beneficiary must have designated — before the signature of this Agreement — a 'legal entity appointed representative (LEAR)'. The role and tasks of the LEAR are stipulated in their appointment letter (see Portal Terms and Conditions).

If the electronic exchange system is temporarily unavailable, instructions will be given on the Portal.

36.2 Date of communication

The sending date for communications made through the Portal will be the date and time of sending, as indicated by the time logs.

The receiving date for communications made through the Portal will be the date and time the communication is accessed, as indicated by the time logs. Formal notifications that have not been accessed within 10 days after sending, will be considered to have been accessed (see Portal Terms and Conditions).

If a communication is exceptionally made on paper (by e-mail or postal service), general principles apply (i.e. date of sending/receipt). Formal notifications by registered post with proof of delivery will be considered to have been received either on the delivery date registered by the postal service or the deadline for collection at the post office.

If the electronic exchange system is temporarily unavailable, the sending party cannot be considered in breach of its obligation to send a communication within a specified deadline.

36.3 Addresses for communication

The Portal can be accessed via the Europa website.

The address for paper communications to the granting authority (if exceptionally allowed) is the official mailing address indicated on its website.

For beneficiaries, it is the legal address specified in the Portal Participant Register.

ARTICLE 37 — INTERPRETATION OF THE AGREEMENT

The provisions in the Data Sheet take precedence over the rest of the Terms and Conditions of the Agreement.

Annex 5 takes precedence over the Terms and Conditions; the Terms and Conditions take precedence over the Annexes other than Annex 5.

Annex 2 takes precedence over Annex 1.

ARTICLE 38 — CALCULATION OF PERIODS AND DEADLINES

In accordance with Regulation No 1182/71[22], periods expressed in days, months or years are calculated from the moment the triggering event occurs.

The day during which that event occurs is not considered as falling within the period.

'Days' means calendar days, not working days.

ARTICLE 39 — AMENDMENTS

39.1 Conditions

The Agreement may be amended, unless the amendment entails changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

Amendments may be requested by any of the parties.

39.2 Procedure

The party requesting an amendment must submit a request for amendment signed directly in the Portal Amendment tool.

The coordinator submits and receives requests for amendment on behalf of the beneficiaries (see Annex 3). If a change of coordinator is requested without its agreement, the submission must be done by another beneficiary (acting on behalf of the other beneficiaries).

[22] Regulation (EEC, Euratom) No 1182/71 of the Council of 3 June 1971 determining the rules applicable to periods, dates and time-limits (OJ L 124, 8/6/1971, p. 1).

The request for amendment must include:

- the reasons why
- the appropriate supporting documents and
- for a change of coordinator without its agreement: the opinion of the coordinator (or proof that this opinion has been requested in writing).

The granting authority may request additional information.

If the party receiving the request agrees, it must sign the amendment in the tool within 45 days of receiving notification (or any additional information the granting authority has requested). If it does not agree, it must formally notify its disagreement within the same deadline. The deadline may be extended, if necessary for the assessment of the request. If no notification is received within the deadline, the request is considered to have been rejected.

An amendment **enters into force** on the day of the signature of the receiving party.

An amendment **takes effect** on the date of entry into force or other date specified in the amendment.

ARTICLE 40 — ACCESSION AND ADDITION OF NEW BENEFICIARIES

40.1 Accession of the beneficiaries mentioned in the Preamble

The beneficiaries which are not coordinator must accede to the grant by signing the accession form (see Annex 3) directly in the Portal Grant Preparation tool, within 30 days after the entry into force of the Agreement (see Article 44).

They will assume the rights and obligations under the Agreement with effect from the date of its entry into force (see Article 44).

If a beneficiary does not accede to the grant within the above deadline, the coordinator must — within 30 days — request an amendment (see Article 39) to terminate the beneficiary and make any changes necessary to ensure proper implementation of the action. This does not affect the granting authority's right to terminate the grant (see Article 32).

40.2 Addition of new beneficiaries

In justified cases, the beneficiaries may request the addition of a new beneficiary.

For this purpose, the coordinator must submit a request for amendment in accordance with Article 39. It must include an accession form (see Annex 3) signed by the new beneficiary directly in the Portal Amendment tool.

New beneficiaries will assume the rights and obligations under the Agreement with effect from the date of their accession specified in the accession form (see Annex 3).

Additions are also possible in mono-beneficiary grants.

ARTICLE 41 — TRANSFER OF THE AGREEMENT

In justified cases, the beneficiary of a mono-beneficiary grant may request the transfer of the grant to a new beneficiary, provided that this would not call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiary must submit a request for **amendment** (see Article 39), with

- the reasons why
- the accession form (see Annex 3) signed by the new beneficiary directly in the Portal Amendment tool and
- additional supporting documents (if required by the granting authority).

The new beneficiary will assume the rights and obligations under the Agreement with effect from the date of accession specified in the accession form (see Annex 3).

ARTICLE 42 — ASSIGNMENTS OF CLAIMS FOR PAYMENT AGAINST THE GRANTING AUTHORITY

The beneficiaries may not assign any of their claims for payment against the granting authority to any third party, except if expressly approved in writing by the granting authority on the basis of a reasoned, written request by the coordinator (on behalf of the beneficiary concerned).

If the granting authority has not accepted the assignment or if the terms of it are not observed, the assignment will have no effect on it.

In no circumstances will an assignment release the beneficiaries from their obligations towards the granting authority.

ARTICLE 43 — APPLICABLE LAW AND SETTLEMENT OF DISPUTES

43.1 Applicable law

The Agreement is governed by the applicable EU law, supplemented if necessary by the law of Belgium.

Special rules may apply for beneficiaries which are international organisations (if any; see Data Sheet, Point 5).

43.2 Dispute settlement

If a dispute concerns the interpretation, application or validity of the Agreement, the parties must bring action before the EU General Court — or, on appeal, the EU Court of Justice — under Article 272 of the Treaty on the Functioning of the EU (TFEU).

For non-EU beneficiaries (if any), such disputes must be brought before the courts of Brussels, Belgium — unless an international agreement provides for the enforceability of EU court judgements.

For beneficiaries with arbitration as special dispute settlement forum (if any; see Data Sheet, Point 5), the dispute will — in the absence of an amicable settlement — be settled in accordance with the Rules for Arbitration published on the Portal.

If a dispute concerns administrative sanctions, offsetting or an enforceable decision under Article 299 TFEU (see Articles 22 and 34), the beneficiaries must bring action before the General Court — or, on appeal, the Court of Justice — under Article 263 TFEU.

For grants where the granting authority is an EU executive agency (see Preamble), actions against offsetting and enforceable decisions must be brought against the European Commission (not against the granting authority; see also Article 22).

ARTICLE 44 — ENTRY INTO FORCE

The Agreement will enter into force on the day of signature by the granting authority or the coordinator, depending on which is later.

SIGNATURES

For the coordinator	For the granting authority

ANNEX 1

Horizon Europe (HORIZON)

Description of the action (DoA)

Part A

Part B

DESCRIPTION OF THE ACTION (PART A)

COVER PAGE

Part A of the Description of the Action (DoA) must be completed directly on the Portal Grant Preparation screens.

PROJECT *Grant Preparation (General Information screen) — Enter the info.*	
Project number:	101103089
Project name:	STOP 2030: TOWARDS THE INTERRUPTION OF TRANSMISSION OF SOIL-TRANSMITTED HELMINTHS: PROMOTING IMPLEMENTATION OF RESEARCH RESULTS OF A FIXED-DOSE COMBINATION OF CO-FORMULATED IVERMECTIN AND ALBENDAZOLE
Project acronym:	STOP2030
Call:	HORIZON-JU-GH-EDCTP3-2022-01
Topic:	HORIZON-JU-GH-EDCTP3-2022-CALL1-01-01
Type of action:	HORIZON-JU-RIA
Service:	RTD/D/01
Project starting date:	fixed date: 1 July 2023
Project duration:	36 months

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PROJECT SUMMARY

Project summary

Grant Preparation (General Information screen) — Provide an overall description of your project (including context and overall objectives, planned activities and main achievements, and expected results and impacts (on target groups, change procedures, capacities, innovation etc)). This summary should give readers a clear idea of what your project is about.

Use the project summary from your proposal.

Soil-Transmitted Helminths (STH) remain a significant public health problem with recognized obstacles for control and elimination with the current benzimidazole regimens in Mass Drug Administration (MDA) campaigns. Renewed targets from WHO for 2030 include elimination of STH morbidity in pre-school and school age children (PSAC & SAC), increased country governance and financial support and a strongyloidiasis control program; 2030 has also been targeted by WHO for controlling NTDs to attain the Sustainable Development Goals.

The current proposal aims at accelerating the implementation of an innovative health technology, a fixed-dose combination (FDC) tablet of co-formulated albendazole and ivermectin, with adequate safety and significantly superior efficacy against T. trichiura in a registrational randomized clinical trial. This trial is being conducted in Ethiopia, Kenya and Mozambique with the guidance of EMA and sponsored by EDCTP (STOP projects) with a Phase II trial completed and a Phase III currently recruiting.

This project, STOP2030, seeks to complement the results of the safety and efficacy trial with a field-based safety and effectiveness clinical study, acceptability studies in Ghana and Kenya, modelling and cost-effectiveness exercises. The resulting information will be consolidated to build a multidisciplinary package for policy making and WHO guidance with the support of advocacy and communication activities to reach stakeholders and maximize the exploitation and impact of the FDC for STH control and elimination.

The Consortium assembled to execute the STOP2030 proposal combines expertise in complementary fields from program assessment and implementation through Ministries of Health in sub-Saharan African countries, advocacy, state of the art technology, leadership in clinical research and a pharma that has shown commitment for generating access to drugs against NTDs and has recently obtained WHO prequalification for generic ivermectin.

LIST OF PARTICIPANTS

PARTICIPANTS

Grant Preparation (Beneficiaries screen) — Enter the info.

Number	Role	Short name	Legal name	Country	PIC
1	COO	Liconsa	LABORATORIOS LICONSA SA	ES	990555950
2	BEN	ISGLOBAL	FUNDACION PRIVADA INSTITUTO DE SALUD GLOBAL BARCELONA	ES	951414122
3	BEN	FMS ESPANA	FUNDACION MUNDO SANO ESPANA	ES	885624551
4	BEN	KEMRI	KENYA MEDICAL RESEARCH INSTITUTE	KE	997741225
5	BEN	GHS	GHANA HEALTH SERVICE	GH	894057343
6	BEN	GRL	GENOME RESEARCH LIMITED	UK	999981343
7	AP	Bridges	BRIDGES TO DEVELOPMENT	CH	896766941

LIST OF WORK PACKAGES

Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
WP1	Consortium Coordination and Management	1 - Liconsa	51.00	1	36	D1.1 – Data Transfer Agreement D1.2 – Terms of reference for project committees D1.3 – Risk management record (Y1) D1.4 – Communication Plan D1.5 – Risk Management record (Y2)
WP2	Biomedical Sciences: Safety and Effectiveness studies	2 - ISGLOBAL	201.00	1	36	D2.1 – Registration number of clinical study D2.2 – Study approval package D2.3 – Clinical monitoring plan D2.4 – Clinical data management plan (cDMP) D2.5 – Midterm recruitment report D2.6 – Report on the status of posting results D2.7 – Genomic protocol
WP3	Modelling and database management	4 - KEMRI	28.00	1	36	D3.1 – Data management plan D3.2 – Locked and cleaned database available D3.3 – Updated Data Management Plan
WP4	Acceptability, feasibility, and adherence	5 - GHS	36.00	1	12	D4.1 – Formative study on Acceptability & Feasibility completed D4.2 – Protocol for KAP study on Acceptability & Feasibility protocol & implementation plan completed

Work packages

Grant Preparation (Work Packages screen) — Enter the info.

Work Package No	Work Package name	Lead Beneficiary	Effort (Person-Months)	Start Month	End Month	Deliverables
						D4.3 – Implementation acceptability & Feasibility study in Ghana D4.4 – Implementation Acceptability & Feasibility study in Kenya D4.5 – Data analysis and interpretation D4.6 – Exploitation and dissemination plan
WP5	Policy, access, advocacy, and communications	7 - Bridges	131.00	1	36	D5.1 – WHO Pathway D5.2 – Communications and Advocacy D5.3 – Draft Stewardship plan D5.4 – Final Stewarship plan D5.5 – Launched Project - WEBSITE D5.6 – Global Access Plan

Work package WP1 – Consortium Coordination and Management

Work Package Number	WP1	Lead Beneficiary	1. Liconsa
Work Package Name	Consortium Coordination and Management		
Start Month	1	End Month	36

Objectives

Obj 1.1 To set-up a project management structure that ensures efficient operational management including administrative, financial, and legal issues, and appropriate liaison with EDCTP.
Obj 1.2 To provide the overall direction and to drive the progress of the project, steering efforts of the partners for the achievement of the project's objectives.
Obj 1.3 To ensure a good project integration enabling the appropriate communication and work dynamics to help drive the whole Consortium as a team towards successful completion.
Obj 1.4 To ensure that the work is appropriately managed according to the project roadmap, undertaken to the highest quality levels and within the established timelines and costs.

Description

Led by Dr. Alejandro Krolewiecki, from Laboratorios Liconsa, S.A. the Scientific Coordination and Management teams will (1) guarantee overall and transdisciplinary management of the project's evolution from the ethical, implementation, and cost perspectives (2) deal with strategic direction by gathering and reacting to new ideas (3) optimizing the use of the capacities and resources of the project partners (4) supervising WP leaders as they execute their role and (5) monitor progress and achievement of objectives.

The coordination of the Consortium will combine expertise in project management in all administrative and financial aspects, including interactions with regulatory agencies and drug importation procedures, of the project with the scientific leadership of Dr. Krolewiecki, who is the Chief Investigator of the ALIVE clinical trial of the STOP project and is joining the Liconsa team for this new stage of the project. Dr. Krolewiecki brings his expertise in global health, dedicated to STH as leading author of multiple scientific projects and member of the STH-Advisory Committee at Task Force for Global Health and of the Drug Efficacy sub-group of the STH & Schisto Technical Advisory Group at WHO.

Task 1.1: Daily management and Contract management (months 1-36)
Task Leader: Liconsa
Partners involved: ISGlobal, FMS España, KEMRI, GHS, GRL, Bridges.

WP1 will guarantee the supervision of the project and strategic decision making. It will also help to promptly identify risks and implement appropriate contingency measures. This task will also deal with:
A. Liaison with the EDCTP.
B. All contractual and other legal issues related to the project, which will primarily focus on partnership management (including enabling relationships with third parties, external collaborators and stakeholders)
C. Formalisation of updates of the work plan, roles and resource assignments as needed.
In particular, it will comprise Grant Agreement and Consortium Agreement implementation and amendments, support to partners in legal issues, production of non-disclosure agreements, and Intellectual Property Rights (IPR) management.

Task 1.2: Communication (months 1-36)
Task Leader: Liconsa
Partners involved: ISGlobal, FMS España, KEMRI, GHS, GRL, Bridges.

Especially important for the success of the project will be the establishment and maintenance of an open and proactive interaction among the members of the Consortium, the main ambassadors of the project.
To this end, an effective internal communication system will be established and formalized to ensure the existence of channels that allow fluid and bidirectional communication among Consortium members. The use of electronic devices (internal e-mail, corporate WhatsApp group, collaborative platforms, and video conferences, etc) will be utilized to facilitate communication needs.
Likewise, the appropriate communication messages and tools will be defined within the organization itself, in order to strengthen and align the members´ communication. In addition, ongoing communication with EDCTP and relevant stakeholders will be a priority.

Furthermore, the communication team will also be responsible for scheduling and organizing annual meetings where all Consortium members will self-assess the progress of the project, review next steps and discuss challenges.

Task 1.3.a: Project quality and risk management (months 1-36)
Task Leader: Liconsa
Partners involved: ISGlobal, FMS España, KEMRI, GHS, GRL, Bridges.

This activity is devoted to support the Coordination and overall management structure in:
A. Support in leadership and linkage of project components. Work plan control and updates, implementation of corrective actions.
B. Identifying and recording risks to have them categorized and prioritized accordingly. Risks will be classified by likelihood and impact based on which they will be prioritized and mitigation actions will be identified.
C. Support to Work Package Leaders (WPL) in day-to-day management, decision-making, conflict resolution and consensus building.
D. Promotion of synergies and efficiency throughout the project. Creation of tools for efficient communication and co-operative work among partners. Support to meeting organisation and production of the corresponding minutes. Implementation of derived actions into the work plan, and follow-up.

High-quality standards will be applied to all the work undertaken. Good performance will be a priority of the project, and this will be fostered by openness about achievements, friendly peer-pressure, and constructive criticism. Special relevance will be given to this activity in General Assembly meetings, where members of all Consortium´s partners attend in order to instil the importance of quality procedures in the Consortium.
Finally, quality control and internal peer-review of deliverables and scientific publications will be implemented in order to ensure that any result arising from the project complies with the highest international standards.

Task 1.3.b: Continuous assessment and evaluation (months 1-36)
Task Leader: Liconsa
Partners involved: ISGlobal, FMS España, KEMRI, GHS, GRL, Bridges.

Project leadership will be enabled by a robust management structure. Leadership decisions will also be influenced substantially by the project's General Assembly, and most importantly by the Steering Committee on the daily running of the project. To monitor project progress closely, regular communications will take place (e.g., at least once every 2 months) in the framework of the Steering Committee.
Additionally, annual meetings of the General Assembly will always include specific sessions for each WP to highlight results and provide public accountability of the progress achieved. These communications will reinforce the timely gathering of contributions, the achieving of milestones, the identification of risks, and the delivery of deliverables.

Task 1.3.c: Reporting and Financing (months 1-36)
Task Leader: Liconsa
Partners involved: ISGlobal, FMS España, KEMRI, GHS, GRL, Bridges.

This activity will be devoted to:
A. Financial management: budget management, cost control and justification, EDCTP contribution distribution control (supporting the contractual obligations of the Scientific Coordinator). Budget assignment is expected to be somewhat flexible and help steer efforts in the most productive way; for that, specific, transparent procedures will be included in the Consortium Agreement
B. Periodic Reporting: setting up of reporting mechanisms, providing education and support to partners in appropriate reporting, including facilitation of the task via web-based systems as needed.
Reporting and administration are usually one of the main areas of difficulty for partners. Thus, it is especially important that: a) partners are aware of important determinants of reporting and finances (including the provision of audit certificates, etc.); b) the processes involved are closely monitored; and c) partners get bilateral support to avoid any distortions in the workflow. This will ensure timely delivery of the required reports to the EDCTP.

All these tasks will be reinforced by giving them appropriate visibility in the different Consortium meetings. Special attention will be paid to the correlation between effort reporting and cost justification, and to help partners manage the relationships between financial flows (funding, justification, expenditure, payments) so as to ensure 'distortion-free' scientific progress. This activity will also include coordination of other administrative procedures as needed during the project, especially those particular procedures that stem from the Grant Agreement but also those created to ensure the fulfilment of contractual obligations.

Work package WP2 – Biomedical Sciences: Safety and Effectiveness studies

Work Package Number	WP2	Lead Beneficiary	2. ISGLOBAL
Work Package Name	Biomedical Sciences: Safety and Effectiveness studies		
Start Month	1	End Month	36

Objectives
Obj 2.1 To design and execute a pragmatic trial for the establishment of the safety and effectiveness of a FDC of co-formulated IVM and ALB against STH, as a single dose in school settings of T. trichiura transmission areas Obj 2.2 To design and conduct a nested study to evaluate the impact of the intervention on the seroprevalence of strongyloidiasis. Obj 2.3 To evaluate the effectiveness of deworming programmes using genomic epidemiology data to understand parasite-diversity, transmission, and predict the emergence of anthelmintic resistance.

Description
This work package will be led by the team at ISGlobal, currently in charge of the registrational safety and efficacy ALIVE trial for the STOP and II projects. As a continuation of those activities, ISGlobal will coordinate the biomedical studies to provide further evidence to be integrated with the data generated in WPs 3 & 4 for evaluation by WHO and other relevant stakeholders of the FDC for the treatment, control, and elimination of STH, based on the promising results obtained up to date. The main activity comprises a pragmatic clinical trial to assess the safety and effectiveness of the FDC. This trial will combine the efforts of the field activities of the partners in GHS and KEMRI as well as the team at the WSI contributing with genomic epidemiology tools and Mundo Sano with contributions in medical monitoring through a medical team experienced in monitoring research activities in SSA. The data generated in this WP will serve to feed the modelling activities coordinated by KEMRI for WP3 and the policy, communication and advocacy objectives by Bridges and Mundo Sano in WP5. Task 2.1. Trial design, implementation and coordination (months 1-36) Task Leader: ISGlobal Partners involved: Liconsa, FMS España, KEMRI, GHS, GRL To prepare the submission package with all study documents for Institutional Review Board (IRB) evaluations (including study protocol, statistical analysis plan, informed consent forms and investigational brochure) as well as periodic reports to DSMB and IRBs. It also includes the coordination of drug importation activities to deliver the FDC, ALB and IVM to the field sites for the studies involving drug procurement within this and other WPs. Task 2.1a Selection of study sites (months 1-6) Task Leader: ISGlobal Partners involved: Liconsa, KEMRI, GHS Activities related to the selection of the areas with the adequate epidemiological setting for the conducting the study with adequate support from local services and endorsement by the Ministries of Health, in coordination with the teams at GHS and KEMRI. Task 2.1b Development of a clinical monitoring plan (months 1-15) Task Leader: ISGlobal Partners involved: Liconsa, FMS España. Procedures will be designed and implemented along with the monitoring system in order to ensure that GCP guidelines are followed. Training and guidelines will be developed for the implementation of adequate, thorough and feasible pharmacovigilance activities through collaboration with the pharmacovigilance team from Laboratorios Liconsa in partnership with national pharmacovigilance teams. Task 2.2 Production of study-related databases and materials (months 4-12) Task Leader: ISGlobal Partners involved: Liconsa, KEMRI.

All the materials for the execution of the study including CRFs, randomization lists and pharmacy logs and the databases for the storage and analysis of the data will be developed by the epidemiology and statistics team at ISGlobal in accordance with regulatory rules. These study specific databases will be designed in coordination with WP3 in order to be imported to the databases designed for the study and modelling activities.

Task 2.3 Develop and implement study protocol for sub-studies (months 1–36)
Task Leader: ISGlobal
Partners involved: Liconsa, FMS España, KEMRI, GHS, GRL

Through the platform of the safety & effectiveness study, nested studies will strengthen the project contribution to demonstrate the opportunities created by the FDC through 2 nested studies.

Task 2.3a. Genomic epidemiology sub-study (months 1– 36)
Task Leader: GRL
Partners involved: ISGlobal, KEMRI, GHS

Protocols and IRB related documents will be generated to incorporate the sequencing of a sub-group of stool samples collected for the prevalence studies of the pragmatic trial. The tasks include sample preparation, storage, shipment to WSI, sequencing and data analysis. Included in this sub-study is the arrangement for a trainee from SSA to be trained at the WSI in the UK.

Task 2.3b. Impact of the intervention on Strongyloides stercoralis prevalence (months 1 – 36)
Task Leader: ISGlobal
Partners involved: FMS España, KEMRI, GHS

As a secondary goal of the pragmatic trial, this nested study in a population subgroup will be developed to assess the serologic responses to the NIE assay performed on blood spots in a subgroup of participants. Study protocols, analysis plan and laboratory SOPs will be developed in coordination with the teams of GHS and KEMRI.

Work package WP3 – Modelling and database management

Work Package Number	WP3	**Lead Beneficiary**	4. KEMRI
Work Package Name	Modelling and database management		
Start Month	1	**End Month**	36

Objectives
Obj 3.1: Data analysis and modelling inform evidence-based decision making on FDC in study countries, by WHO, regulators, development partners and Pharma for publication, and presentation Obj 3.2: A database that is cleaned, locked and available for scientifically robust statistical analysis on FDC effectiveness, safety, acceptability, and feasibility is available

Description
Modelling of FDC impact on the prevalence and intensity of infection and costing/cost-effectiveness is required to support introduction planning, policy and national decision making. This work will be led by KEMRI and conducted in partnership with other Consortium members and builds on the outputs from STOP. The STOP2030 modelling will work in the new selected sites in Ghana and Kenya incorporating new data available from safety and effectiveness trials as well as acceptability and feasibility as appropriate. The modelling results will inform decision-making on policies and guidelines, as well as development partners and pharma in preparation for sustainable supply and financing (WP5). In order for these multicentre studies to be successful the Consortium will need scientifically robust, aligned databases, data management, and analysis support for aggregated results to support policy making and decision making. The resulting data systems will ensure a robust database for use in generating the full range of study results including regulatory submissions. Task 3.1a: Model scenario for FDC vs routine treatment with monotherapy in the national programmes in Ghana and Kenya, including impact on prevalence and intensity of infection and costing (Months 1-24).

Task Leader: KEMRI
Partners involved: ISGlobal, GHS, Bridges

KEMRI will first construct the model, running and refining the model based on currently available data from STOP trial which includes safety and efficacy from the clinical trials as well as the incremental cost-effectiveness ratio of FDC compared with ALB per case averted and DALY averted. KEMRI will then use the model to propose the optimal use of FDC in Ghana and Kenya for maximum impact. As the project progresses, KEMRI will refine the modelling of effectiveness and cost-effectiveness based upon the emerging research data (effectiveness, acceptability, feasibility)

Task 3.1b: Model potential global impact based on implementation scenario developed in partnership with Bridges (WP5) (Months 18-36)
Task Leader: KEMRI
Partners involved: FMS España, GHS, Bridges

Building on the work based on Ghana and Kenya, the KEMRI team will work to model the broader impact and cost effectiveness of use of FDC in support of STH control and elimination globally.

Task 3.2a: Data management plan and system developed (Month 6)
Task Leader: KEMRI
Partners involved: Liconsa, ISGlobal, FMS España, GHS

Data management plan and system established in coordination with multicentre study sites and managed to support study data collection and analysis. KEMRI will decide on database structure, management, and software to be used for both the safety and effectiveness trials, as well as the acceptability and feasibility studies. KEMRI will work with ISGlobal on the needs for the safety and effectiveness trials, and Ghana on the acceptability, feasibility and adherence.

Task 3.2b: Data management and cleaning (Month 7-33)
Task Leader: KEMRI
Partners involved: ISGlobal, GHS, GRL

The team will support cleaning of data, reconciling with partners, and locking of the database for analysis in collaboration with Consortium partners. Data set will be completed, locked, and primary analysis conducted by the KEMRI team per the analysis plan, and shared with partners for analysis per WP3, WP4 and WP5.

Work package WP4 – Acceptability, feasibility, and adherence

Work Package Number	WP4	**Lead Beneficiary**	5. GHS
Work Package Name	Acceptability, feasibility, and adherence		
Start Month	1	**End Month**	12

Objectives
Obj 4.1 To conduct a multi-country knowledge, attitudes and practices (KAP) survey to inform the design of the feasibility and acceptability study Obj 4.2 To develop a multi-country acceptability, feasibility and adherence study design aligned to the needs of WHO and MOHs of endemic countries for FDC use within STH programmes Obj 4.3 To conduct a multi country acceptability, feasibility and adherence study and make findings available for use by WHO, national governments and supporting partners.

Description
Completing clinical studies and manufacturing a new medicine alone is not sufficient to ensure it will be used in LMICs. Among the key considerations governments, WHO and development partners will want to understand are the product's acceptability to individuals, parents and communities, the feasibility of implementing it within the health system, and the adherence to dosing schedules being considered. These data contribute to the establishment of guidance from WHO and inform national policies (addressed in WP5).

The Consortium, under Ghana's leadership, will develop a protocol and support the implementation of a multicentre study to address acceptability, feasibility, and adherence. It is anticipated that the study will have three arms:
· Comparator: Tablets of IVM and ALB per WHO dosing guidance
· Oro-dispersible FDC: Single dose (Directly Observed Therapy)
· Oro-dispersible FDC: Single dose for 3 consecutive days (first day Directly Observed Therapy)
The multicentre study will be implemented by study teams in Ghana and Kenya. Ghana, under the leadership of Dr Abraham Oduro (Director, Research and Development Division, Ghana Health Service) and Dr Kofi Asemanyi-Mensah (Programme Manager of Neglected Tropical Diseases), will lead the development of the protocol in consultation with Consortium members. They will also lead the implementation of the protocol in Ghana and support implementation by the study team in Kenya, under the leadership of Charles Mwandawiro and Stella Kepha.
A two-phased study is envisaged. The first phase would be a formative study to explore programme and community factors related to feasibility and acceptability of FDC. The second phase of the study would be a comparative study across the 3 arms above on acceptability and feasibility, in the two countries and a study of adherence to the 3-day regimen.
Task 4.1 (Month 1-4) Design and implement the formative study
Task leader: GHS
Partners involved: FMS España, KEMRI, Bridges

GHS will develop and lead the implementation of a formative study in Ghana and Kenya to inform the acceptability and feasibility of FDC. The formative qualitative study will examine NTDP implementation and identify contextual (programme and community) factors related to MDA that could influence the feasibility and acceptability of an FDC. We will conduct document review of the MDA programmes in Ghana and Kenya, as well as key informant interviews with key stakeholders of NTDP. A protocol for the formative study will be submitted to all relevant IRBs in both countries for review and approval prior to implementation.
Task 4.2a (Month 1-6) Acceptability & Feasibility Protocol & Implementation Plan Completed
Task leader: GHS
Partners involved: FMS España, KEMRI, Bridges

The Ghana team will develop the acceptability and feasibility study protocol with input from Consortium members, particularly KEMRI and Bridges, and in consultation with WHO. The target population for this study will be informed by the endemicity of STH in Kenya and Ghana. Both quantitative and qualitative methods will be used in the study. The quantitative component will be a survey using a structured questionnaire targeting students, teachers, and parents. The qualitative component will include focus group discussions with selected members of the same groups plus IDI with community drug distributors, and program implementers. Assessment of feasibility will involve key informant interviews with NTDP managers at various levels of service delivery, and teachers. Follow up visits to a sample of Arm 3 recipients would be made to assess adherence to the 3-day regimen. The protocol will be submitted to all relevant IRBs in both countries for review and approval prior to implementation.

In addition to providing data to support the value proposition and communications on the FDC, these results will be used to help define and advise on the best integration of FDC into STH programs for maximum impact
Task 4.2b (Months 1-6) Coordination of trial design with data management and analysis plan in WP3
Task leader: GHS
Partners involved: ISGlobal, KEMRI, Bridges

Based on the protocols in 4.1 and 4.2 as well as in consultation with KEMRI (WP3), finalize the data management plan, including collection, storing, cleaning and analysis.
Task 4.3a (after trial design is complete 12 Months) Study Implementation Ghana (GHS)
Task leader: GHS
Partners involved: KEMRI, Bridges

Ethical clearance from the Ghana Health Service Ethics Review Committee will be obtained and study sites for the study identified. The study sites will be selected to represent the major STH endemic areas in Ghana. Qualitative and quantitative data will be collected.
Task 4.3b (after trial design is complete 12 Months) Study Implementation Kenya (KEMRI)
Task leader: KEMRI
Partners involved: GHS, Bridges

Coordinate with KEMRI team to obtain relevant IRB clearance, identify study sites, and conduct study in Kenya. The study sites will be selected to reflect major STH endemic areas in Kenya. Qualitative and quantitative data will be collected.
Task 4.3c (after trial is complete 6 Months) Data analysis and interpretation
Task leader: KEMRI

Partners involved: Liconsa, ISGlobal, FMS España, GHS, Bridges

After data cleaning by KEMRI, Ghana will lead on data analyses and interpretation in collaboration with Consortium members.
Task 4.3d (after analysis is complete 12 Months) Report and dissemination
Task leader: GHS
Partners involved: FMS España, KEMRI, Bridges

Ghana will lead in the development of reports for sharing and presenting the data in consultation with Consortium members including preparation of publication/s on study findings. Dissemination will be coordinated with WP5 for sharing with WHO and the Consortium's communications and advocacy plan.

Work package WP5 – Policy, access, advocacy, and communications

Work Package Number	WP5	**Lead Beneficiary**	7. Bridges
Work Package Name	Policy, access, advocacy, and communications		
Start Month	1	**End Month**	36

Objectives

Obj 5.1 Define a pathway to WHO guidance for use of FDC in STH and other NTD control and elimination efforts (Bridges)
Obj 5.2 Support the development of scenarios for a sustainable supply and financing of FDC (Bridges, Liconsa)
Obj 5.3 Develop and implement a Comprehensive Communication and Promotion Plan that will contribute to the dissemination and application of the Project's results, have an impact on the community, and influence the decision-making of policymakers on the use of the FDC. (Mundo Sano)

Description

Development of a new medicine needs to be complemented by activities that anticipate and address factors that otherwise risk slowing or stopping implementation and therefore impact. Wherever possible such activities should be implemented in parallel in order to compress timelines, accelerate pace to impact, and improve project efficiency.
This WP is led by Alan Brooks, RN PHD and Dr Julie Jacobson of Bridges to Development, who will lead work on objective 5.1. Objective 5.2 will be led by Bridges and Liconsa. Objective 5.3 will be led by Mundo Sano with support of Bridges. Consortium members KEMRI and GHS will have particularly important complementary roles in this work package but their contribution to the work is accounted for in other work packages.

Task 5.1a (Months 1-4) Implementation Scenarios
Task leader: Bridges
Partners involved: Liconsa, ISGlobal, FMS España, KEMRI, GHS, GRL.

Bridges will work with Consortium members, most notably, KEMRI and GHS, to determine the most feasible scenarios for scaling up the use of FDC in MDA. The scenarios will be developed by first considering current MDA approaches in different contexts within each country and the epidemiological settings in the country, followed by how an FDC might optimally be implemented within those contexts to realize public health impact aligned with the 2030 goals. The team will then consult with WHO and key partners to help refine the scenarios for use in additional contexts and settings. The scenarios will inform modelling and WHO guidance tasks for the project. This work will also be communicated back to WP3 to inform modelling efforts.
Task 5.1b (Months 1-30) Engage WHO to define mechanisms for providing guidance on use of a FDC
Task leader: Bridges
Partners involved: Liconsa, FMS España.

LMICs and development partners will look for guidance from WHO on the use and scale up of the FDC in NTD programmes, particularly to treat STH, supporting control and elimination efforts. Bridges will facilitate exploration with WHO of potential mechanisms available to provide FDC product recommendations for NTD programmes, leading to a decision on the most efficient and appropriate pathway for FDC guidance. Pathways to be explored include Essentials Medicine List, Pre-qualification, WHO guidance, WHO guidelines, operationalization manuals, and the new Consolidated Scientific Advice process. WHO's policy information needs will provide guidance on initial field study

designs, such as rationale for study sites including baseline prevalence and intensity of infection data as well as sample size across the multi-centre studies. WHO will be briefed approximately twice yearly on study progression to ensure close adherence to identified guidance processes.
Task 5.2a (Months 12-36) Explore supply models and implications for sustainable access (supply and financing) and recommend access strategy
Task leader: Bridges
Partners involved: Liconsa, FMS España, KEMRI, GHS

The Consortium will work in parallel with the field trials to determine options for ensuring access to FDC in African countries following completion of the project. From the supply perspective, Liconsa anticipates making manufacturing plans at pace with emerging models of and insights into potential demand. The planning will take into account current uses of ALB and IVM, the burden of disease, introduction scenarios, and emerging insights into financing.

Liconsa and Bridges will consider alternative pricing models tailored to the needs of LMICs, for example tiered relative to those of middle-income countries. They, primarily Bridges, will also review and engage with other development partners who are considering alternatives to traditional donation programmes for NTD medicines like paediatric praziquantel and moxidectin. The pricing models and demand will be used to inform financing estimates for development partner and country planning and development of an access strategy.

The data emerging from this task will inform and be informed by WP3 modelling activities including its impact and cost-effectiveness estimates.
Task 5.3a (Months 1-4) Develop a Comprehensive Communication and Promotion Plan
Task leader: FMS España
Partners involved: Liconsa, ISGlobal, KEMRI, GHS, GRL, Bridges

Mundo Sano will develop a plan as a tool at the service of the Consortium's institutional image and management, with internal and external communication goals, strategies and specific actions. It is not a static piece, but characterized by its flexibility and ease of adaptation to the Consortium's priorities and objectives as the project progresses. The Communications Plan will have the following specific goals:
1) To put on the agenda the implementation of FDC in SSA countries.
2) To position the STOP2030 Consortium, increasing the visibility of the brand and its reputation.
3) Contribute to the positioning of the funding entity.
In order to achieve the proposed goals, Mundo Sano, with the support of Bridges, will design communication strategies and actions to be implemented in the short, medium and long term, which includes: activities such as mapping stakeholders, internal and external, developing the Consortium's visual identity, creating and FAQ, and website for the project. The team will also create a crisis communications plan and train Consortium members in media communications skills. The plan will also include identifying opportunities for Consortium members (KEMRI, GHS) to inform other countries about the study results, e.g. through NTD programme manager meetings. Communication and advocacy activities will keep pace with emerging field data and project results.

Task 5.3b (Months 5-36) Engage stakeholders to utilize (exploit) emerging study data to inform decision making
Task leader: FMS España
Partners involved: Liconsa, KEMRI, GHS, Bridges

Mundo Sano, with the support of Bridges, will implement the communication and promotion plan, once the communication strategies and actions have been defined. As an example:
· We will work on installing the use of FDC in specialized media in countries of interest for the project (Africa and other countries where the Consortium partners come from); and in journals and/or newsletters of the Consortium members, strategic allies and NGOs.
· Be content creators of news about the project that will be shared on the Consortium's institutional website.
· Implement training and updating campaigns for health personnel, and communication and prevention campaigns for nearby communities in order to generate a positive impact on them and on health personnel.
· Create digital content to be published periodically on the Consortium's digital channels.
All of this will be supported by quarterly activity reports to evaluate progress and results

STAFF EFFORT

Staff effort per participant

Grant Preparation (Work packages - Effort screen) — Enter the info.

Participant	WP1	WP2	WP3	WP4	WP5	Total Person-Months
1 - Liconsa	36.00	1.00				37.00
2 - ISGLOBAL	6.00	96.00	3.00		1.00	106.00
3 - FMS ESPANA	5.00	11.00			55.00	71.00
4 - KEMRI		21.00	25.00	20.00	20.00	86.00
5 - GHS	3.00	48.00		16.00	2.00	69.00
6 - GRL		24.00				24.00
7 - Bridges	1.00				53.00	54.00
Total Person-Months	51.00	201.00	28.00	36.00	131.00	447.00

LIST OF DELIVERABLES

Deliverables

Grant Preparation (Deliverables screen) — Enter the info.

The labels used mean:

Public — fully open (⚠ automatically posted online)
Sensitive — limited under the conditions of the Grant Agreement
EU classified —RESTREINT-UE/EU-RESTRICTED, CONFIDENTIEL-UE/EU-CONFIDENTIAL, SECRET-UE/EU-SECRET under Decision 2015/444

Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D1.1	Data Transfer Agreement	WP1	1 - Liconsa	R — Document, report	PU - Public	6
D1.2	Terms of reference for project committees	WP1	1 - Liconsa	R — Document, report	PU - Public	6
D1.3	Risk management record (Y1)	WP1	1 - Liconsa	R — Document, report	PU - Public	12
D1.4	Communication Plan	WP1	1 - Liconsa	R — Document, report	PU - Public	6
D1.5	Risk Management record (Y2)	WP1	1 - Liconsa	R — Document, report	PU - Public	24
D2.1	Registration number of clinical study	WP2	2 - ISGLOBAL	R — Document, report	PU - Public	6
D2.2	Study approval package	WP2	2 - ISGLOBAL	R — Document, report	PU - Public	12
D2.3	Clinical monitoring plan	WP2	2 - ISGLOBAL	R — Document, report	PU - Public	12
D2.4	Clinical data management plan (cDMP)	WP2	2 - ISGLOBAL	R — Document, report	PU - Public	12
D2.5	Midterm recruitment report	WP2	2 - ISGLOBAL	R — Document, report	PU - Public	20
D2.6	Report on the status of posting results	WP2	2 - ISGLOBAL	R — Document, report	PU - Public	36
D2.7	Genomic protocol	WP2	6 - GRL	R — Document, report	PU - Public	12
D3.1	Data management plan	WP3	4 - KEMRI	DMP — Data Management Plan	PU - Public	6

Deliverables

Grant Preparation (Deliverables screen) — Enter the info.

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Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D3.2	Locked and cleaned database available	WP3	4 - KEMRI	DATA — data sets, microdata, etc	PU - Public	24
D3.3	Updated Data Management Plan	WP3	4 - KEMRI	DMP — Data Management Plan	PU - Public	18
D4.1	Formative study on Acceptability & Feasibility completed	WP4	5 - GHS	R — Document, report	PU - Public	3
D4.2	Protocol for KAP study on Acceptability & Feasibility protocol & implementation plan completed	WP4	5 - GHS	R — Document, report	PU - Public	3
D4.3	Implementation acceptability & Feasibility study in Ghana	WP4	5 - GHS	R — Document, report	PU - Public	12
D4.4	Implementation Acceptability & Feasibility study in Kenya	WP4	4 - KEMRI	R — Document, report	PU - Public	12
D4.5	Data analysis and interpretation	WP4	5 - GHS	R — Document, report	PU - Public	6
D4.6	Exploitation and dissemination plan	WP4	5 - GHS	R — Document, report	PU - Public	12
D5.1	WHO Pathway	WP5	7 - Bridges	R — Document, report	PU - Public	34
D5.2	Communications and Advocacy	WP5	3 - FMS ESPANA	R — Document, report	PU - Public	36
D5.3	Draft Stewardship plan	WP5	7 - Bridges	R — Document, report	PU - Public	18
D5.4	Final Stewarship plan	WP5	7 - Bridges	R — Document, report	PU - Public	36

Deliverables

Grant Preparation (Deliverables screen) — Enter the info.

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EU classified —RESTREINT-UE/EU-RESTRICTED, CONFIDENTIEL-UE/EU-CONFIDENTIAL, SECRET-UE/EU-SECRET under Decision 2015/444

Deliverable No	Deliverable Name	Work Package No	Lead Beneficiary	Type	Dissemination Level	Due Date (month)
D5.5	Launched Project - WEBSITE	WP5	3 - FMS ESPANA	DEC —Websites, patent filings, videos, etc	PU - Public	3
D5.6	Global Access Plan	WP5	7 - Bridges	R — Document, report	PU - Public	36

Deliverable D1.1 – Data Transfer Agreement

Deliverable Number	D1.1	**Lead Beneficiary**	1. Liconsa
Deliverable Name	Data Transfer Agreement		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	6	**Work Package No**	WP1

Description
Safeguard the data protection as per the applicable laws: define the clauses for the transfer or personnel data

Deliverable D1.2 – Terms of reference for project committees

Deliverable Number	D1.2	**Lead Beneficiary**	1. Liconsa
Deliverable Name	Terms of reference for project committees		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	6	**Work Package No**	WP1

Description
Define the different project Committees, scope, frequency and participant

Deliverable D1.3 – Risk management record (Y1)

Deliverable Number	D1.3	**Lead Beneficiary**	1. Liconsa
Deliverable Name	Risk management record (Y1)		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP1

Description
List of potential risk and mitigation plans to either avoid or minimize

Deliverable D1.4 – Communication Plan

Deliverable Number	D1.4	**Lead Beneficiary**	1. Liconsa
Deliverable Name	Communication Plan		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	6	**Work Package No**	WP1

Description
Internal Communication plan to define the internal communication channels and tools to promote the exchange of ideas and the sharing of information among the Consortium's members.

Deliverable D1.5 – Risk Management record (Y2)

Deliverable Number	D1.5	Lead Beneficiary	1. Liconsa
Deliverable Name	Risk Management record (Y2)		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	24	Work Package No	WP1

Description
List of potential risk and mitigation plans to either avoid or minimize

Deliverable D2.1 – Registration number of clinical study

Deliverable Number	D2.1	Lead Beneficiary	2. ISGLOBAL
Deliverable Name	Registration number of clinical study		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	6	Work Package No	WP2

Description
Trial registration in public access trial repositories

Deliverable D2.2 – Study approval package

Deliverable Number	D2.2	Lead Beneficiary	2. ISGLOBAL
Deliverable Name	Study approval package		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	12	Work Package No	WP2

Description
Final version of study protocol, regulatory and ethics approval

Deliverable D2.3 – Clinical monitoring plan

Deliverable Number	D2.3	Lead Beneficiary	2. ISGLOBAL
Deliverable Name	Clinical monitoring plan		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	12	Work Package No	WP2

Description
Plan establishing the guidelines for conducting monitoring visits and timelines

Deliverable D2.4 – Clinical data management plan (cDMP)

Deliverable Number	D2.4	**Lead Beneficiary**	2. ISGLOBAL
Deliverable Name	Clinical data management plan (cDMP)		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP2

Description
Description of the data management life cycle for the data to be collected, processed and/or generated by STOP2030 project

Deliverable D2.5 – Midterm recruitment report

Deliverable Number	D2.5	**Lead Beneficiary**	2. ISGLOBAL
Deliverable Name	Midterm recruitment report		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	20	**Work Package No**	WP2

Description
Detail on patient recruitment numbers for the time point when 50% of the study population were expected to be recruited and future patient recruitment numbers

Deliverable D2.6 – Report on the status of posting results

Deliverable Number	D2.6	**Lead Beneficiary**	2. ISGLOBAL
Deliverable Name	Report on the status of posting results		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP2

Description
Overview of the status of posting results in the study

Deliverable D2.7 – Genomic protocol

Deliverable Number	D2.7	**Lead Beneficiary**	6. GRL
Deliverable Name	Genomic protocol		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP2

Description
Protocol for reporting on genomic data generation and submission to open access repositories, standardisation of code description and availability

Deliverable D3.1 – Data management plan

Deliverable Number	D3.1	Lead Beneficiary	4. KEMRI
Deliverable Name	Data management plan		
Type	DMP — Data Management Plan	Dissemination Level	PU - Public
Due Date (month)	6	Work Package No	WP3

Description
Includes Safety/Effectiveness and Acceptability/Feasibility studies

Deliverable D3.2 – Locked and cleaned database available

Deliverable Number	D3.2	Lead Beneficiary	4. KEMRI
Deliverable Name	Locked and cleaned database available		
Type	DATA — data sets, microdata, etc	Dissemination Level	PU - Public
Due Date (month)	24	Work Package No	WP3

Description
Database for safety and effectiveness and acceptability, feasibility, and adherence cleaned and locked ready for analysis

Deliverable D3.3 – Updated Data Management Plan

Deliverable Number	D3.3	Lead Beneficiary	4. KEMRI
Deliverable Name	Updated Data Management Plan		
Type	DMP — Data Management Plan	Dissemination Level	PU - Public
Due Date (month)	18	Work Package No	WP3

Description
Includes Safety/Effectiveness and Acceptability/Feasibility studies

Deliverable D4.1 – Formative study on Acceptability & Feasibility completed

Deliverable Number	D4.1	Lead Beneficiary	5. GHS
Deliverable Name	Formative study on Acceptability & Feasibility completed		
Type	R — Document, report	Dissemination Level	PU - Public
Due Date (month)	3	Work Package No	WP4

Description
Protocol for the formative study on acceptability and feasibility to be implemented in Ghana and Kenya

Deliverable D4.2 – Protocol for KAP study on Acceptability & Feasibility protocol & implementation plan completed

Deliverable Number	D4.2	**Lead Beneficiary**	5. GHS
Deliverable Name	Protocol for KAP study on Acceptability & Feasibility protocol & implementation plan completed		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	3	**Work Package No**	WP4

Description
Protocol for the KAP study on acceptability and feasibility study to be implemented in Ghana and Kenya

Deliverable D4.3 – Implementation acceptability & Feasibility study in Ghana

Deliverable Number	D4.3	**Lead Beneficiary**	5. GHS
Deliverable Name	Implementation acceptability & Feasibility study in Ghana		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP4

Description
Obtain ethical clearance and complete data collection in Ghana

Deliverable D4.4 – Implementation Acceptability & Feasibility study in Kenya

Deliverable Number	D4.4	**Lead Beneficiary**	4. KEMRI
Deliverable Name	Implementation Acceptability & Feasibility study in Kenya		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP4

Description
Obtain ethical clearance and complete data collection in Kenya

Deliverable D4.5 – Data analysis and interpretation

Deliverable Number	D4.5	**Lead Beneficiary**	5. GHS
Deliverable Name	Data analysis and interpretation		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	6	**Work Package No**	WP4

Description
Analyse and interpretate data in collaboration with Consortium members

Deliverable D4.6 – Exploitation and dissemination plan

Deliverable Number	D4.6	**Lead Beneficiary**	5. GHS
Deliverable Name	Exploitation and dissemination plan		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	12	**Work Package No**	WP4

Description
Develop reports for sharing, presentation and publications in consultation with Consortium members

Deliverable D5.1 – WHO Pathway

Deliverable Number	D5.1	**Lead Beneficiary**	7. Bridges
Deliverable Name	WHO Pathway		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	34	**Work Package No**	WP5

Description
Efficient pathway from clinical studies to WHO normative guidance, contributing to WHO guidance for use of FDC in national STH and NTD programmes

Deliverable D5.2 – Communications and Advocacy

Deliverable Number	D5.2	**Lead Beneficiary**	3. FMS ESPANA
Deliverable Name	Communications and Advocacy		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP5

Description
Design and implementation of a comprehensive communication and promotion plan that contributes to the Consortium's general medium-, short- and long-term objectives

Deliverable D5.3 – Draft Stewardship plan

Deliverable Number	D5.3	**Lead Beneficiary**	7. Bridges
Deliverable Name	Draft Stewardship plan		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	18	**Work Package No**	WP5

Description
Report outlining how to achieve the optimal use of an intervention, including, for example, how to avoid irrational use, overuse or abuse of health technologies

Deliverable D5.4 – Final Stewarship plan

Deliverable Number	D5.4	**Lead Beneficiary**	7. Bridges
Deliverable Name	Final Stewarship plan		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP5

Description
Report outlining how to achieve the optimal use of an intervention, including, for example, how to avoid irrational use, overuse or abuse of health technologies

Deliverable D5.5 – Launched Project - WEBSITE

Deliverable Number	D5.5	**Lead Beneficiary**	3. FMS ESPANA
Deliverable Name	Launched Project - WEBSITE		
Type	DEC —Websites, patent filings, videos, etc	**Dissemination Level**	PU - Public
Due Date (month)	3	**Work Package No**	WP5

Description
Project Website and as per good practices, all work packages leads will be listed.

Deliverable D5.6 – Global Access Plan

Deliverable Number	D5.6	**Lead Beneficiary**	7. Bridges
Deliverable Name	Global Access Plan		
Type	R — Document, report	**Dissemination Level**	PU - Public
Due Date (month)	36	**Work Package No**	WP5

Description
The global access plan covers registration targets, plans to meet demand, flexible approaches to IP and other strategies that reflect ability to pay and ensure that economic barriers to access are low.

LIST OF MILESTONES

Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
1	Kick-off meeting	WP1	1-Liconsa	Meeting minutes	1
2	Annual project meeting (Y2)	WP1	1-Liconsa	Meeting minutes	12
3	Annual Project Meeting (Y3)	WP1	1-Liconsa	Meeting minutes	24
4	FDC Regulatory evaluation and approval	WP1	1-Liconsa	Submission registration and Marketing Authorizations. This is not included within the scope of this Call, but previous one. But this represent overall a key MILESTONE. Planned to at least submit for Marketing Authorization and hopefully the be approved.	24
5	Study Institutional Review Board (IRB) approval	WP2	2-ISGLOBAL	Countries' Institutional Review Board (IRB) report	12
6	First participant enrolled in the trial	WP2	2-ISGLOBAL	Updates at clinical trial registries' webpages	12
7	50% of subjects included in trial	WP2	2-ISGLOBAL	Recruitment Report (includes an overview of recruited subjects by study site, potential recruiting problems, and, if applicable, a detailed description of implemented and planned measures to compensate delays in the study subject recruitment), updates at clinical trial registries' webpage	18
8	Last patient- last visit (LPLV)	WP2	2-ISGLOBAL	Updates at clinical trial registries' webpages	27
9	Database lock	WP2	2-ISGLOBAL	Extract of database	30
10	Primary data analysis complete	WP4, WP2, WP5, WP3	6-GRL	Report issued and publication in peer-review journal prepared	32

Milestones

Grant Preparation (Milestones screen) — Enter the info.

Milestone No	Milestone Name	Work Package No	Lead Beneficiary	Means of Verification	Due Date (month)
11	Formative Research implemented	WP4	4-KEMRI	Formative study report	4
12	Ethical approval obtained	WP4	5-GHS	Ethical approval certificate	6
13	Report and dissemination	WP4	5-GHS	Final study report	36
14	Summary of anticipated WHO guidance pathway for FDC	WP5	7-Bridges	Report Issued	10
15	White paper on sustainable supply and financing models	WP5	7-Bridges	Report Issued	15
16	Communications & advocacy plan	WP5	7-Bridges	Report Issued	6

LIST OF CRITICAL RISKS

Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
1	Reporting and administration challenges (low likelihood, medium severity)	WP1	Providing both indications/templates, processes involved closely monitored and awareness of important determinants of reporting and finances.
2	Insufficient reporting of adverse events (low likelihood, medium severity)	WP2	Analysis of demography, variability among schools and spatial distribution of adverse event occurrence. Selection of a sub-set of school for in depth monitoring. Retraining of the teams in study procedures and use of questionnaires adapted to each culture along with use of Health Centre data to confirm

Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
3	Delay in trial start due to delays of the IRB approval (medium likelihood, medium severity)	WP2	In case the results of the pilot study are delayed, the activities of the trial will start later than expected. We will ensure communication with countries' IRB through African partners who have close relationship and experience with local IRB.
4	Unexpected safety issues with the experimental arms (low likelihood, high severity)	WP2	There is a pharmacovigilance system in place to detect these events. In case unexpected safety events appear, the investigators will follow a detailed "adverse event management plan" that will be included in the final trial protocol. The DSMB is part of this plan
5	Available baseline data particularly in Ghana may not be reflective of current endemicity (medium likelihood, low severity)	WP4	Baseline surveys will be required and should be considered for site selection if burden is insufficient to meet study objectives. Alternative sites should be considered early in case they are required.
6	Regulatory authorities in Ghana and Kenya do not give or delay decision on FDC Dossier (medium likelihood; medium risk)	WP4, WP2, WP5, WP1, WP3	Parallel submission to EMA will also provide support to the national decision-making process. Pragmatic trial will be amended to a Safety & effectiveness trial should it be required by the IRBs and Informed Consent Forms will be ready to be incorporated. Close engagement with WHO for proper channel for WHO support (PQ, EML etc) which will also support national decision-making
7	Public health emergency of international concern (low likelihood; low risk)	WP4	Suspend community activities until recovery; use PPEs as per WHO and national policies.
8	Changes in leadership at WHO may change perspectives on the value of the FDC and/or slow response (low likelihood; medium risk)	WP5	Early engagement with new WHO STH Focal point when current focal point retires and early engagement with new Director of the NTD Team when hired
9	Failure in the safety of the drug that transcends the media (low likelihood; high risk)	WP5	In the face of an adverse scenario, we must spend time dealing with the problem and not thinking about how to deal with it. To this end, we will previously work on the design of the crisis strategy, the protocol to be implemented, the training of the spokesperson(s) and the crisis team. During the crisis, the published information will be compiled, and the evolution of the situation will be monitored and analyzed in all its aspects in order to define how and when to act
10	The combination treatment is not seen as a valuable	WP5	Define the value proposition and additional benefit to the program and clearly communicate

Critical risks & risk management strategy

Grant Preparation (Critical Risks screen) — Enter the info.

Risk number	Description	Work Package No(s)	Proposed Mitigation Measures
	contribution to the STH program WP5 Mitigation (low likelihood; medium risk)		this to partners and countries working closely with the WHO and pharma partners as donation programs transition

PROJECT REVIEWS

Project Reviews

Grant Preparation (Reviews screen) — Enter the info.

Review No	Timing (month)	Location	Comments
RV1	18	To be decided	Tentative review meeting to take place after the periodic report is received
RV2	36	To be decided	Tentative review meeting to take place after the final report is received

JU CONTRIBUTIONS

PIC	Legal Name	Membership	IKOP	Non-EU part of IKOP	Financial Contribution	IKAA
885624551	Fundación Mundo Sano España	No	€ 0.00	€ 0.00	€ 0.00	€ 0.00
894057343	GHANA HEALTH SERVICE	No	€ 0.00	€ 0.00	€ 0.00	€ 0.00
951414122	FUNDACION PRIVADA INSTITUTO DE SALUD GLOBAL BARCELONA	No	€ 0.00	€ 0.00	€ 0.00	€ 0.00
990555950	Laboratorios Liconsa, S.A.	No	€ 0.00	€ 0.00	€ 0.00	€ 0.00
997741225	KENYA MEDICAL RESEARCH INSTITUTE	No	€ 0.00	€ 0.00	€ 0.00	€ 0.00
999981343	GENOME RESEARCH LIMITED	No	€ 0.00	€ 0.00	€ 0.00	€ 0.00

STOP 2030: TOWARDS THE INTERRUPTION OF TRANSMISSION OF SOIL-TRANSMITTED HELMINTHS: PROMOTING IMPLEMENTATION OF RESEARCH RESULTS OF A FIXED-DOSE COMBINATION OF CO-FORMULATED IVERMECTIN AND ALBENDAZOLE INTO POLICY PRACTICE.

TABLE OF HISTORY OF CHANGES		
Version	**Date**	**Changes**
		Annex 1 Part A
1.0	30.08.2022	▪ Initial version/Submitted proposal
1.1	11.01.2023	▪ Removal of periodic and final reports from deliverables, since indeed a requirement of the Grant Agreement. ▪ Included new deliverables as per the Instructions received from Project officer (i.e. Launched project website, Stewardship plan, updated Data management plan)
1.2	03.02.2023	▪ Removal of HCB, Chemo Research and Bridges (associated partner) from JU Contribution Section. ▪ Updated researchers table of Liconsa (removal of one researcher) not within initial proposal. ▪ Included within Working Packages section, for each task both Leading party and Participants. ▪ Included Global Access Plan (GAP) within Deliverables section and removed the overlapping ones with GAP (i.e. Sustainable Supply plan and Sustainable Financing plan) ▪ Included within Risks Section and for each Risk, likelihood, and impact as in the proposal. ▪ Kept GRL (UK) as Beneficiary since their participation is essential. (as aligned with Project Officer and Legal Officer) ▪ GEP (in place for GRL and being drafted by Fundación Mundo Sano) will be self-declared.
		Annex 1 Part B
1.0	30.08.2022	▪ Initial version/Submitted proposal (Form B)
1.1	11.01.2023	▪ Removal of sections already included in Part A (online) ▪ Added Self-assessment section as per instructions ▪ Methodology of the acceptability, feasibility and adherence study was more detailed. ▪ Edited slightly the impact trying to address reviewer feedback. ▪ Added Clinical studies details at the very end.
1.2	03.02.2023	▪ Kept GRL (UK) as Beneficiary since their participation is essential. (as aligned with Project Officer and Legal Officer) ▪ Removal of sections already included in Part A (online): List of Participants, List of Work packages and description (Table 3.1.a, Table 3.1b), List of Deliverables (Table 3.1c), List of Milestones (Table 3.1d), Critical Risks (Table 3.1e) and Staff Effort (Table 3.1.f) ▪ Added Table of contents (Page 1-2) and List of Abbreviations (Page 2) ▪ Methodology of the Section 1.3.2 Acceptability, feasibility and adherence study was more detailed to address reviewer feedback (pages 11-12) ▪ Edited slightly the Section 2. Impact trying to address reviewer feedback (pages 16-17) ▪ Updated Section 3.1.2 Gant Chart, Deliverables and milestone numbering to match Form A (page 24) ▪ Updated Section 3.1.3 Organigram (page 25) to remove the General Assembly. Only one strategic level proposed Steering Committee. Aligned with proposed Consortium Agreement. ▪ Elaborated further tables 3.1.h description of the expense (page 26-27) ▪ Removed "in-kind contribution" linked to Liconsa (page 27) since not applicable. ▪ Corrected the number of beneficiaries in tables 3.1h, 3.1i, 3.1j in line with Part A. (pages 27-28) ▪ Added Section 4. Ethics Self-assessment as per instructions (pages 30-31) ▪ Added Section 6, Info on Clinical studies (pages 34-44)

Table of Contents

List of Abbreviations listed in order of appearance within the text

ALB – albendazole
IVM – Ivermectin
STH – Soil-transmitted helminths
NTDs – Neglected tropical diseases
SSA - Sub-Saharan African
FDC - Fixed-dose combination
MDA – Mass Drug Administration
WHO – World Health Organization
EMA - European Medicines Agency
EDCTP – European and Developing Countries Clinical Trials Partnership
DEC – Diethylcarbamazine
WPs – Working packages
AEs – Adverse Events
ELISA - Enzyme-linked immunosorbent assay
SACs – School-aged children
CR – Cure rate
DSMB – Drug Safety Management board
WSI – Wellcome Sanger Institute
DNA - Deoxyribonucleic acid
PAC - Principal component analysis
FGD - Focus Group Discussions
IDI - In-depth Interviews
KII - Key informant interviews
CI - Confidence interval
GEE - Generalized estimating equation
aOR - Adjusted odds ratio
SEs - Standard errors
IRRs - Incidence rate ratios
LMICs - Low and Low Middle Income Countries
IDDO - Infectious Diseases Data Observatory
ENA - European Nucleotide Archive
YLD - Lived with disability
SOPs - Standard Operating Procedures
GLP - Good Laboratory Practices
HQ – Headquarters
ESPEN - Expanded Special Project for the Elimination of NTDs
IPR - Intellectual Property Rights
CA - Consortium Agreement
STAB – Scientific and Technical Advisory board
ERC – Ethical Review Committee

1. Excellence

1.1 Background

Burden and control of soil-transmitted helminths, at a glance

Soil-transmitted helminths (STH) are a group of parasitic worms that cause a major cumulative burden of disease worldwide. The World Health Organization (WHO) estimates that 1.5 billion people are infected with at least one of four STH species, including: the roundworm, *Ascaris lumbricoides*; the whipworm, *Trichuris trichiura*; and the two hookworms, *Necator americanus* and *Ancylostoma duodenale*.(1) According to 2019 Global Burden of Disease estimates, STH infections collectively causes 1.9 million disability-adjusted life years (DALYs) due to various symptoms associated with moderate or heavy infections, including malnutrition, anaemia, wasting, impaired physical and cognitive development, and abdominopelvic problems such as diarrhoea, abdominal pain, and intestinal obstruction. (2)

WHO guidelines for STH have called for controlling morbidity through mass drug administration (MDA) of the benzimidazole-class anthelmintics - albendazole (ALB) or mebendazole (MBZ) - mainly to pre-school aged children (PSAC), school-aged children (SAC) and women of reproductive age. Benzimidazoles are administered as a single dose once or twice a year, depending on the estimated prevalence of STH in the area. Targets set for 2020 include reaching at least 75% of PSAC and SAC in high-risk areas with regular treatment in 75 STH-endemic countries. However, data from 2019 show that these targets were not attained with only 59% of children in 21 countries receiving the recommended treatment, respectively. (1)

In addition to the above-mentioned group of STH species, *Strongyloides stercoralis* is transmitted similarly to other STH, and can cause hyper-infection syndrome leading to death. However, *Strongyloides* infections have not been addressed comparably with other STHs, as benzimidazole monotherapy is not an effective treatment option.

New Guidelines and Gaps in MDA programmes for STH

WHO's 2021-2030 NTD Roadmap sets a more ambitious target to achieve and maintain elimination of STH-associated morbidity in PSAC and SAC. This target is defined as <2% prevalence of STH infections of moderate and heavy intensity. In addition to the elimination goal for STH, the new targets include the establishment of an efficient strongyloidiasis control programme with an indicator of the number of countries including ivermectin in preventive chemotherapy. (1,3,4)

MDA with benzimidazoles has been and continues to be the cornerstone of WHO's control strategy. However, there are increasing concerns that the ongoing success of these programmes is at risk due to the almost complete reliance on a treatment strategy with a single drug. Although the widespread use of benzimidazoles is effective at controlling *A. lumbricoides* and hookworms, they are less effective against *T. trichiura* and *S. stercoralis*. The lower efficacy of treatment in some species will enable sustained transmission, thereby increasing the time needed to reach targets. The efficacy of benzimidazoles against some STH seems to have further decreased in recent years, particularly against *T. trichiura.* (5) One hypothesis is that the widespread and frequent use of benzimidazole monotherapy has led to the selection of anthelmintic resistant populations of parasites, consistent with the early stages of what is now widespread benzimidazole resistance in a number of veterinary helminth species. If this hypothesis is true, the evolution of resistance to MDA treatment by STH is a significant threat to the progress made to date and to futureplans of transmission interruption once morbidity is controlled. A lack of understanding of parasite populations from a genetic perspective means that it is unclear what proportion of parasites are exposed to drugs, if there is recrudescence or transmission from untreated populations, including zoonotic reservoirs, or if drug resistance is evolving. Therefore, an understanding of the drivers of treatment response is critically needed to ensure drug efficacy is maintained. (6)

New treatment strategies for STH

Given the low efficacy of current treatment regimens against *T. trichiura* and *S. stercoralis*, and the potential risk of developing anthelmintic resistance by relying on monotherapy, a combination therapy using multiple existing drugs with complementary but different modes of action is a possible near-term solution. The co-administration of IVM and ALB has been evaluated as a potential alternative to ALB alone for the treatment of STH. (7,8) This new approach has repeatedly shown improvements in efficacy in trichuriasis treatment compared to the current standard treatment

(ALB 400 mg), reaching cure rates close to 90% when IVM was administrated at higher doses (600 µg/kg). (9) Furthermore, considering IVM is the drug of choice to treat strongyloidiasis, the combined treatment has the added benefit of targeting all STH species with greater efficacy, thereby enhancing progress towards the WHO targets for 2030. (4,10)

Currently, IVM is administered on either a weight-based, height-based or age-based dosing schedule, which makes MDA campaigns more complicated due to the need to measure individual-based parameters before administration and may result in inaccurate dosing. (11) A fixed-dose combination (FDC) of co-formulated IVM and ALB has the potential to simplify drug administration during MDA and prevent underdosing of IVM. Both drugs possess complementary pharmacokinetic properties that make them ideal for co-formulation. The shipping and distribution of FDC in integrated control programmes are likely to be significantly more cost effective compared with the delivery of two individual drugs for MDA. Previous use of co-formulations to treat other diseases like tuberculosis, HIV, or malaria, have resulted in an increased therapeutic efficacy, reduced pill burden, improved adherence, and prevented the emergence of drug resistance. (12,13) Together, these factors will contribute to achieving greater coverage and, therefore, improved control when using an FDC.

Preliminary results of STOP project the ALIVE clinical trial to evaluate the safety and efficacy of FDC

In the search for safe, efficient and logistically simple solutions to distribute and administer therapeutic alternatives, our group, the "Stop Transmission of intestinal Parasites" (STOP) Consortium, established an international public-private partnership to design and validate innovative products and strategies for the control of STH as a public health problem. These products include an oro-dispersible tablet combination of fixed-dose IVM (9 mg or 18 mg) and ALB (400 mg) as a single dose (FDCx1) or three-day regimen (FDCx3). These co-formulations are being evaluated as part of an adaptive study phase II/III superiority trial (called the ALIVE trial) that focuses on measuring safety and efficacy of the FDCx1 and FDCx3 treatment arms against ALB (400 mg) alone (NCT05124691). (14) To evaluate the safety and pharmacokinetic profile of the three dosing regimens, members of the team conducted a phase I clinical trial with 54 healthy adult volunteers who sequentially received two experimental treatments using a new 18 mg IVM tablet in a fixed-dose strategy of 18 and 36 mg single dose regimens, compared to the standard, weight-based 150-200 µg/kg, regimen. (15) Safety data showed no significant differences between regimens and no serious adverse events, and was one of the main pillars to demonstrate that IVM can be safely given in fixed doses. In addition, it was observed that the two experimental treatments of 18 mg and 36 mg showed higher systemic bioavailability compared to the weight-based 150 to 200 µg/kg regimen.

A study focusing on the comparative bioavailability of FDC versus each of its components was funded by Laboratorios Liconsa and also carried out by the STOP Consortium. At a formal Scientific Advice with EMA, after noting that there are no PK/PD parameters established for anthelmintics against STH, it was concluded that although bioequivalence versus ALB alone was not shown this study demonstrated adequate drug exposure to pursue safety and efficacy goals (16) The Phase II component of the ALIVE randomized clinical trial was completed in March this year and evaluated the safety of the FDCx1 and FDCx3 compared to ALB alone. The safety analysis includes 127 SAC in three different weight groups. No alterations in vital signs or serious adverse events (SAE) were observed in any of the participants. A total of 35 adverse events (AE) of mild severity were recorded in 27 participants. The most common AEs were abdominal pain and diarrhoea. All AEs resolved without medical intervention within 48 hours. There was no significant difference in the frequency of total or related AEs among the different treatment arms (Table 1).

Table 1: Summary of adverse events in Phase II ALIVE trial (n=127). AE: adverse event; ALB albendazole

	ALB (n=27)	**FDCx1 (n=49)**	**FDCx3 (n=51)**	**FDCx1 and FDCx3 (n=100)**	**Total**
Total AEs	**5**	**12**	**18**	**30**	**35**
Related AEs	**3**	**10**	**13**	**23**	**26**
Subjects with at least 1 AE	**5 (19%)**	**10 (20%)**	**12 (24%)**	**22 (22%)**	**27**
Subjects with at least 1 related AE	**3 (11%)**	**8 (16%)**	**9 (18%)**	**17 (17%)**	**20**
Fisher exact test against ALB	**-**	**0.40**	**0.34**		**-**

Following the DSMB clearance, the Phase III component of the trial started in May 2022 and is scheduled to complete recruitment in March 2023. Its objective is to evaluate the efficacy of the FDCx1 and FDCx3 compared to ALB alone, specifically for the treatment of *T. trichiura,* but also for hookworms, and *S. stercoralis*. An interim analysis was recently conducted and, in the population recruited so far, statistically significant higher cure rates and egg reduction rates (ERR) for *T. trichiura* infections were observed in the FDCx1 and FDCx3 treatment arms compared to ALB alone (Table 2), without any SAEs or significant safety findings.

Table 2. Preliminary cure and Egg Reduction Rates by Treatment Arms in ALIVE clinical trial (n=465)

***T. trichiura* infections (n=465)**			
	ALB	**FDCx1**	**FDCx3**
Positive before treatment	95	184	186
Cured after treatment	29	148	182
Cure rate (CI 95%)*	30.5% (22.1,40.3)	80.4% (74.1,85.5)	97.8% (94.6,99.1)
P value (vs ALB)**		P<0.0001	P<0.0001
P value ** (vs FDCx1)	P<0.0001		P<0.0001
Baseline Mean EPG (IC 95%)*	387 (-174,66)	438 (-264,684)	361 (-230,545)
Anova (Welch correction) Baseline EPG	P=0.89		
Arithmetic mean ERR (CI 95%)*	54.2% (44.6,59.7)	95.1% (94.4,96.5)	99.7% (99.6,99.9)
Hookworm infections (n=60)			
	ALB	**FDCx1**	**FDCx3**
Positive before treatment	13	25	22
Cured after treatment	11	18	22
Cure rate (CI 95%)*	84.6% (57.8-95.7)	72.0% (52.4-85.7)	100% (85.1-100)
P value (vs ALB)**		P=0.45	P=0.13
P value **(vs FDCx1)	P=0.45		P=0.01
Baseline Mean EPG (IC 95%)*	408 (80-838)	244 (134-388)	202 (101-339)
Anova (Welch correction) Baseline EPG	p=0.63		
Arithmetic mean ERR (CI 95%)*	90.0% (88.0-100)	90.4% (88.7-95.3)	100

*95% CIs were calculated using bootstrap resampling methods with 500 replicates.
**Fisher exact test

In addition to the ALIVE clinical trial, the STOP project includes a set of work packages (WP) that will complement the efficacy results of the FDC, as well as investigate the potential added benefits of this new drug formulation, including but not limited to the acceptability and palatability of the FDC by the participants in ALIVE trial and the relative cost effectiveness if implemented in control programmes. The project will also use molecular biology-based methods to better understand drug efficacy and treatment failures.(17) Finally, the ongoing STOP project includes the use of genome-wide approaches to characterize anthelmintic resistance in STH, focused on the optimization and validation of scalable protocols for sample processing and sequencing to assess anthelmintic resistance alleles in STH.(18)

1.2 Objectives and ambition of STOP2030

Aim

The overall goal of STOP2030 is to test and ensure availability of a new and affordable anthelmintic fixed-dose combination of co-formulated ALB and IVM to increase the safety and effectiveness of regimens against STH in paediatric populations in endemic countries.

This aim is fully aligned with the roadmap for NTDs 2021-30 by supporting the new programmatic goals for 2030 and addressing the three pillars outlined to support global efforts to control, eliminate, and eradicate NTDs: 1. Accelerate programmatic action; 2. Intensify cross-cutting approaches; and 3. Facilitate country ownership. (1) STOP2030 will contribute to all these pillars with enhanced efficacy, improved ability to integrate across diseases and strengthening country ownership. This new therapeutic tool has a potential for integration across several NTDs beyond STH like scabies. Through STOP2030, we have added to the goal of submitting its registration in national regulatory agencies in both participating Sub-Saharan African (SSA) countries This approach encourages country ownership in defining their own national NTD plans, and in turn, provides an opportunity to demonstrate the progress of the roadmap for STH control.

General objective

To facilitate the uptake of a new oro-dispersible fixed-dose combination (FDC) of albendazole (ALB)/ivermectin (IVM) tablet by NTD Control Programmes in MDA activities within the current WHO elimination strategy for STH, including enhanced efficacy against *T. trichiura* and *S. stercoralis*, and by providing additional tools to detect and respond to the emergence of ALB (monotherapy) resistance.

Specific objectives

- To complete the **submission process** of the oro-dispersible FDC of ALB and IVM tablet to national agencies in Ghana and Kenya (submission to European Medicines Agency – EMA - via EUM4all will be completed through ongoing STOP & STOP II projects).
- Provide evidence on **safety and effectiveness** tailored to policy makers for a FDC of ALB and IVM for the control of STH, including *S. stercoralis*, and potentially useful for integration with other neglected tropical diseases (NTDs) in communities qualifying for MDA activities in SSA and scalable to populations at the global scale.
- Provide **acceptability, feasibility, and adherence** indicators to the evidence package to support WHO guidance on the use of FDC in STH control and elimination programmes.
- Develop a model for **sustainable supply and costing** appropriate for widespread use in endemic country settings; and engage in the global dialogue on the deployment and financing of new NTD products and the availability of FDC within this context
- Upscale the **capacity of partner research centres in SSA** for clinical research and pharmacovigilance activities to pharma industry and regulatory standards.
- **Model the impact of different use cases and scenarios** for highest impact to promote product introduction, national decision making, and donor support for STH programmes and other NTDs.
- Implementing a pilot **antihelmintic resistance** surveillance approach based on genetic epidemiology nested in the STH control programmes.
- **Engage stakeholders including policy and decision makers** as well as end-users to identify and overcome barriers to have the FDC adopted by health systems to support uptake and scale up in STH control and elimination programmes.

The STOP2030 project is designed to progress from clinical trial data to provide evidence from use in field settings to support WHO guidance for use of the FDC in national NTD programmes. This will make available the first new treatment for STH in decades. The use of FDC in MDA programmes could increase impact and progress towards the 2030 goal of elimination of STH as a public health problem in 96% of countries. The STOP2030 Consortium builds on the STOP programme funded by EDCTP which supported the development and testing of the FDC in a multicentre clinical trial in three sites in Africa. As part of that scope of work, STOP demonstrated the safety and

superior efficacy of the FDC compared to the standard monotherapy. This next scope of work will now take the FDC on an accelerated pathway to introduction and scale-up, building on the recent experience accelerating access to the triple drug therapy with IVM, DEC, and ALB for lymphatic filariasis.

1.3 Methodology

To achieve the project goal and objectives, we have gathered a highly experienced multidisciplinary and multinational South-North team that includes clinical physicians, nurses, epidemiologists, pharmacologists, modellers, researchers, and parasitologists, as well as professionals of the pharmaceutical industry to provide support in regulatory affairs, pharmacovigilance, intellectual property rights and business development.

The project will include capacity building, networking and communication activities around a multicentre clinical safety and effectiveness trial, and studies on acceptability, feasibility, and adherence for FDC in programmatically relevant scenarios. Classic microscopy-based procedures will be used to detect STH. Modelling studies will be conducted to identify the scenarios with highest potential impact on transmission and economic benefits of the new treatment regimen within NTD programmes. Genome-wide approaches will be used to assess parasite response to drug treatment. The scientific results will be translated into key messages and presented to the scientific community, local governments and other implementation actors and stakeholders and used to inform WHO guidance and national decision makers on the use of FDC in NTD programmes.

The activities will be organized in five strategic WPs with clear deliverables and responsibilities. The WPs intersect to maximize the interaction between researchers and institutions. This allows for better coordination of the transnational and multidisciplinary nature of the project.

1.3.1 Intervention studies

This project will include two main studies, to be conducted in Kenya and in Ghana:

1.3.1.1 Safety and effectiveness pragmatic trial

A multicentre pragmatic trial will be conducted involving two study sites in SSA, Ghana and Kenya, to evaluate safety and effectiveness of the newly developed FDC as a single dose to treat STH, compared to the standard dose ALB (400 mg single dose) for the treatment and control of STH.

Study design and justification

The ALIVE trial (STOP project 2018-2023) was designed to provide the highest quality information on the efficacy and safety of the FDC in a controlled environment with registrational purposes. We aim now to validate the benefits of FDC through a pragmatic trial in a programme context to evaluate the safety and effectiveness profile in a large population of participants.

We have designed an open-label pragmatic trial, randomized by school, two-arm safety and effectiveness study which will be carried out to evaluate implementation parameters of a treatment regimen of FDC to treat STH (including *S. stercoralis*) compared to the standard 400 mg ALB single-dose in children attending primary schools in *T. trichiura* transmission settings currently included in local MDA programmes for STH in two SSA countries.

As a pragmatic trial it will reproduce real programme structure and activities; as such, the criteria for participation will be equal to those applying to MDA activities within the STH control programmes. Application for temporary-preliminary approval of FDC will be submitted to the drug regulatory agencies (Ghana Food and Drug Authority and Pharmacy and Poisons Board of Kenya) for the purpose of these implementation evaluations. *Please see Table 3.1e addressing Critical risks for implementation and the proposed mitigation measures*.

Schools of the two study sites will be randomly assigned to one of the treatment arms, where the entire school population will be offered treatment according to the assigned treatment arm, and a sample of participants per school will be sampled at different time points to measure prevalence. One intervention will be carried in a period of one year in each school. Prevalence will be measured at the school level, prior to the first intervention (baseline), at one-month post intervention and within the month prior to the second yearly intervention. It is expected that at each time point, the selected participants will vary. Adverse effects will be monitored through a specific surveillance system established in schools, sentinel hospitals and health centres near schools. Safety surveillance will be performed for seven days after each MDA, allowing for the identification of AEs in subpopulations (in terms of gender, age, body weight, comorbidities, and additional risk factors) for better estimation of safety.

Objectives of the trial

Primary objective

- To evaluate and compare **safety** of a FDC against ALB alone via MDA in two study areas in Kenya and Ghana.

Secondary objectives

- To evaluate the effectiveness of one round of MDA with FDC compared to ALB against STH (T. trichiura, A. lumb*ricoides,* hookworms by microscopy
- To evaluate the effectiveness of one round of MDA with FDC compared to ALB against *S.stercoralis* by serology.

Target population

The main target population of this trial are school-aged children, currently prioritized by the WHO strategy and currently included in the national STH-control programme in each country. (19)

Inclusion and Exclusion criteria

Inclusion and exclusion criteria are those applying to MDA programmes.

Study arms

The trial will have two study arms. Schools will be randomized to receive either:

1. ALB: 400 mg single dose
2. FDC: IVM and ALB single dose:
   a. 9/400 mg to subjects <45 kg body-weight
   b. 18/400 mg to subjects≥ 45 kg body-weight

Method of allocation

The randomization unit will be the schools in the study area. Allocation of schools to study arms will be performed by block randomization.

Protection against bias

Due to the characteristics of the study (MDA conditions), treatment concealing is considered not to apply to this trial. Laboratory personnel will be blinded to the treatment received by school participants.

Pharmaceutical products

Laboratorios Liconsa S.A. will manufacture, test and release the IVM/ALB FDC. Afterwards, the drug will be distributed to the partners in SSA for its use in the pragmatic trial.

ALB 400mg tablets used by STH control programs in the sites.

Trial procedures

The clinical trial will be conducted in schools of the participating countries following the same programmatic activities used in the deworming programme, with the addition of a thorough monitoring of safety and effectiveness. This will include:

- Community mobilization: as is routine for deworming activities in both field sites, local teams in each field site will facilitate the approach to candidate schools through professionals already engaged in the local programmes and allow those in the community to identify this trial as a locally owned process. Activities to promote, advertise and inform about the trial through mechanisms and tools approved by the respective bioethics committee will include interactions with local community leaders, members of the educational community, health care providers, local press and other community gathering points.
- Enrollment: the intervention will be described in full to parents and children. All school aged children attending the study schools and not having contraindications will be offered treatment with one of the two study interventions, following standard procedures of the programme.
- School intervention: All participants attending a selected school will receive all doses of study treatment (ALB or FDC) at school under the direction of local MDA programme implementer.
- Outcome evaluation:
  - Safety cohort: All children receiving either ALB or FDC will participate in the safety cohort (a total

of 20,000 participants). We will monitor AEs at the schools with active surveillance using a pharmacovigilance system during the first 2 days and passively through sentinel hospitals through the full week.

- Effectiveness cohort: We will select a sample of 87 children for each of the 23 schools by each study arm participating in the two countries to evaluate effectiveness of the interventions (a total of 2001 participants by arm). Those participants will be requested to bring one stool sample to evaluate the prevalence of STH at baseline, month+1 and month+11 by Kato-Katz evaluation . Participants for this analysis will be selected randomly for each timepoint, and it is expected that different participants will contribute to each analysis. To evaluate and compare the effectiveness of the MDA with FDC and ALB on *S. stercoralis*, serology against NIE through ELISA will be conducted at baseline and at month +11 to all the participants of the effectiveness cohort.

Laboratory methods

- Stool samples will be examined by duplicate Kato-Katz smear examination for each of the time points of the clinical trial. A single stool sample will be collected from each participant.
- Serum samples will be evaluated with serology by measuring antibody titer against NIE through in-house Luminex.

1.3.1.1.a Pragmatic clinical trial outcomes

Primary outcomes

Number, type, severity and relationship to study drugs for all AEs registered through the pharmacovigilance system reported in the seven days after treatment in the FDC arm, compared with ALB.

Secondary outcomes

- Prevalence reduction of STH (*T. trichiura, A. lumbricoides,* hookworms), between baseline and month +1 and +11 after MDA with FDC compared to ALB, measured by microscopy
- Prevalence reduction of *S. stercoralis* by measuring antibody titer against NIE through in-house Luminex at baseline and month +11.

Data management

- Each study site will be responsible for the internal quality management of study conduct, data and biological specimen collection, documentation and accurate completion of study documents. A data management plan will be developed for each site in coordination with the coordinating center of WP3 (Data management and modelling).
- All data storage will be encrypted and password protected.

Sample size calculation

The sample size was estimated to detect a frequency of severe adverse events (p_0) of 1/3000. Since this frequency is less than 0.02, we use the zero-patient method to estimate the necessary sample size (n) with a one-sided significance level of 0.05, as follows: $n= 3/p_0$, giving a total of 10000 participants per treatment arm(ref). Considering that on average schools have 450 SACs in Kenya and Ghana, 23 schools are required per treatment arm.

To measure effectiveness, stool samples will be collected in each school at different time points. We assume that the baseline prevalence of STH in the study sites will be 30%, that ALB has an average efficacy of 69% for the three STH (*A. lumbricoides* CR: 96%, hookworms Cr: 80%, and Cr: 31%), and we expect the same cure rates for hookworm and A. lumbricoides and higher cure rates for *T. trichiura* (CR=72%) in schools treated with FDC, so FDC would have an average efficacy of 83% for the three STH. Therefore, after one month of treatment we expect a prevalence of 9% in the ALB arm and 5% in the FDC arm. To measure the difference in difference: of the reduction in prevalence in schools treated with FDC vs. reduction in prevalence in schools treated with ALB, 2000 children per treatment arm are required (significance level=0.01) at each time point. These children will be divided among the 23 schools, and 87 children will be recruited at each school.

1.3.1.1.b Protection of human subjects

The evaluation will be conducted in accordance with all applicable study participant privacy requirements and the guiding principles of the Declaration of Helsinki.

- A favorable opinion/approval to conduct the assessment will be obtained prior to a site commencing study-

related activities in each country, in accordance with local ethics requirements.

- For the pragmatical trial, we will work with the local Ministries of Health in each country. They will be in charge of carrying out the MDA in the different schools, through their offices involved in the Consortium (GHS and KEMRI).
- Months before the start of the study, promotional and publicity activities about the pragmatic trial will be carried out. Meetings will be held at the community level and in the school setting to inform the population about the objectives of the trial. Then, the informed consent of the parents or legal guardians of the children of the schools selected to participate in the trial will be requested. In addition, signed informed consent, approved by the corresponding ethics committee, will be requested from the parents or guardians of the children who participate in the collection of biological samples and epidemiological data.
- Even though the current trial results are showing a favourable outlook for the safety of the intervention, the trials included in this proposal will again be supervised by a DSMB with specific go/no go criteria.

1.3.1.2 Genetic monitoring of MDA effectiveness substudy

Drug resistance is widespread in many veterinary helminth species, having evolved from the overuse of anthelmintic drugs. The rapid rate in which resistance has evolved to the same drug classes used to control human infective helminths represents a significant threat to MDA campaigns if it were to establish and spread. The genetic cause of resistance is largely unknown in human-infective helminths such as STH; although some candidate genes have been proposed and investigated, the evidence for variation in these genes associated with resistance is poor. Recent genome-wide approaches have provided new insight into the genetics of anthelmintic resistance, highlighting similarities and importantly differences between human- and veterinary-infective helminths in their response to treatment, and revealing new variants that show significant greater diagnostic potential than candidate genes alone. To date, there has been no coordinated genetic monitoring and evaluation of resistance in MDA interventions worldwide. As seen for other infectious diseases, genomic data from whole-genome sequencing can provide unprecedented information that could be used to define the response of parasites to MDA treatment, transmission zones of parasites to differentiate between reinfection and recrudescence, and to detect genetic evidence of suboptimal responses to the drug.

Main goal

The main objective of this substudy is to implement genomic surveillance as a tool to evaluate MDA effectiveness during STH control programmes.

- For this substudy, we expect to sequence a total of 690 STH positive samples, which will be equally distributed by school (5 positive samples per school, per time point, and per treatment arm).

Sample size:

- 5 participants from each school participating in the stool surveys, for a total of 690 samples.

Sampling times:

- Baseline, month 1, month 11.

Laboratory methods

After the completion of informed consent process, documented through the signature of informed consent forms (and assent when indicated), those stool samples collected from SAC previously selected for the genetic surveillance substudy will be subjected to egg concentration. (18) This method has been previously validated by members of the STOP Consortium and it is currently being used in whole-genome sequencing for the assessment of anthelmintic resistance. Three grams of stool will be concentrated and the resulting sediment (around 250 mg) will be stored in each study site at -80ºC before shipment to the Wellcome Sanger Institute in UK (WSI) for DNA extraction and sequencing.

Once at the WSI, DNA will be extracted from the sediment using a previously validated, highly efficient DNA extraction method for *T. trichiura.* Briefly, the method follows three consecutive lysis steps: (i) a bead-beating step using PowerBeads tubes (ceramic 1.4mm; Qiagen) followed by one freeze-thaw cycle, (ii) a 2 h proteinase K incubation, and (iii) DNA extraction using the QIAamp DNA Mini Kit (Qiagen).

DNA sequencing libraries will be prepared following established protocols by the sample management team at the WSI. These protocols have been used successfully for a range of helminth species by Doyle and colleagues. (20) In the case of very-low input samples, a modified low-input protocol will be followed. DNA input and the resulting

sequencing library will be checked for quantity and quality prior to committing for sequencing. Libraries will be sequenced using 150 bp paired-end chemistry on an Illumina NovaSeq platform at the WSI. We will aim to sequence each sample at 200X coverage of the *A. lumbricoides*, *T. trichiura* or hookworm (mainly *N. americanus*) genome, with an 80% mapping efficiency to account for some variation associated with mapping and likely contamination. This will require approximately 17.5 Gb of data per sample, which can be achieved by sequencing ~40 samples multiplexed per NovaSeq sequencing lane. In total, we aim to use 18 NovaSeq sequencing lanes to sequence approximately 690 samples.

Bioinformatics and data analysis

Population structure. We will perform principal component analysis (PCA) and evaluate relatedness and admixture. By estimating all these parameters, we will be able to understand the relatedness between samples within and between communities in the different study sites. We will also examine the impact of the two different treatment arms in the genetic structure of the different populations of parasites. We will also explore if the new infections between the month 1 and month 11 are due to recrudescence, or the introduction of parasites from other geographical areas.

Genetic diversity. We will measure genetic diversity (measured as nucleotide diversity (pi), Watson estimator, Tajima's D) as an estimation of effective population size and a proxy for successful control programmes, as seen for other parasites (it is expected that diversity will be lower in populations closed to elimination). (21) In addition, we will evaluate the genetic differentiation (Fst) between baseline parasites and the parasites collected after the interventions. Thus, we will be able to evaluate the impact of both treatments in genetic selection and potentially identify genes associated with treatment failure and anthelmintic resistance.

Genome-wide association. We will use two approaches to test the relationship between parasite genetics and parasite clearance in response to treatment: (i) a logistic regression genome-wide association between samples from children with 'good clearance' phenotypes and post interventions samples from children with poor clearance phenotypes; and (ii) a linear regression genome-wide association study with the ERR estimates for all samples collected before treatment. We will include other variables as potential confounders such as sex, age, school and/or community. We will also characterize the predicted effects of genetic variation, and identify relationships between genes associated with the outlier variation by functional enrichment analyses. Finally, we will assess the association of beta-tubulin gene variants and resistance, in the context of variants identified in the genome-wide analyses. Once resistant parasite populations are identified, we will be able to evaluate the impact of the two treatment strategies in the selection of resistant strains.

1.3.2 Acceptability, feasibility, and adherence study

Research Questions

- What is the perception of providers and clients about the current management of STH in Ghana and Kenya?
- Will a FDC of IVM and ALB be acceptable to clients and providers in Ghana and Kenya?
- Would clients adhere to a 3-day regimen of FDC of IVM and ALB in Ghana and Kenya?
- What contextual and process factors are likely to influence the feasibility and acceptability of a FDC of IVM and ALB in Ghana and Kenya?

Main goal

To explore the acceptability, feasibility and adherence of a FDC of IVM and ALB for the control of STH in Ghana and Kenya.

Specific objectives

- To describe the perceptions and attitudes towards the current management strategy for _STH.
- To explore the feasibility of using a FDC of IVM and ALB in the management of STH.
- To assess the acceptability of the use of FDC in the management of STH to clients and providers.
- To assess adherence to a 3-day regimen of FDC of IVM and ALB in Ghana and Kenya.
- To examine contextual and process factors that could influence the feasibility and acceptability of the FDC.

Methodology

A two-phased study is envisaged. The first phase would be a formative study using qualitative methods to explore the perceptions of the STH control programme. The formative phase will consist of document review, and selected Focus Group Discussions (FGD)/ In-depth Interviews (IDI with program implementors. Phase one will provide an opportunity to better understand the strengths and challenges of the current programme implementation. Stakeholder

views on the proposed FDC of IVM and ALB in the management of STH will be explored. We will also identify areas to explore further in phase 2.

The second phase will be a three-arm comparative study comparing acceptability and feasibility of FDC versus co-administered ALB and IVM in school-based STH MDA programmes. Schools will be randomly assigned to one of the treatment arms. The three arms are schools where MDA is conducted with:

1. Co-administered IVM and ALB directly observed treatment
2. FDC single directly observed treatment
3. FDC single directly observed treatment followed by 2 doses for the student to take home and take daily (total of 3-day dosage)

A structured questionnaire on acceptability will be targeted at students, teachers, and parents, followed by FGD. IDI will be used to gather information on acceptability and feasibility of FDC with teachers, drug distributors and programme implementers. A final follow- up with a subsample of students in schools that received the 3-day dosing will be done to determine adherence with taking all 3 doses over the 3-day period.

We will explore whether the perceptions of the proposed FDC of IVM and ALB in the management of STH and the expectations of stakeholders, including advantages and disadvantages, reaction to proposed intervention, and benefits to stakeholders. We will also explore how best the information obtained can be used to guide integration into the STH programme.

Study area:

One STH endemic region each in Ghana and Kenya will be selected for the study. In this region three districts will be selected (one for each arm of the study) with three schools in the district receiving the intervention.

Study Population:

In communities with intervention schools, participants for the formative phase of the study will include key stakeholders in the NTD programme including teachers, parents, drug distributors, and programme implementers. For the comparison arms schools will be randomly selected to receive one of the treatment regimens. Schools with a minimum population of 100 students will be randomly selected to receive one of the 3 treatment options. All the students in the sampled school would receive the intervention with a subset selected for the survey. The qualitative component will involve FGDs and IDI with students, teachers, community drug distributors, and program implementers. We will explore appropriate ways to interview younger students to have their views reflected in the assessment.

Sampling and sample size estimation:

A total of 9 schools will be selected for quantitative survey

- **District A-** Co-administered IVM and ALB 3 randomly selected schools with 50 students will be selected per school to participate in the acceptability survey; at the district level all teachers and 50 parents will be surveyed
- **District B-** FDCx1 3 randomly selected schools with 50 students will be selected per school to participate in the acceptability survey; at the district level all teachers and 50 parents will be surveyed
- **District C-** FDCx3 3 randomly selected schools with 50 students will be selected per school to participate in the acceptability survey: at the district level all teachers and 50 parents will be surveyed

FGD- per school

- 5 to 7 students 11-15 years of age
- 5 to 7 parents

FGD- Per district

- 5 to 7 teachers
- 5 to 7 drug distributors

IDI/Key informant interviews (**KII)- per district**

- The programme manager
- 2 drug distributors

Data collection and analysis:
Trained individuals will conduct the interviews. KIIs and FGDs will be tape recorded and transcribed. We will develop a codebook using the KII and FGD guides as well as the objectives of the study to guide the coding of transcripts. Data will be analyzed thematically, focusing on key themes and sub-themes that cut across various respondent groups. Qualitative data will be analyzed using NVivo to categorize text in the transcripts based on the codebook.

Quantitative data will be collected through surveys or interviews as appropriate with respondents. Interviewers will use tablets that have questionnaires designed on them to facilitate speedy processing of data. The electronic version of the questionnaire on tablet will have built-in consistency checks to reduce errors in data collection. Completed questionnaires will be submitted electronically to a data server. Quantitative data will be analyzed using Stata software.

1.3.3 Data management

All the quantitative data collection tools (questionnaires, acceptability tool, laboratory forms, etc) for the safety, effectiveness, and acceptability studies will be programmed onto android-based smartphones (e.g. Samsung Galaxy M31 series of android version 12 or posterior) which will be used to capture data electronically using Open Data Kit (ODK) system. The ODK system will incorporate in-built data quality checks to reduce data entry errors and duplications of records. The system will allow sending data from the field in real time. Additionally, barcodes will be designed using P-Touch software and printed using Brother Barcode Printer QL-800. The QR barcodes will be printed preferably on paper label of size 23mm by 23mm on a white background. The barcode will be used to link all the samples collected in the field and those processed in the laboratory to the respective individual interviewed. All data will be submitted to ODK central database for safe storage. Only key study team members will be given login credentials to the database. Different user access rights will be assigned to each user based on their perceived roles. ODK Central is easy to use, very fast, and secure online database maintained by the ODK Team (https://getodk.org/#odk-cloud). After the completion of the study, all the collected experimental and field observational datasets will be anonymized and deidentified before being deposited into an open access stable public repository to enable the data and all the associated research outputs to be findable, accessible, interoperable and reusable in accordance with the FAIR principles and standards (https://fairsharing.org). We will use figshare repository (https://figshare.com) to deposit all the field-based data and a subject-specific public repository for the laboratory-based sequencing data. All the statistical modelling codes will be deposited in GitHub (https://github.com).

1.3.4 Modelling

Modelling will be conducted to analyze and integrate the following outcomes across the project; acceptability, feasibility, effectiveness, safety, adherence, fidelity, and genomic resistance. Some of these outcomes are primary (i.e., acceptability, feasibility, and safety) while others are secondary (i.e., effectiveness at 21 days and 1 year, adherence, fidelity, and genomic resistance) in the two study countries.

The modelling will aim to determine the FDC impact on STH infection prevalence and intensity as well as its cost-effectiveness. This analysis is required to support introduction planning, policy and national decision-making; it will be constructed based on data being currently generated in the context of the EDCTP-funded STOP project and complemented with the data and analysis that will be collected in the acceptability (WP4) and safety and effectiveness (WP2) studies of this proposal.

Modelling the impact of FDC on infection prevalence
Impact of FDC vs. monotherapy on infection prevalence will be determined. Infection prevalence for each STH species will be calculated at school level with a 95% confidence interval (CI) using generalized linear models (specifying the binomial family function) while accounting for the school clusters. The impact of the various treatment interventions (particularly FDC) on infection prevalence will be first analysed by fitting a generalized estimating equation (GEE) model assuming within-subject correlation and binomial family function that will test whether the proportion of individuals positive for each STH species varied significantly among the treatment arms. The covariates included in the model will be treatment interventions, age, gender, schools, and study site. Additionally, multivariable mixed effects logistic regression model at three levels will be separately fitted; individuals nested within schools selected within treatment groups and finally within a study site, with age and gender

retained as fixed terms in the model and reporting the adjusted odds ratio (aOR). The results from the first and second models will be compared and model with significantly better results will be reported.

Modelling the impact of FDC on infection intensity

Impact of FDC on infection intensity will be determined. Infection intensity for each STH species will be calculated at school level with a 95%CI using generalized linear models (specifying the negative binomial family function) while accounting for the school clusters. The impact of the various treatment interventions (particularly FDC) on infection intensity will be analysed by fitting a GEE model allowing for within-subject correlation using robust variance estimator to calculate the standard errors (SEs). From the GEE model, the incidence rate ratios (IRRs) will be reported.

Modelling cost-effectiveness of the FDC intervention

The primary purpose of this analysis is to compare the cost-effectiveness of FDC (either administered once or three-days consecutively) against the routine monotherapy (ALB 400 mg) across a variety of epidemiologic and socio-demographic settings.

Costing methods: Costs and cost-components will be retrospectively compiled from the current STOP study and will also be prospectively collected in this study. Cost records will be reviewed and expert opinion of the survey implementers regarding the frequency and specifics of the survey costs will be obtained. An ingredients-based approach will be used to compile costs, review individual cost component and apportioning them to respective cost categories. However, we will exclude all economic costs and in-kind resources e.g., opportunity cost of school teachers' time, and investigators' time on protocol development and analysis. We will estimate the total value of goods or services by multiplying the unit price by the total number of such items. Thus, the total costs will be extrapolated by intervention arm, school, and individuals sampled to be able to capture the variation in cost-precision.

Cost-effectiveness: A precision metric will be derived to determine relative effectiveness of comparative intervention arms. Details of the simulation exercise that will be used to derive the metric will be provided later.

All statistical analysis will be performed using STATA version 17.0 (STATA Corporation, College Station, TX, USA). Visualizations and graphical analysis will be performed using R/RStudio (https://www.r-project.org) (particularly, the ggplot package).

1.3.5 National or international research and innovation activities supporting STOP2030

STOP2030 builds upon encouraging results emerging from the Phase II component and preliminary analysis included in the DSMB report of the Phase III component of the ALIVE trial within the EDCTP-supported STOP project (2018-2023). These studies have already achieved 70% of the target recruitment of T. trichiura cases required, and successfully demonstrated adequate safety and palatability of the FDC, and superior efficacy of the FDC regimens compared to ALB alone against T. trichiura infections (Tables 1 & 2). These results are further supported by a trial completed by members of the STOP Consortium in Honduras, where co-administration of ALB with high dose-IVM at 600 µg/kg in single dose or 3-consecutive days single dose was significantly superior to ALB monotherapy in either single or 3-day regimens, with no safety concerns and no relationship between IVM exposure and adverse events. Notably, cure rates of 100% were achieved in the 3-day ALB/IVM arm (9). Further evidence on the safety of high dose IVM comes from a systematic review and meta-analysis highlighted the fact that despite the limited number of studies, doses up to 800 µg/kg were as safe as regular doses of 150 to 200 µg/kg. (22)This data on the innovative FDC product and regimens, open opportunities for achieving goals of control for STH that would be very difficult to achieve with benzimidazole monotherapy (23) without compromising the safety, simplicity of administration and logistics necessary for MDA campaigns. While the current STOP projects provide safety and efficacy data for the registration of FDC against STH at EMA through the EU-M4all programme and WHO Prequalification, an additional set of supportive data is necessary for the intervention to be considered and implemented by the global health community and WHO for incorporation into global guidelines.

The recently published American Journal of Tropical Medicine and Hygiene, Accelerating Innovation to Impact: Learning from Triple-Drug Therapy (IDA) for Lymphatic Filariasis and from Other Innovations (hereafter referred to as the IDA Supplement)(24) provides a useful roadmap for accelerating product development and access for NTDs. Bridges was instrumental in the work on the IDA triple therapy when at the Bill & Melinda Gates Foundation and led the development of the journal supplement to document that experience as well as some selected other examples including a vaccine, new drug, and diagnostic. Four members of Bridges team contributed to the supplement. Drawing from this experience and others, the Bridges team is uniquely placed to be able to help guide the FDC from

clinical studies to programmatic use in their role in the Consortium.

The genetic analysis of parasite transmission and drug resistance relies on research expertise and innovation from the parasite genomics group at the WSI led by PI Doyle. The Institute and the wider Wellcome Genome Campus operate under the name of Genome Research Limited (GRL). Examples include the recently published genome-wide analysis of *T. trichiura* sampled from around the world, which provided the first framework for genetic epidemiology in this species which will be used as a baseline to compare genetic variation of samples sequenced in STOP2030, and analysis of genome-wide genetic variation including zoonotic relationships between parasites that infect humans and non-human primates (6) Additional examples include genetic mapping of drug resistance-associated mutations for benzimidazole and IVM in veterinary parasites, which have provided new insight into the genetic mechanisms of drug resistance and importantly genetic markers that can be translated into diagnostic tests for monitoring resistance in the field (25), which will be a long-term objective of STOP2030.

1.3.6 Multidisciplinary expertise and methods integrated in pursuit of project objectives

The work packages lead brings a wealth of expertise from diverse disciplines essential to an efficient path from field trial to product availability to informing WHO guidance and national decision-making on implementation of an FDC. Work package leads will serve on the Steering Committee ensuring regular project oversight and effective and timely integration across disciplines and methods. Protocols and WP activity plans will be shared for review and input from all Consortium members.

Individual WPs have been designed with multiple contributing disciplines accountable for success. Implementation of field studies for Safety and Effectiveness (WP2) will require expertise and methods blended from, but not limited to, clinical research, parasitology, genetics, data management, public health programming, lab sciences, social sciences, and regulatory. Data management and modelling (WP3) will require multiple methods and expertise including clinical research, modelling, policy-making and advocacy. Work package 5 will leverage disciplines such as public health programme, clinical research, social sciences, pharma, regulatory, advocacy, and modelling to inform policy making processes by WHO and national NTD programmes.

1.3.7 Integration of social sciences and humanities

The STOP2030 Project blends a multidisciplinary approach to accelerate the use of FDC therapy in NTD programmes by anticipating questions such as the acceptability, feasibility, and adherence of implementation in communities. Social scientists in Ghana will lead WP4, working in collaboration with social scientists in Kenya, and also contribute to the design and implementation of the other WPs. The lead of WP4 will be part of the Steering Committee, fully integrated into generating the evidence base for dissemination and to inform exploitation of the FDC.

The WP4 data is essential to supporting the development of guidance by WHO which requires eight factors (GRADE criteria) to inform WHO Guideline Committee recommendations. These include acceptability, feasibility, values and preferences, ethics and human rights, and balance of benefits and harms. Social scientist contributions to all the WPs, and leadership of WP4, will provide supportive evidence related to such factors and contribute to policy-making by WHO and governments.

1.3.8 Accounting for gender dimensions in research and innovation content

Mass drug administration (MDA), which will be the method for administration of the FDC, is generally considered to be an equitable or neutral platform for provision of medicines to females and males in a community. However, equity in MDA will be monitored. STH programmes are frequently school-based which could add a bias towards males who may be enrolled more frequently, especially in the later years (26). While both boys and girls face barriers to complete formal schooling for many reasons, some factors affect girls differently, such as cost, late or no school enrollment, forced withdrawal of married adolescents, the social influence of family members concerting the traditional roles of girls and women, early pregnancy, as well as menstrual health leading to school absenteeism. (27,28) The field study designs (WPs 2 and 4) will accommodate administration through either a school or community-based platform based on the approach used in the study country. This will allow for an analysis of sex-related differences in access with either platform. Data collected through the field studies will be disaggregated for analysis and interpretation according to gender (26). Currently, there is a lack of available and accessible quality sex- and age-disaggregated data related to NTDs, and there is a clear need to introduce gender considerations during programme design and delivery. With that in mind, our project acknowledges the possible gender biases and barriers, and works on providing data on the differences and disparities between genders in the access of either school or community-based MDA delivery, focusing on STH and LMICs.

1.3.9 Implementation of open science practices as an integral part of the methodology

This project will be conducted embracing open science concepts which are well aligned with the project goals of getting data and evidence put into action in national programmes for impact. This starts from the very inception of the work. Preliminary research design will be shared for input and guidance with NTD programmes in Ghana and Kenya, and WHO (headquarters and Regional Office for Africa). As the studies are initiated, progress will routinely be shared among the Consortium members, sharing knowledge, lessons learned, and collaboratively work on problem solving in real time. To support rapid use of data, study results will be made available to WHO and WHO committees, as needed, aiming to support guidance and decision making prior to publication. The study results can be submitted for independent data analysis, if requested by WHO.

The STOP Consortium has initiated interactions with the Infectious Diseases Data Observatory (IDDO), a clinical data platform for the collation, curation, standardization and reuse of individual participant data on treatments for multiple infectious disease, whose coordinating office is based in the Centre for Tropical Medicine and Global Health at the University of Oxford (https://www.iddo.org). By joining this network of global health researchers, the data emerging from the current and future trials will be public and available for reuse, also providing the members of our STOP2030 Consortium access to a wide array of data generated by network members for re-analysis and modelling exercises. With the goal of an ethical and equitable environment for sharing and reuse of clinical data supporting the elimination of NTDs, the recently launched chapter dedicated to STH and schistosomiasis provides the ideal setting for data sharing and community work of our Consortium members.(29) Registration in clinicaltrials.gov will also be done as is the case with the registrational clinical trial under way by the STOP Consortium (ID: NCT05124691). (14) As part of the dissemination and communication activities, the publication policy of the Consortium will be to use open-access peer-review scientific journals.

1.3.10 Research data management and management of other research outputs

A large volume of parasite genome sequencing data will be generated by WSI. Raw sequencing data will initially consist of FASTQ format files of forward and reverse reads, which will be mapped to a reference genome to generate BAM files. Variant data will be stored as VCF format files. Sequencing data will be automatically submitted to the European Nucleotide Archive (ENA) within 12 months of generating the data in line with WSI data sharing policies and commitment to open access (https://www.sanger.ac.uk/about/research-policies/open-access-science/). These data will be perpetually maintained and freely available. Reproducible analytical pipelines and presentation of these analyses, in the form of computational code. All computer code use to analyse and visualise these data will be archived with a stable DOI in publicly available GitHub and Zenodo code repositories.

2. Impact

2.1 Project's pathways towards impact- Overall

This proposal will complement and build on the results of the safety and efficacy clinical trial of the FDC of co-formulated ALB and IVM for the treatment of STH (EDCTP funded STOP project 2018-2023). This proposal for STOP2030 will generate the evidence needed by policy makers at both the national scale (STH-endemic countries in SSA) and the global scale (WHO) to modify STH programme recommendations for achieving control and elimination of STH thereby improving the health and wellbeing of populations at risk. The expected impact of the project involves four different levels (listed below) with inter-related outcomes:

Accelerate the implementation and registration of a FDC of co-formulated ALB/IVM for the control of STH in SSA countries and beyond.

Through the generation of safety, effectiveness, acceptability, feasibility, and cost effectiveness data during implementation trials and modelling activities, this proposal seeks to complete the data collection necessary to demonstrate to programme managers and policy makers at country level the benefits and utility of incorporating the FDC to their programmes. The data will also support the addition of the FDC to the list of the pharmaceutical products registered at their national or regional regulatory agencies; in that respect, the registration process in Ghana and Kenya will serve as a case model for its replication in other endemic countries. Still, the incorporation of FDC to WHO recommendations and Essential Medicines List allows its use in NTD control programs in all endemic countries. Overall, these results will provide an evidence base for policy changes among the different stakeholders

in the field, including the WHO Department of Control of NTDs, the NTD NGO Network, and governments broadly across endemic countries. STOP2030 will work in parallel to the already initiated interaction with EMA for the current ALIVE trial, which has been accepted for participation in the M4all Programme and has already had 3 Scientific Advice meetings. The current proposal includes the submission for registration in both countries where field activities will be executed; therefore, facilitating the engagement and governance of endemic countries and National NTD Programmes.

Ultimately the FDC could have impact across all STH-endemic geographies, much of the evidence generated by this project will also support use in other regions although some replication may be required. STOP2030 includes modelling and stakeholder engagement to identify the best scenarios for wide-scale implementation with other donors and implementers.

Foster progress towards Sustainable Development Goals (SDG)

At a larger scale and longer term, our proposal will contribute to the achievement of the SDGs, especially SDG3: "Ensure healthy lives and promote wellbeing for all at all ages" by tackling diseases with the highest burden of morbidity in SSA countries. According to the 2019 Global Burden of Disease data, STH causes 1.9 million DALYs. They are, collectively, the NTDs that contribute the highest number of years lived with disability (YLD), estimated in 2015 to be 3.17 million years (30).

This proposal will also contribute to improving SDG1, "ending poverty", SDG4, "quality education", and SDG8, "economic growth" (30). There are many consequences to this large burden of disability and morbidity that contribute to the cycle of poverty in communities affected by STH. Infection with STH can result in poor educational outcomes for children due to malnutrition, anaemia, and impairments in physical and cognitive development (31–33). Infection can have an adverse effect on pregnancy outcomes and worker productivity (32). These factors together reduce the ability for children to receive a quality education and communities to break the cycle of poverty through economic development. Therefore, addressing the significant morbidity associated with STH infection represents a largely untapped development opportunity to alleviate poverty and improve educational outcomes. This will directly contribute to the SDGs and also help fulfil WHO's mission of ensuring attainment of the highest standard of health as a fundamental human right of all peoples (34). Furthermore, the impact of attaining control of STH goes beyond morbidity determinants, in view of the demonstrated effects of deworming in improving outcomes like school absenteeism and even future wage earning in adult life; all of which foster equity and productivity (35).

This project, by developing a new intervention for STH, can contribute to addressing the significant burden of these infections be ensuring a sustainable supply of a highly effective treatment. Moreover, an ALB/IVM combination can surpass and amplify the impact against STH, by providing an equally significant effect on other NTDs like scabies, LF and onchocerciasis all of which contribute to the cumulative DALYs due to NTDs. In addition, the FDC provides a unique single tablet with anthelmintic activity against *S. stercoralis*, an infection targeted by WHO for incorporation into 96% of control programmes by 2030.(3) Altogether, this project, which will generate the evidence for inclusion of the FDC into deworming programmes, can help accelerate progress towards reducing the burden of all these diseases where they are endemic.

Upscale the capacity of Research and Public Health units in SSA in clinical research and pharmacovigilance activities with Pharma and Regulatory standards.

The STOP2030 Consortium has two African Institutions leading two of the five work packages. Both African partners will be leading multicentre studies in two countries, highlighting and adding their research study design, data management, and analytic capacity to the Consortium and across borders. They also both fully participate in the Steering Committee guiding the project. Kenya will support the development of the models for use of the new FDC in different settings to help prioritize the best use-case scenarios to maximize impact and cost-effectiveness (WP3). Ghana will develop and lead the acceptability, feasibility, and adherence multicentre study (WP4). This work will provide essential data to support WHO guidance and national-level decision-making strengthening endemic country researchers' roles in policy making which will impact this work and beyond.

This proposal seeks to include the registration of an innovative pharmacologic tool for the control of STH with the potential to be used for several other endemic diseases in SSA countries. The path to implementation and access of this pharmacologic tool includes its registration in regulatory agencies and, as such, it requires strengthening within-

country capacity for the generation and registration of quality data. It also requires the capacity for monitoring and surveillance activities for pharmacovigilance of products recently introduced in the market or expanding their indications to new population groups. Pharmacovigilance activities will be provided through the Standard Operating Procedures (SOPs) and protocols by Laboratorios Liconsa. These SOPs are usually applied for equivalent activities in their portfolio of products in Europe and other regions. The application of these SOPs in this project will be coordinated by ISGlobal as part of WP2 who will implement and provide tools to both countries in SSA. This will include the provision of state-of-the-art tools for a wider use by the implementing countries in the vigilance of the safety of medical interventions. Beyond that, the proposal aims to establish within the participating centres a new standard for pharmacovigilance of anthelmintics that meets regulatory demands.

Survey capacity will also be strengthened through the incorporation of new technological advances to assess anthelmintic resistance as well as training on the methods for genomic epidemiology. The project will initiate technology transfer of these new techniques and methods from WSI to SSA partners as part of WP2, which includes the placement of a trainee from one of the SSA partners to the laboratories of Stephen Doyle (WSI) in the UK.

The execution of randomized clinical trials with EMA registration targets, in the context of the EDCTP-funded STOP project, has upgraded the capacities of the three participating centres to standards of Good Clinical Practices (GCP) and Good Laboratory Practices (GLP). This improved capacity will be furthered bolstered as this project moves to carrying out studies focused on the identification of safety in larger populations under the same standards of GCP.

GCP training will upscale local capacities for readiness to implement and evaluate rapid responses to emergencies and outbreaks. As seen in the recent crisis created by the COVID-19 pandemic, research capacity is essential in low-resource countries to avoid creating a dependency on foreign centres with lack of local knowledge and priorities and its consequent risks on research priorities and missed opportunities in pharma sponsored clinical research (36).

In summary, building capacity within the local partner organizations is central to the success of this project and can have impacts beyond the lifetime of this work. As such, the project will provide the tools and trainings for upscaling the capacity to implement pharmacovigilance activities and train local teams in its application.

Integration of genome-based epidemiology for the evaluation of anthelmintic drug efficacy and monitoring for resistance.

The utility of genomic surveillance is perhaps best exemplified by monitoring the emergence and spread of SARS-COV-2 variants during the current COVID pandemic and has motivated the implementation of the Global Genomics Surveillance Strategy by the WHO over the next 10 years. In this proposal, we aim to apply genomic epidemiology of STH during MDA activities for the first time. Using genetics to understand where parasites come from and how they respond to treatment will provide unprecedented information that adds value to existing and planned operational activities to eliminate STH as a public health problem. Using whole-genome sequencing of parasites from both Kenya and Ghana, supported by existing global parasite genome datasets generated by Doyle and colleagues, we will characterise the genetic relatedness of parasites within and between countries; these data will inform to what degree parasites are shared between regions and in turn, the scale in which management of parasites must be considered. For example, MDA efforts (such as scale and duration) may be optimised depending on whether genetically related parasites are widespread, or alternatively, genetically distinct parasites are found in discrete focal areas. By combining parasitological data (e.g., parasite prevalence before and after treatment) with genomic data, we will aim to identify genetic variants associated with response to treatment. Although genetic variants associated with benzimidazole resistance are well established for veterinary parasites, e.g., three canonical resistance variants at positions P167, P198, and P200 of the beta-tubulin gene, homologous variants in beta-tubulin of STH parasites only show poor association with resistance in the field (37), (work also developed by members of the STOP Consortium). Our unbiased whole-genome approach to investigate and monitor anthelmintic resistance offers the highest probability of identifying resistance associated variants if they exist. These data will be invaluable for developing simple diagnostic tools that can be applied in endemic countries to monitor for anthelmintic resistance variants during MDA. Besides the immediate benefits of its implementation to MDA activities, we will also pilot the development of simple, cheap amplicon sequencing technologies (similar to that used for SARS-COV-2 sequencing) based on genome-wide data predictive of resistance, as well as quantifying species composition, which will be the basis for technology transfer from WSI to SSA (described above).

Ultimately this work will support STH programmes but will be of relevance to all NTD programmes especially those working with MDA and striving for elimination. The relevance beyond NTDs has already been intimated through the recent pandemic and would be similarly relevant and of value in Africa for future epidemics.

2.2. Dissemination, exploitation and communication

Plan for dissemination and exploitation

The audience for the dissemination and communication activities of the project are diverse including:

- STH-endemic **African countries** in particular Ghana, Kenya, and other **STH-endemic countries**
- C**ommunities** endemic for STH and other NTDs in African countries
- **WHO** NTD Programme (HQ and regional offices) and complementary departments (e.g., PQ, Guidelines Development Group)
- **EMA and African Regulatory** bodies
- **Development and technical partners** working in STH-endemic countries (e.g., Children Without Worms; STH Advisory Committee; US Agency for International Development)
- **Pharmaceutical partners** engaged in STH programmes (e.g., GlaxoSmithKline; Johnson & Johnson)

To ensure that each stakeholder has the appropriate information at the appropriate time in the best format, WP5 activities include analysing and identifying stakeholders needs relative to the project timelines to guide an appropriately-timed and impactful dissemination, communication and exploitation plan as an early deliverable in the project. This plan will also include targeting communication tools and approaches to the various stakeholder needs.

The **dissemination and communication** plan will ensure tailored materials are developed for the varied audiences noted above. These will include, for example, one-pagers, FAQs, social media postings, PowerPoint presentations, conference presentations by WP leads (e.g., Coalition on NTD Research (COR-NTD), and a bespoke website for Consortium activities. The communication tool and approach will be designed to reach stakeholders where it may be most effective. For example, it may work most effectively for implementing partners to bring communications to the NTD NDGO Network meeting in contrast to working directly with WHO to reach National programme leads, The dissemination and communication activities will proceed iteratively according to project timelines, sharing the rationale for the project and FDC and "what to anticipate" timelines early on. Activities will progressively shift to a greater focus on results from each stage of the project, followed by final project results from field studies and modelling (e.g., impact, cost-effectiveness) tailored to those who will be instrumental in policy and decision-making processes in WHO, SSA countries, development partners and pharma.

WHO will be a key target for the exploitation of study results. After consulting them on study design during the project's formative stages, WP5 will facilitate a regular cadence (e.g., every 3-6 months depending on project stage) for disseminating data emerging from the study in a manner tailored for WHO exploitation through guidelines and guidance documents. The team will disseminate the final study results to WHO and discuss implications for their use and public health practice in STH-endemic countries prior to publication. Results will be submitted for **peer-reviewed publication** (open access priority), and relevant databases shared through formats like IDDO.

Project plans, interim findings from WPs and final project results will also be disseminated through and discussed in bilateral consultations with the **NTD programmes in Ghana and Kenya,** as well as with WHO's Regional Office for Africa, the Expanded Special Project for the Elimination of NTDs (ESPEN), and targeted development partners engaged in SSA. This will contribute to a discussion of the exploitation of the results by stakeholders to inform policy and investment decisions. Consortium members from Ghana and Kenya will disseminate findings for exploitation through key NTD-related fora in Africa such as NTD Programme Manager Meetings.

The project will create a **website** to transparently communicate information on the Consortium and disseminate progress. This will allow a central place for questions to be addressed that may arise during the project. The team will also embrace social media as a tool for communications including twitter to share interim updates with partners.

As noted above, the use of study results by WHO, African countries and development partners will inform each organization's role in developing guidance and policies for use of FDC, however **a key exploitation will be in guiding pharma decisions.** As a Consortium member, Liconsa will be directly engaged in ensuring that supply and financial sustainability approaches build from the project results. This will include decisions on manufacturing

quantities, and financing strategies. These decisions will guide the project and inform and be informed by discussions in the wider NTD and development community on changes to current donation models for NTD medications.

Strategy for the management of intellectual property

Intellectual Property Rights (IPR) will be tackled from the beginning of the project and will be specifically addressed as part of a Consortium Agreement (CA). Confidentiality among participants during the project development and confidentiality towards external participants, access rights, ownership and protection of results, will be covered in detail within the CA that will be enforced before the official project start. **All research and results will be available through open access.**

During the project, the team will look beyond the lifetime of the project and will consider the IP rights of stakeholders such as Consortium members that may be involved in bringing the STOP2030 project results to market.

As claimed specifically for this call topic, participants will – up to four years after the end of the action – use their best efforts to ensure that resulting health technologies and services will be broadly available and accessible, as soon as possible and at fair and reasonable conditions. In this respect, if, despite a participants´ best efforts, the results are not exploited within one year after the end of the action, beneficiaries must (unless otherwise agreed in writing with the granting authority) use the Horizon Results Platform to find interested parties to exploit the results.

In case the participants cannot fulfil the preceding obligation, the participants must (if requested by the granting authority) grant non-exclusive licences - under fair and reasonable conditions - to their results to legal entities that commit to rapidly and broadly exploiting the resulting health technologies and services and ensure that they are broadly available and accessible, as soon as possible and at fair and reasonable conditions.

In case of transfer of the ownership or licensing of results, participants must pass on such additional exploitation obligations to the legal entities exploiting the results.

For up to four years after the action, the funding body must be informed every year about the status of the development of the product or any other exploitation of the results through an annual report that is due on each anniversary of the end of the grant agreement.

2.3 Summary

KEY ELEMENT OF THE IMPACT SECTION

SPECIFIC NEEDS	EXPECTED RESULTS	D & E & C MEASURES
Case 1: **Current drug regimens** for the control of STH **lack adequate efficacy** against *T. trichiura*; therefore, reducing the impact of MDA interventions and limit opportunities for elimination goals Case 2: **New 2030 targets for STH** incorporates the establishment of a strongyloidiasis control programme Case 3: Experience in veterinary parasitology highlights the need for proper and timely surveillance of **anthelmintic resistance**. MDA campaigns carry a still undefined risk for this event that threatens the impact of the programmes. Case 4: SDGs, especially **SDG3 ,**(Ensure healthy lives and promote wellbeing for all at all ages) are **dependent on success in NTD control and elimination** as a marker of access to adequate primary health and linked to the perpetuation of the poverty-disease and equity axis.	Case 1: **Generate a FDC** of co-formulated ALB/IVM approved by EMA, registered in Ghana and Kenya and included in list of Essential Medicines of WHO against STH. Case 2: Provide a therapeutic regimen that in addition to being accessible, affordable and safe, incorporates efficacy against *S. stercoralis* in an **"all STH" spectrum.** Case 3: Upscale the **capacity for local monitoring of anthelmintic resistance** in countries targeted for deworming activities with the implementation of new up-to-date techniques. Case 4: More effective preventive chemotherapy strategy will **accelerate control and elimination** and build on SDG efforts for water and sanitation that are critical for lifting communities from structural poverty.	Case 1: **Exploitation:** Product registration in target countries. **Dissemination** towards the scientific community and stakeholders: Scientific publication of safety & effectiveness clinical study, acceptability studies and modelling cost effectiveness. **Communicatio**n towards citizens: community mobilization activities based on KAP studies. Case 2: **Exploitation**: Product registration in target countries. **Dissemination** towards the scientific community and stakeholders: Scientific publication, policy papers. Case 3: **Exploitation:** Generation of algorithms and guiding investments. **Dissemination** towards the scientific community and stakeholders: Scientific publication, policy papers. Case 4: **Exploitation**: Focused on the communication of the cost effectiveness of achieving SDGs and the role of NTD **Dissemination** towards the scientific community and stakeholders: Scientific publication, policy papers. **Communication** towards citizens: targeted communication to stimulate uptake and coverage

TARGET GROUPS	OUTCOMES	IMPACTS
Case 1: • **WHO NTD Department.** • **NTD Control Programmes in 101 countries targeted** for elimination of STH as a public health problem. • **NTD Partner Organizations.** Case 2: • **WHO NTD Department.** • **National NTD Control programmes.** • **Heath care providers** in endemic settings. • **NTD Partner Organizations.** Case 3: • **WHO Technical Advisory Group on Schisto & STH (TAGSS).** • **National NTD Control Programmes.** Case 4: • **UN-WHA.** • **WHO NTD Department.** • **NTD Partner Organizations.**	Case 1: **Inclusion of FDC in recommendations** for the control and elimination of STH. Countries have **sustainable access to FDC.** Case 2: **Establishment of a strongyloidiasis control programme** integrated into STH control programmes. Case 3: Incorporation of genetic epidemiology into mapping activities and **anthelmintic monitoring** to guide the strategy and use of appropriate tools. Case 4: Stimulate the commitment for **investment in innovative safe health technologies for the control of NTDs** as a mean to address inequalities	Case 1: Reduction of burden of STH **achieving the 2030 NTD roadmap elimination goal d**efined as **<2% proportion of STH infections of moderate and heavy intensity.** Case 2: **Quantum leap in the impact of preventive chemotherapy strategy for STH** through a regimen with adequate spectrum and potency against all species of interest. Case 3: Rational use of anthelmintic for STH control while **preventing the emergence of resistance**. Mitigating the risk of anthelmintic resistance through the **understanding and quantification of the risk**. Case 4: **Strengthen poverty reduction** through increasing school achievement and earning potential by implementation of FDC in STH control programs.

3. Quality and efficiency of the implementation

3.1 Work plan and resources

3.1.1 Overall structure of the work plan

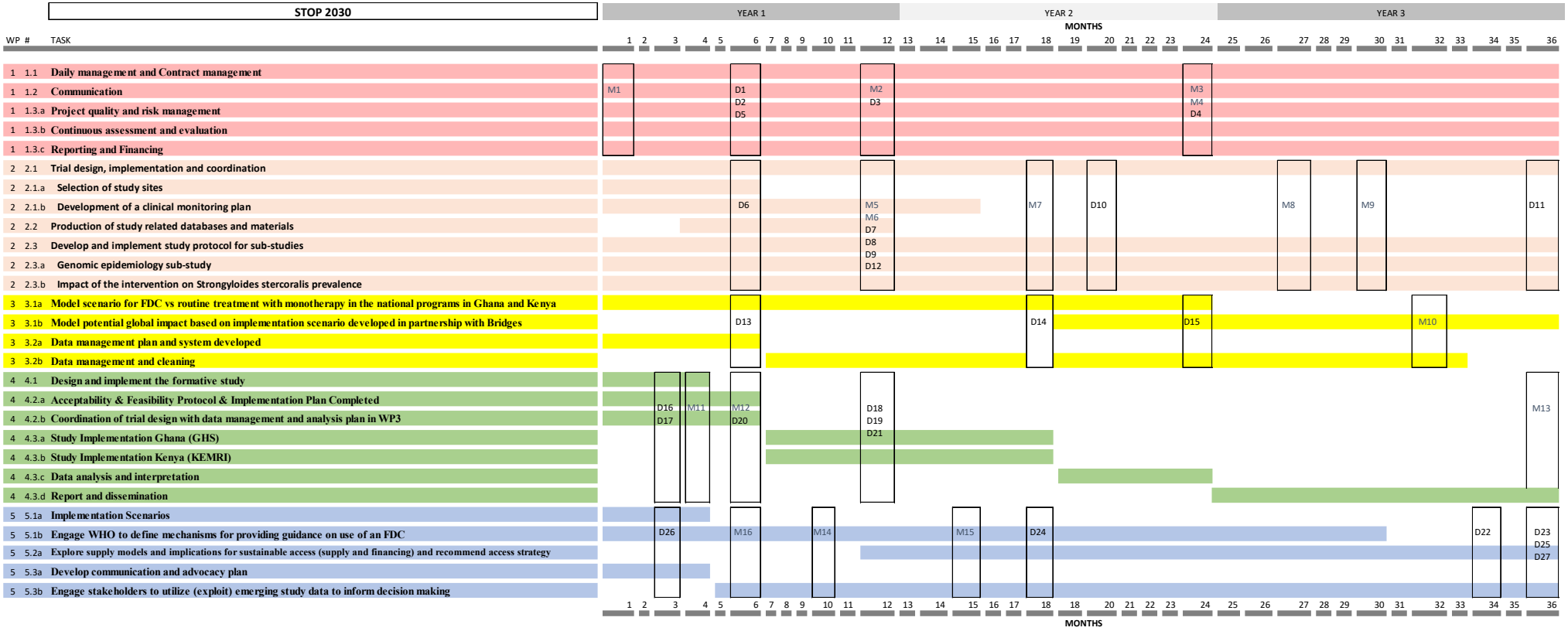
Further clinical studies are needed to support the use and safety of the FDC in programmatically relevant settings and real-world conditions; demonstrating further safety and enhanced effectiveness when used at scale in NTD programmes. This is the aim of WP2 led by ISGlobal and involving two-African sites. The clinical studies outlined in this proposal will provide additional evidence at a larger scale to demonstrate the public health benefit from a safety and effectiveness standpoint, to stakeholders and decision-makers in local African communities and beyond, to advance the usage of this new, more convenient, and more efficient therapy that is as safe as current standards of care. WP2 will also have contributions from the Sanger Institute in genomics-based monitoring of antihelmintic resistance and a substudy to define the impact of the interventions on *S. stercoralis* seroprevalence.

The STOP2030 Consortium model will bring the African Consortium colleagues into higher leadership roles, leading two of the five work packages. In their roles, both African partners will lead multicentre studies in their respective countries, highlighting and adding their research study design, data management, and analytic capacity to the Consortium and across borders. Kenya will support the development of the models for use of the new FDC in different settings to help prioritize the best use-case scenarios to maximize impact and cost-effectiveness (WP3). Ghana will develop and lead the acceptability, feasibility, and adherence multicentre study (WP4). Both WP3 and WP4 will provide essential data to support WHO guidance and national-level decision-making.

In addition to the clinical trials and modelling, the Consortium has brought in a new partner, Bridges to Development, who worked closely with the triple drug therapy for lymphatic filariasis mentioned above. Bridges will lead a complementary scope of work (WP5) to support the development of WHO guidance and decision-making on the use of FDC in national programmes. This workstream will engage stakeholders to understand their needs for evidence to support their role in decision-making on use of FDC. This work will also support the development of models for access and affordability in partnership with Liconsa to ensure that the FDC is able to be deployed widely. The goal of this WP is to remove barriers to access and use of the FDC and help to target the introduction to maximize impact and accelerate progress to WHO NTD Roadmap goals and attainment of SDG3.

Last but not least, WP1, namely the coordination package, will guarantee the supervision of the project and all WP to guarantee all team members jointly work towards the common goals.

3.1.2 Timing of the work packages and their components (GANTT chart or similar)



3.1.3 Graphical presentation of project components and how they inter-relate (PERT chart or similar)

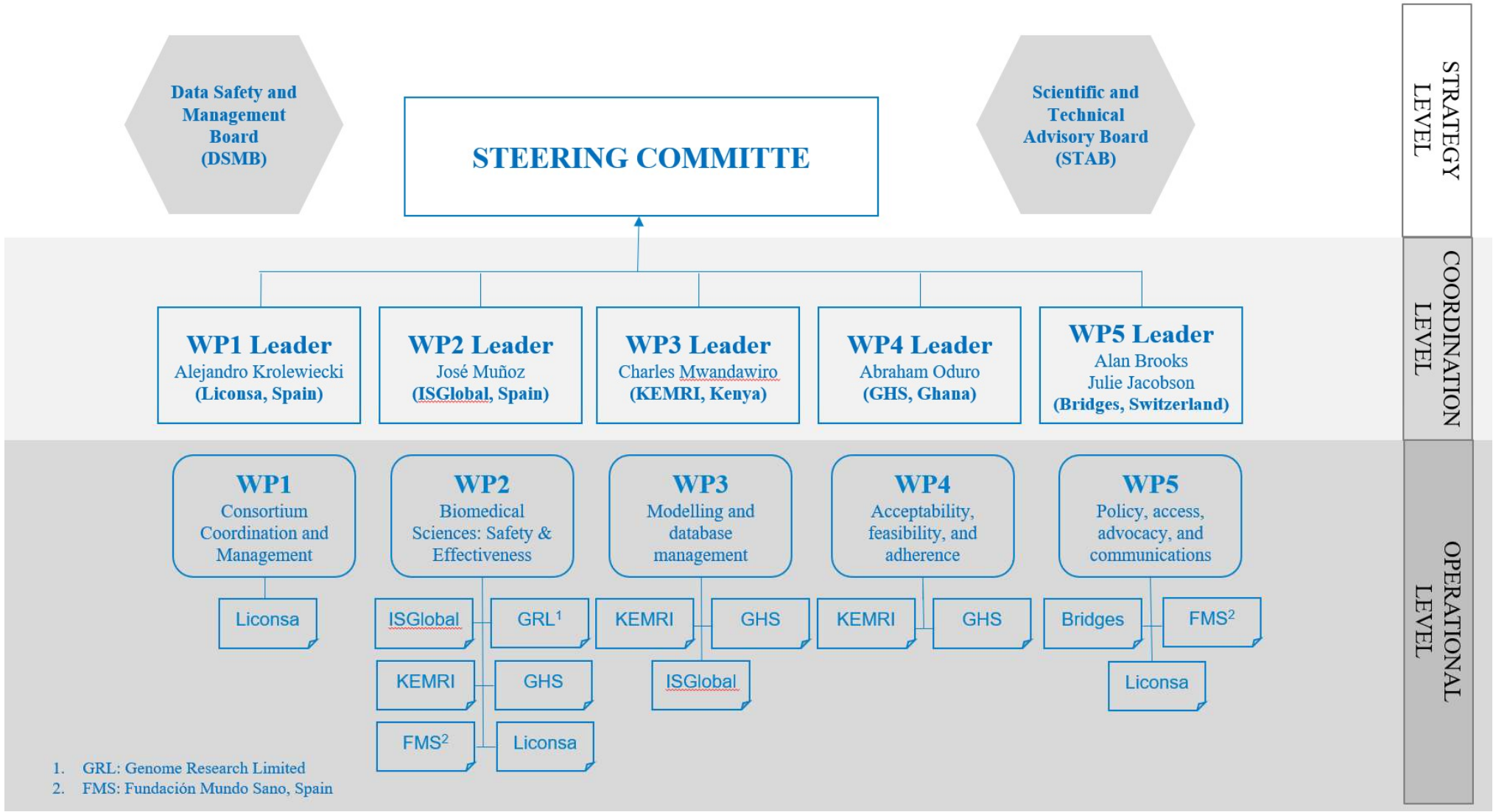


Table 3.1h: 'Purchase costs' items (travel and subsistence, equipment and other goods, works and services)

Participant #1/Liconsa		
	Cost (€)	**Justification**
Travel and subsistence	60.200	Organization of First Annual meeting, additional two annual meetings travels, Steering committee face to face meetings, on-site (Africa) visit
Equipment	3.160	Depreciation costs Laptop, Monitor and Earphones
Other goods, works and services	34.500	Medication shipment cost and customs management (8.000€), registration fees and consultancy fees including audit certificates (25.000€) and stationary material (1.500€)
Remaining purchase costs (<15% of pers. Costs)	0	
Total	97.860	

Participant #3/FMS		
	Cost (€)	**Justification**
Travel and subsistence	24.800	Travel to three annual meetings and on-site travel to the clinical study sites for monitoring among other activities.
Equipment	0	
Other goods, works and services	47.120	Publication fees and other materials and supplies and audit certificates.
Remaining purchase costs (<15% of pers. Costs)	0	
Total	71.920	

Participant #4/KEMRI		
	Cost (€)	**Justification**
Travel and subsistence	75.000	Travel to annual meetings, local subsistence and travel between sites
Equipment	3.000	Depreciation costs Smartphones
Other goods, works and services	331.012	Goods and services required for the execution of the pragmatic study including Kato-Katz (specific diagnostic kits), serology processing samples tools and all lab materials required, execution of acceptability study, advocacy and mobilization for sensitization and mobilization, publication fees and office and field supplies. Also audit certificates.
Remaining purchase costs (<15% of pers. Costs)	0	
Total	409.012	

Participant #5/Ghana		
	Cost (€)	**Justification**
Travel and subsistence	218.300	Travel to 3 annual meetings and to 6 in country meetings as well as travel and subsistence for project implementation
Equipment	0	
Other goods, works and services	216.300	Goods and services required for the execution of the pragmatic study and acceptability study, Lab supplies, Study and Ethics application fees the latest to Ethical Review Committee (ERC), and in-country dissemination forums and participation fees and audit certificates.
Remaining purchase costs (<15% of pers. Costs)	0	
Total	434.600	

Participant #6/GRL		
	Cost (€)	**Justification**
Travel and subsistence	21.000	Attendance at Annual Meetings and Hosting of African Participant at Sanger
Equipment	8.412	Depreciation costs Laptop and Qiagen PowerLyzer 24 Homogenizer
Other goods, works and services	53.860	Consumables and cost of transport for samples
Remaining purchase costs (<15% of pers. Costs)	0	
Total	83.273	

Table 3.1i: 'Other costs categories' items (e.g. internally invoiced goods and services)

Participant #1/Liconsa		
	Cost (€)	**Justification**
Internally invoiced goods and services #1 Liconsa	11.734	FDC (test product) to be used for the clinical studies: 285 packs of 40 tabs, and a unit cost of 10,06€/pack.

Participant #6/GRL		
	Cost (€)	**Justification**
Internally invoiced goods and services #7 GRL	93.067	Library preparation, QC and Sequencing performed by core facilities at WSI

Table 3.1j: 'In-kind contributions' provided by third parties

Participant #2/ISGlobal			
Third party name	**Category**	**Cost (€)**	**Justification**
Hospital Clinic de Barcelona (HCB) PIC number: 905096816	Seconded Personnel	83.033,21	Appropriate full-time salary of Dr. Jose Muñoz who will be working as the lead and principal epidemiologist for WP2 through with ISGlobal.

3.2 Capacity of participants and consortium as a whole

The Consortium includes seven institutions from: one European Union member state; two African states; and two European states. Each Consortium members has been selected due to their ability to carry out their critical role in the successful completion of the project using stringent and standardised methodologies. Several team members are part of the previous STOP Consortium which developed the FDC to its current state, which speaks to the experience and strong commitment of the group. The Consortium will benefit from the synergies of five European and two Sub-Saharan partners, each of whom brings distinctive yet highly complementary expertise. This combination of partners will enhance south-south, south-north and north-north cooperation and networking and bring expertise in clinical research, social science, modelling, cost-effectiveness, and implementation planning. The project will be managed such that the Consortium members will work closely together, support each other's strengths, and increase each other's capacity.

This project is built on several years of collaboration between Laboratorios Liconsa (the coordinating institution), KEMRI and ISGlobal, during which time they developed and tested a fixed dose of IVM in adults under the hypothesis that this drug should not need to be adjusted by body weight. This was an important step towards the development of the FDC and was followed by bioavailability studies of the FDC vs co-administration of each of the active components (ALB and IVM) funded by Liconsa to provide further support to the EDCTP-funded STOP project. As the partners of the STOP project also wanted to contribute to the knowledge of anthelminthic resistance, this Consortium brought in the expertise of WSI who has worked closely with ISGlobal on the genomic research components previously. Now, moving into this next phase, the Consortium will be strengthened by the incorporation

of new partners including a second country partner, the Ghana Health Service, and two non-governmental organizations (NGOs) Bridges to Development (Bridges) and Fundacion Mundo Sano.

The Consortium is coordinated by Laboratorios Liconsa S.A. in Spain, a pharmaceutical company belonging to Chemo. Established in 1977, it has been operating in the pharmaceutical world for 45 years. Liconsa does not commercialize directly to the patients, instead they work through other pharmaceutical companies, public institutions (WHO), or non-profit organizations who can access the production and act as distributors for public sector use. Liconsa has wide regulatory experience in pharmaceuticals and has regular engagement with regulators to obtain marketing authorization from a highly regulated and recognized health authority (EMA/WHO). A recent milestone was the achievement of the WHO-prequalification for IVM 3 mg tablets. Liconsa has promoted early engagement with EMA for their assessment and recommendations during the project development and their recommendations and feedback have been taken into account in development. Liconsa assures both (1) approvability of the product through the regulatory expertise and (2) a highest quality and supply of the product through the industrial capacity of their site. Finally, Liconsa has production capacity and capabilities to manufacture the FDC under GMP and compliant with FDA and EMA ensuring a continuous supply. Liconsa's contributions to this project are multiple: (1) to develop and manufacture the experimental drug, a novel formulation, FDC of IVM and ALB, (2) to support with specific pharma industry expertise (regulatory affairs, business development, pharmacovigilance etc.), and (3) at the end of the EDCTP Project, to continue with the process of marketing authorization, manufacturing and supply of the product.

The two African Consortium members will be responsible for leading and directing their own work packages as well as conducting the field studies. KEMRI as the research branch of the Ministry of Health has long term relationships with local communities and has considerable experience implementing similar studies in STH and other NTDs (38). KEMRI will support the smooth implementation in Kenya of the safety and effectiveness studies as well as the acceptability, feasibility, and adherence. The KEMRI team specifically will bring to the partnership the cross-consortium database management and analytic support. Because of their extensive modelling experience, they will also lead all of the project's modelling activities (WP3). KEMRI also has laboratory capacity and access to a Luminex machine which will allows for multiplex detection of multiple analytes simultaneously in blood. Therefore, they will be able to provide a high level of laboratory support to the project.

The Ghana Health Service is the primary agency of the Ministry of Health responsible for health service delivery in Ghana. The Neglected Tropical Diseases Programme (NTDP) of the Public Health Division of the Ghana Health Service is responsible for programming and management of NTDs in Ghana. The Research and Development Division (RDD) generates evidence to inform health policy and programmes. RDD has a multidisciplinary team of researchers experienced in clinical trials as well as epidemiological and social research. Both the NTDP and RDD have long standing relationships with the communities and the health system. The NTDP and RDD will be responsible for the design and coordination of the acceptability, feasibility, and adherence studies across the consortium. They are also well placed to conduct the safety and effectiveness studies in Ghana.

Mundo Sano is a family foundation created in 1993 with the mission of reducing the impact caused by neglected tropical diseases (NTDs) through research, innovation, access to health and cooperation. Currently, Mundo Sano implements programs and projects in the Americas, Europe and Africa and seeks to position NTDs in the global and regional cooperation agendas, working in consortiums that include public health systems as well as the academic and the private sector. Benznidazole is one of the only two existing drugs for the etiological treatment of Chagas disease, and in 2011 there was a global lack of supply. Mundo Sano promoted and achieved the production of benznidazole, guaranteeing its availability in all the world. In 2017, benznidazole was approved by the Food and Drug Administration (FDA), becoming the first drug for the treatment of Chagas Disease registered in the US.
On STH, since 2010 Mundo Sano has participated in programs for its the prevention and control in Argentina as well as in Mozambique and Ethiopia. Particularly in Ethiopia, Mundo Sano works on STH activities, focused on *S. stercoralis*, with the main aim of filling gaps of the national control program. In addition, their expertise in communications for neglected tropical diseases as demonstrated by the announcement as recipients of the International Public Relations Association's (IPRA) 2022 Golden World Award which recognizes excellence in public relations practice. Mundo Sano will contribute their expertise in communications by leading activities focused on developing and implementing a stakeholder engagement, advocacy, and communications plan, in collaboration with Bridges (WP5).

The Wellcome Sanger Institute (WSI; the research institute and activities on the Wellcome Genome Campus operates under the name of Genome Research Limited (GRL)) is a not-for-profit research organisation and is one of the world's leading genome centres focused on using genomics to improve human and animal health. The WSI's defining characteristic is that it conducts biomedical research on a scale that few other organisations can match. Institute researchers and their collaborators capitalise on high-throughput sequencing and informatic pipelines and the Institute's skills in DNA sequencing to produce new understanding and resources that are widely shared with the worldwide research community. The Doyle group, within the Parasites and Microbes Programme at WSI, uses genomic approaches to understand the mechanisms by which helminths have become successful parasites and to characterise their potential for future adaptation. Research includes population genomic analyses of human (eg. *Onchocerca volvulus, T. trichiura, Schistosoma mansoni, Dracunculus medinensis*) and veterinary infective helminths (eg. *Haemonchus contortus, Teladorsagia circumcincta, Dirofilaria immitis)*, genome-wide analyses of drug response including identifying causal genetic variants associated with resistance, and building and maintaining genetic resources such as reference genomes for the global parasitology community. The experience and capacity of the Doyle group led to the establishment of collaborations with ISGlobal to validate protocols for STH genome sequencing to investigate anthelmintic resistance._

Lastly, the Consortium includes one organization that is not automatically eligible for EU funding. Bridges to Development is a non-profit organization based, Switzerland since 2018. Bridges to Development will contribute to the partnership as an associated partner, due to the fact that Switzerland is not yet an affiliated country to the European Commission. Of the total project budget of 4.351.002,25 EUR, 797.500 EUR is related to the costs of Bridges, and this contribution would be covered by the Swiss government. The Bridges team members bring unique experience accelerating new interventions from R&D into use in public health programmes in low and-middle income countries. As demonstrated on Form A, team members have played roles similar to those proposed here for medicines, vaccines and diagnostics. The team also brings a proven expertise working with pharma and leading public-private product development partnerships.

The new consortium member, Bridges, is headquartered in Geneva and has proximity to WHO and policy makers and is currently serving as the Secretariat for the Immunization Agenda 2030 (IA2030) for WHO. One of Bridges Managing Partners, Dr Julie Jacobson, is the Chair of the WHO Strategic and Technical Advisory Groups Working Group on Monitoring Evaluation and Research which puts the team in close contact with WHO NTD staff and enables a high level of awareness of WHO processes and procedures across multiple NTDs. In addition, Dr Jacobson has been a member of the Scientific and Technical Advisory Board (STAB) of the original STOP project. The Bridges team has experience in accelerating the introduction of a new combination therapy (IDA) for lymphatic filariasis into country programmes. This work provides the knowledge necessary to navigate and strategize how to work with the WHO to have a new more effective and efficient treatment for NTDs brought into the WHO guidelines. This experience has recently been published in a journal supplement on the accelerated policy development and implementation process. (24) Bridges will lead the work focused supporting country-level decision-making on introduction of the FDC in close partnership with WHO by packaging and providing evidence for guidance to countries. The Bridges team has a strong and trusted relationship with partners and a commitment to supporting the achievement of the WHO NTD Roadmap goals through their work which makes them a neutral broker between those that produce new products or strategies and those that could benefit from them.

One of the key factors for the success of this project is that, thanks to the composition of the Consortium, it can provide long-term exploitation of the product. The Consortium has the ultimate goal of having WHO guidance on use of the FDC in STH programmes. There is growing concern with the current model relying on donations of anthelmintics for programmes as not promoting country ownership and not being sustainable. There is also the recognition that: (1) current donations are insufficient for the newly incorporated target for anthelmintics of women of reproductive age (WRA); and (2) the elimination goals will not be achieved with monotherapy particularly where *trichuriasis* and strongyloidiasis are issues. There is a renewed interest in strategies for control plans beyond the drug donations; which includes clearer paths for WHO-PQ of generics through innovative technical partnerships. (3) Having high quality generic producing partners is essential to moving beyond the donation model. Making use of the regulatory approval expertise of Liconsa, the Consortium will be submitting the research and development plan of the FDC to the European Medicines Agency (EMA) evaluation through the regulations of Article 58, No 726/2004. This special programme of EMA in cooperation with the WHO can provide scientific opinions on high priority human

medicines that are intended exclusively for markets outside of the European Union (EU). The aim of this procedure is to facilitate patient access to essential medicines in low- and middle-income countries, including new or improved therapies for unmet medical needs, which are intended to prevent or treat diseases of major public health interest. The project requires a commercial partner to undertake this activity and to take on the responsibility of ongoing production of FDC and provision to the market.

4. Ethics Self-assessment

4.1. Ethical dimension of the objectives, methodology and likely impact

Research with human participants: The aim of the proposal is to evaluate the safety of a new treatment for STH human infection.
Recruitment of volunteers for social or human sciences research: The aim of the proposal is to evaluate effectiveness of a new treatment for STH human infection.
Recruitment of healthy volunteers for medical studies: It is planned to recruit healthy volunteers.
Research with patients: It is planned to recruit school age children with a STH infection.
Research with vulnerable individuals or groups: It is planned to recruit children above 4 years old.
Research with children or minors: It is planned to recruit children above 4 years old.
Research with persons unable to give informed consent: It is planned to recruit children above 4 years old.
Research involving physical interventions on the study participants: It is planned to administer treatment to participants.
Research involving invasive techniques: It is planned to take blood samples from participants.
Research involving collection of biological samples: Stool samples are needed to evaluate effectiveness.
Research involves conducting a clinical study as defined by the Clinical Trial Regulation (EU 536/2014): This study is a clinical study as defined by the Clinical Trial Regulation as it is using pharmaceutical products.
Research is a clinical trial: This research is a clinical trial.
Research is a low intervention clinical trial: This research is a low intervention trial as parts of the trial are carried out by already established country programmes rather than clinical trial staff. The trial is based in “real-world” programmes as opposed to high intervention controlled randomized clinical trials.
Research involving personal data collection and/or processing: Personal data such as age or body weight are needed.
Research involving the collection and/or processing of special categories of personal data: Sensitive personal data is needed such as health status in order to determine if the children have an STH infection.
Research involves processing genetic, biometric and health data: This research will analyse the genetic material of STH.
Research involves profiling, systematic monitoring of individuals, or processing of large scale of special categories of data or intrusive methods of data processing: Monitoring of adverse effects will be carried out at the schools with active surveillance during the first 2 days and passively through sentinel hospitals through the full week after the MDA.
Research involving further processing of previously collected personal data (secondary use): It will be used data of the census (demographic surveillance system) previously collected, in case the census is available.
Research involving the importation of personal data from non-EU countries into the EU or from non- EU countries to another non-EU country: Data will be exported from Kenya and Ghana and imported into Spain and UK. This includes personal and health data as well as parasite DNA.
Research involving activities to be carried out in non- EU countries: Research carried out in Kenya and Ghana.
Research involving non-EU countries raise potential ethical issues: The administration of an experimental drug in children could potentially be seen as an ethic issue. However, besides the fact that the two drugs used in the study (albendazole and ivermectin) have been safely used in millions of people worldwide, safety and pharmacokinetic studies of high doses of ivermectin are being conducted before the beginning of this project. There is evidence of the absence of interaction when combining albendazole with ivermectin. Local IRBs will be involved to evaluate all clinical studies involving human subjects.
Research planning to use local resources (e.g. animal and/or human tissue samples, genetic material, live animals, human remains, materials of historical value, endangered fauna or flora samples,etc.) This research study will use human stool samples.
Research project planning to export any material (other than data) from the EU to non-EU countries: Parasite eggs and DNA of STH´s will be imported for further processing into UK.

Study will use material (other than data) from the EU to non-EU countries: The fixed dose combination will be exported from Spain to the non-EU countries where the study/ies are to be planned.
Research in low and/or middle-income countries with benefits sharing actions planned: The outcome of this project benefit directly the populations affected by intestinal parasites in endemic countries in sub-Saharan Africa, with the ultimate aim of approving a new treatment for STH´s.
Research that, considering the situation in the country, puts the individuals taking part in the research at risk: We do not anticipate major risks in this section. However, we cannot disregard possible risks related to conducting field work in remote and areas that could be especially vulnerable to a possible adverse situation in the country.

4.2. Compliance with ethical principles and relevant legislations

Research studies in Ghana and Kenya are regulated by both international and national legal and ethical rules. In each centre, national legal and ethical requirements will be fullfilled. The candidate is aware and will conform to the International, European and National legislations in all the various aspects of the research as detailed below.

The candidate project is aware of further relevant guidance and codes, including:

- The Revised Declaration of Helsinki in its last version of 2013.
- The convention for the protection of human rights and dignity of human being with regard to the application of biology and medicine called the "Convention on Human Rights and Biomedicine" (Council of Europe, 1997) and its additional protocol on biomedical research (2005).
- The Recommendation Rec (2006)4 of the Committee of Ministers to member states on research on biological materials of human origin (Council of Europe) are the main international guidelines for medical research.
- The Spanish Law on Biomedical Research (14/2007, of 3rd July) which regulates biomedical research in Spain.
- The charter of Fundamental rights of the EU Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to processing of personal data and on the free movement of such data.
- UN Convention on the Rights of the Child (1990).
- The Royal Decree (RD) that establishes the basic requirements for the authorisation and functioning of biobanks with biomedical research purpose and for the processing of human samples and regulating the functioning and organisation of the National Register of Biobanks for Biomedical Research (1716/2011, of 18th November).
- The New Brunswick Declaration: A Declaration on Research Ethics, Integrity and Governance resulting from the 1st Ethics Rupture Summit, Fredericton, New Brunswick, Canada (2013).
- The Respect Code focused in socio-economic research (http://www.respectproject.org).
- The Code of Ethics of the Spanish Sociological Association provides guidelines for social research, which are the same as the guidelines in the Code of Ethics of the International Sociological Association (http://www.isa-sociology.org/about/ isa_code_of_ethics.htm).

We have reviewed the guidance available on the webpages:

- http://ec.europa.eu/research/participants/docs/h2020-funding-guide/cross-cutting-issues/ethics_en.htm
- http://ec.europa.eu/research/science-society/index.cfm?fuseaction=public.topic&id=1433

ISGlobal is bond to the Hospital Clínic Ethics Committee (Clinical Research Ethics Committee of the Hospital Clínic de Barcelona, created and accredited for the first time on November 11th, 1993 by the General Direction of Health Resources of the Department of Health of the Government of Catalonia, in accordance with the Order of 26 October 1992). The Hospital Clinic CEIC evaluates all research protocols in humans conducted by ISGlobal researchers. According to Spanish regulations, our local Ethic Committee will follow the implementation of the study by giving its approval to every protocol (including Participant Information Sheet and Consent Form) that will be developed through the study. All ISGlobal researchers are self-regulated by the Code of Good Scientific Practice (http://www.isglobal.org/en/research/what-we-do)

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6. Info on Clinical studies

1. Description of the clinical study

1.1. Title, acronym, unique identifier (e.g. EudraCT Number[1], or identifier from ISCRTN[2], ClinicalTrials.gov[3] if available) of the clinical study.

An open-label pragmatic trial to evaluate the safety and effectiveness of a single-dose of an oro-dispersibleAlbendazole-Ivermectin co-formulation vs Albendazole single-dose for the treatment of Soil-Transmitted Helminth Infections (*Trichuris trichiura*, hookworm, *Strongyloides stercoralis*) in Paediatric Subjects.

Study is not yet registered and consequently there is not unique identifier available. This is one of the deliverables (2.1) within WP2.

1.2. Study rationale

Current WHO guidelines for STH call for controlling morbidity through mass drug administration (MDA) of the benzimidazole-class anthelmintics - albendazole (ALB) and mebendazole (MBZ), mainly to pre-school children (PSAC), school-aged children (SAC) and women of reproductive age.

The first and main target of WHO included in the 2021-2030 roadmap for STH is to achieve and maintain elimination of STH morbidity in PSAC and SAC. This target is defined as a reduction in the prevalence of STH in areas with moderate to heavy infections to below 2%. To achieve this, MDA with benzimidazoles is the cornerstone of the strategy. However, there are increasing concerns that the ongoing success of these programs is at risk due to the almost complete reliance on a single drug treatment strategy. Although the widespread use of these drugs appears effective at controlling *A. lumbricoides* and hookworms, they are less effective against *T. trichiura* and *S. stercoralis*. In addition, the efficacy of benzimidazoles against STH seems to have further decreased in recent years, particularly against *T. trichiura* (5). One hypothesis is that the widespread and frequent use of benzimidazole monotherapy has led to the selection of anthelmintic resistant populations of parasites. If true, the evolution of STH resistance to MDA treatment is a significant threat to the progress made to date and to future plans of transmission interruption.

Given the low efficacy of current treatment regimens against *T. trichiura* and *S. stercoralis*, and the risk of developing anthelmintic resistance by relying on monotherapy, combination therapy with existing drugs with complementary but different modes of action is a possible solution. The co-administration of ivermectin (IVM) and ALB has been evaluated as a potential alternative to ALB alone for the treatment of STH (7,8). This new approach has repeatedly shown improvements in efficacy in trichuriasis treatment compared to the current standard treatment (ALB 400 mg), reaching cure rates close to 90% when IVM was administrated at higher doses (600 µg/kg) (9). Furthermore, IVM is the drug of choice to treat strongyloidiasis, providing the combined treatment the added benefit of targeting all STH species with improved efficacy (4,10).

Currently, IVM is administered on either a weight-based, height-based or age-based dosing schedule, which makes MDA campaigns more complicated due to the need to measure individual-based parameters before administration and may result in inaccurate dosing (11). A fixed-dose formulation (FDC) of IVM and ALB has the potential to simplify drug administration during MDA and prevent underdosing of IVM. Both drugs possess complementary pharmacokinetic properties that make them ideal for co-formulation. An FDC will likely have additional, immediate benefits over conventional treatment strategies. The shipping and distribution of FDC in integrated control programmes are likely to be significantly more cost effective compared with the delivery of two individual drugs for MDA. Previous use of FDC to treat other diseases like tuberculosis, HIV, or malaria, have resulted in an increased therapeutic efficacy, reduced pill burden, improved adherence, and prevented the emergence of drug resistance. Together, these factors will contribute to achieving greater community-wide coverage and, therefore, improved control when using an FDC.

1.2.1 Extent and evaluation of current knowledge directly linked to the scientific question(s) to be answered by the clinical study

Our group, the "Stop Transmission of intestinal parasites" (STOP) consortium, developed and tested a combination tablet of fixed-dose ivermectin (9 mg or 18 mg) and albendazole (ALB: 400mg) (FDC) as a single dose (FDCx1) or three-day regimen (FDCx3). These co-formulations are being evaluated as part of an adaptive study phase II/III superiority trial (called the ALIVE trial) that focuses on measuring safety and efficacy of the FDCx1 and FDCx3 treatment arms against ALB (400 mg) alone. The ALIVE trial protocol has been also published (NCT05124691) (14). As a preliminary step, members of our team conducted a phase I clinical trial with 54 healthy adult volunteers who sequentially received 2 experimental treatments using a new 18 mg ivermectin tablet in a fixed-dose strategy of 18 and 36 mg single dose regimens, compared to the standard, weight-based µg/ 150±200 /kg, regimen (15). This study was designed to evaluate the safety and pharmacokinetic profile of the 3 dosing regimens. Safety data showed no significant differences between regimens and no serious adverse events and was one of the main pillars to demonstrate that IVM can be safely given in fixed doses. In addition, it was observed that the two experimental treatments of 18 mg and 36 mg, showed higher systemic bioavailability compared to the weight-based 150±200 µg/kg regimen.

A study focusing on the comparative bioavailability of FDC versus each of its components was funded by Liconsa Labs and carried out by the STOP Consortium. This study demonstrated that adequate drug exposure to pursue safety and efficacy goals was achieved, though bioequivalence versus ALB alone was not shown; although provided no PK/PD data has been established for antihelmintics against STH, a Scientific Advise with EMA defined that the data was adequate to progress to Phase II/III trials (16).

The Phase II component of the ALIVE randomized clinical trial was completed in March 2022 and evaluated the safety of the FDCx1 and FDCx3 compared to ALB alone. The safety analysis included 127 participants in three different weight groups. No alterations in vital signs or serious adverse events (SAE) were observed in any of the participants. A total of 35 adverse events (AE) of mild severity were recorded in 27 participants. The most common AEs were abdominal pain and diarrhoea. All AEs resolved without medical intervention within 48 hours. There was no significant difference in the frequency of total or related AEs among the different treatment arms (Table 1).

Table 1: Summary of adverse events in Phase II ALIVE trial (n=127)

	ALB (n=27)	FDCx1 (n=49)	FDCx3 (n=51)	FDCx1 and FDCx3 (n=100)	Total
Abdominal pain	**1**	**5**	**7**	**12**	**13**
Diarrhea	**1**	**2**	**6**	**8**	**9**
Nausea	**1**	**1**	**2**	**3**	**4**
Vomiting	**0**	**1**	**1**	**2**	**2**
Stomach Ache	**0**	**0**	**1**	**1**	**1**
Toothache	**1**	**0**	**0**	**0**	**1**
Rhinitis	**1**	**0**	**1**	**1**	**2**
Fever	**0**	**1**	**0**	**1**	**1**
Nasal congestion	**0**	**1**	**0**	**1**	**1**
Upper respiratory tract infection	**0**	**1**	**0**	**1**	**1**
Total AEs	**5**	**12**	**18**	**30**	**35**
Total related AEs	**3**	**10**	**13**	**23**	**26**
Total subjects with at least 1 AE	**5 (19%)**	**10 (20%)**	**12 (24%)**	**22 (22%)**	**27**
Total subjects with at least 1 related AE	**3 (11%)**	**8 (16%)**	**9 (18%)**	**17 (17%)**	**20**
Fisher exact test against ALB	**-**	**0.40**	**0.34**	**0.34**	**-**

Following the DSMB clearance, the Phase III component of the trial started in May 2022 and is scheduled to complete recruitment in March 2023. Its objective is to evaluate the efficacy of the FDCx1 and FDCx3 compared to ALB alone, specifically for the treatment of *T. trichiura,* but also for hookworms, and *S. stercoralis*. An interim analysis was recently conducted and, in the population recruited so far a good safety profile and higher cure rates and egg reduction rates (ERR) for *T. trichiura* infections are observed in the FDCx1 and FDCx3 treatment arms compared to ALB alone (Table 2).

Table 2. Preliminary cure and Egg Reduction Rates by Treatment Arms in ALIVE clinical trial (n=465)

***T. trichiura* infections (n=465)**			
	ALB	**FDCx1**	**FDCx3**
Positive before treatment	95	184	186
Cured after treatment	29	148	182
Cure rate (CI 95%)*	30.5% (22.1,40.3)	80.4% (74.1,85.5)	97.8% (94.6,99.1)
P value (vs ALB)**		P<0.0001	P<0.0001
P value ** (vs FDCx1)	P<0.0001		P<0.0001
Baseline Mean EPG (IC 95%)*	387 (-174,66)	438 (-264,684)	361 (-230,545)
Anova (Welch correction) Baseline EPG	P=0.89		
Mean EPG at 21 days post_treatment (IC 95%)*	177 (-105,258)	21 (-10,39)	1 (-0,2)
Anova (Welch correction) EPG at 21 days post_treatment	P<0.00001		
Tukey Test EPG at 21 days post_treatment (vs ALB)		P<0.00001	P<0.00001
Tukey Test at 21 days post_treatment (vs FDCx1)	P<0.00001		P=0.52
Arithmetic mean ERR (CI 95%)*	54.2%(44.6,59.7)	95.1%(94.4,96.5)	99.7% (99.6,99.9)
Hookworm infections (n=60)			
	ALB	**FDCx1**	**FDCx3**
Positive before treatment	13	25	22
Cured after treatment	11	18	22
Cure rate (CI 95%)*	84.6% (57.8-95.7)	72.0% (52.4-85.7)	100% (85.1-100)
P value (vs ALB)**		P=0.45	P=0.13
P value ** (vs FDCx1)	P=0.45		P=0.01
Baseline Mean EPG (IC 95%)*	408 (80-838)	244 (134-388)	202 (101-339)
Anova (Welch correction) Baseline EPG	p=0.63		
Mean EPG at 21 days post_treatment (IC 95%))*	40 (0-100)	24 (6-44)	0
Anova (Welch correction) EPG at 21 days post_treatment	p=0.59		

Arithmetic mean ERR ((CI 95%)*	90.0% (88.0-100)	90.4% (88.7-95.3)	100

*95% CIs were calculated using bootstrap resampling methods with 500 replicates.
**Fisher exact test

The current proposal builds on our previous experience with the clinical development plan of the FDC and is aiming at evaluating safety with a larger sample of participants, and effectiveness, to guide the policy process for the control and elimination of STH.

1.2.1.1. Outcomes (efficacy, safety) of completed and number of ongoing clinical studies utilising the same intervention in the same indication (including review of public registers)

A series of clinical trials have been developed and conducted by our team in the recent years to provide robust evidence of the use of FDC:

- **Safety and pharmacokinetic profile of fixed-dose ivermectin with an innovative 18mg tablet in healthy adult volunteers (DOI:10.1371/journal.pntd.0006020)**
  We conducted a phase I clinical trial with 54 healthy adult volunteers who sequentially received two treatments using 18 mg IVM tablet in a fixed-dose strategy of 18 and 36 mg single dose regimens, compared to the standard, weight based 150–200 μg/kg, regimen. Volunteers were recruited in 3 groups based on body weight. Plasma concentrations of ivermectin were measured through HPLC up to 168 hours post treatment. Safety data showed no significant differences between groups and no serious adverse events. Pharmacokinetic parameters showed a half-life between 81 and 91 h in the different treatment groups. When comparing the systemic bioavailability (AUC0t and Cmax) of the reference product (WA-ref) with the other two study groups using fixed doses, we observed an overall increase in AUC0t and Cmax for the two experimental treatments of 18 mg and 36 mg. Body mass index (BMI) and weight were associated with t1/2 and V/F, probably reflecting the high liposolubility of IVM with longer retention times proportional to the presence of more adipose tissue. Systemic exposure to ivermectin (AUC0t or Cmax) was not associated with BMI or weight in our study.

- **Pharmacokinetic Characterization and Comparative Bioavailability of an Innovative Orodispersible Fixed-Dose Combination of Ivermectin and Albendazole: A Single Dose, Open Label, Sequence Randomized, Crossover Clinical Trial in Healthy Volunteers (DOI: 10.3389/fphar.2022.914886).**
  The aim was to characterize pharmacokinetics and to evaluate the comparative bioavailability of an innovative fixed-dose combination of IVM/ALB 18/400 mg compared with the marketed references. Seventy-eight healthy volunteers were included in this laboratory-blinded, randomized, three-treatment, three-period crossover study. Each subject received a single dose of IVM/ALB 18/400 mg (1 tablet); IVM 3 mg (6 tablets); and ALB 400 mg (1 tablet). Serial blood samples for the pharmacokinetic analysis were obtained pre-dose and up to 72 h post-dose. Plasma concentrations of ivermectin H2B1a, IVM H2B1b, ALB, and albendazole sulfoxide (ALBSO) were analyzed by LC-MS/MS. Pharmacokinetic parameters were estimated by a non-compartmental analysis and bioavailability compared through a bioequivalence analysis. Safety and tolerability were assessed throughout the study. Main pharmacokinetic parameters of the fixed combination were estimated for both, IVM [Cmax (mean, confidence interval): 86.40 (30.42-39.23) ng/ml; AUC0-72 (mean, CI): 1,040 (530-1,678) ng·h/mL; tmax (median, min., and max.); 4.50 (2.50-5.50)] and ALB [Cmax (mean, CI): 22.27 (1.89-111.78) ng/ml; AUC0-72 (mean, CI): 94.65 (11.65-507.78) ng·h/mL; tmax (median, min., and max.): 2.50 (1.00-12.00) h]. The 90% confidence interval of the geometric mean ratios demonstrated the bioequivalence in the case of IVM (Cmax: 110.68%-120.49%; AUC0-72: 110.46%-119.60%) but not in the case of ALB (Cmax: 53.10%-70.34%; AUC0-72: 61.13%-76.54%).

- **ALIVE Phase II Adaptive randomized, superiority trial to compare the safety of the active control arm (current standard of care, single dose of 400 mg ALB) against two experimental arms (single day or three-day single dose FDC of ALB+IVM).**
  We conducted a phase II clinical trial with 127 individuals aged between 5 to 17 years in Kenya from February to March 2022. Individuals were sequentially recruited into three weight groups to determine safety as a primary outcome and efficacy as a secondary outcome result of an ALB-IVM fixed-dose combination (FDC) (ALB-IVM) administered as single dose (FDCx1) or 3-day regimen (FDCx3) compared to ALB. No

severe adverse events or alterations in vital signs were observed in the treatment arms and the frequency of total and related adverse effects did not present significant differences between the three treatment arms. Most related adverse events in all treatment arms were gastrointestinal. The efficacy analysis showed statistically significant higher cure rates and higher egg reduction rates (ERRs) for the FDCx1 and FDCx3 treatment arms with respect to ALB.

- **ALIVE Phase III Adaptive randomized, superiority trial to compare the efficacy of the active control arm (current standard of care, single dose of 400 mg ALB) against two experimental arms (single day or three-day single dose FDC of ALB+IVM).**
  Phase III started in May 2022 and will end in March 2023, being its objective the evaluation of the efficacy of the FDCx1 and FDCx3 compared to ALB for the treatment mainly of *T. trichiura*, but also hookworms, and *S. stercoralis*. In the population recruited so far (n=465) in Kenya, higher cure rates and ERR for *T. trichiura* infections are observed in the FDCx1 and FDCx3 treatment arms compared to ALB.

1.2.1.2. Level of evidence related to the mechanism of action of the intervention in the planned clinical study population

The evidence for the use of ALB and IVM is rather large. Albendazole acts on STH by its inhibitory effect on tubulin polymerization which results in the loss of cytoplasmic microtubules. IVM binds selectively and with high affinity to glutamate-gated chloride ion channels in invertebrate muscle and nerve cells of some parasites. There is increasing evidence of the very good safety profile and increased efficacy of the combination of both drugs for the treatment of STH, as described above. This treatment is usually delivered in mass drug administration campaigns that have shown over the years the capacity to reduce prevalence and intensity of STH infections for morbidity control.

1.3. Objective(s) of the clinical study

Primary objective

- To evaluate and compare safety of a FDC against ALB alone via MDA in two study areas in Kenya and Ghana.
-

Secondary objectives

- To evaluate the effectiveness of one round of MDA with FDC compared to ALB against STH (*T. trichiura*, *A. lumbricoides*, hookworms) by microscopy
- To evaluate the effectiveness of one round of MDA with FDC compared to ALB against *S.stercoralis* by serology.

1.4. Characteristics of the study population (size, age group, sex distribution, inclusion and exclusion criteria)

The main target population of this trial are school-aged children, currently prioritized by the WHO strategy and currently included in the national STH-control program in each country (19).

The study population will be all school-aged children (both male and female) ageing more than 5 years old and weighting more than 15 kg attending primary and secondary schools in the study area.

This pragmatic trial will be implemented by the Ministries of Health of both countries through the Ghana Health Services, in Ghana, and the Kenyan Medical Research Institute/Eastern and Southern Africa Centre of International Parasite Control (KEMRI ESACIPAC), in Kenya, through respective national deworming programmes targeting schools in the study area. Thus, no specific inclusion and exclusion criteria are needed since this will be generating real world evidence through the existing programme. Consequently, inclusion and exclusion criteria are those applying to MDA programmes.

1.4.1 Details on sample size and power calculation

The sample size was estimated to detect a frequency of severe adverse events (p0) of 1/3000. Since this frequency is less than 0.02, we use the zero-patient method to estimate the necessary sample size (n) with a one-sided significance level of 0.05, as follows: n= 3/p0, giving a total of 10000 participants per treatment arm. Considering that on average schools have 450 SACs in Kenya and Ghana, 23 schools are required per treatment arm.

To measure effectiveness, stool samples will be collected in each school at different time points. We assume that the baseline prevalence of STH in the study sites will be 30%, that the ALB has an average efficacy of 69% for the three STH (A. lumbricoides CR: 96%, hookworms Cr: 80%, and Cr: 31%), and we expect the same cure rates for hookworm and A. lumbricoides and higher cure rates for T. trichiura (CR=72%) in schools treated with FDC, so the FDC would have an average efficacy of 83% for the three STH. Therefore, after one month of treatment we expect a prevalence of 9% in the ALB arm and 5% in the FDC arm. To measure the difference in difference: of the reduction in prevalence in schools treated with FDC vs. reduction in prevalence in schools treated with ALB, 2001 children per treatment arm are required (significance level=0.01) at each time point. These children will be divided among the 23 schools, and 87 children will be recruited at each school.

1.5. Design of the clinical study (controlled / uncontrolled; randomised; open / blinded; parallel group / cross over / other; please justify the appropriateness of the selected design)

The ALIVE trial is a phase II/III trial designed to provide the highest quality information on the efficacy and safety of the FDC in a controlled environment with registration purposes. This trial is now ongoing but preliminary results support the evidence of a good safety profile and a good efficacy to treat STH. We aim now to validate the benefits of the FDC through a pragmatic trial in a real program context, to evaluate effectiveness and the safety profile in a large population of participants.

We have designed an open-label cluster randomized pragmatic trial to evaluate safety and effectiveness of a treatment regimen of FDC to treat STH (including *S. stercoralis*) compared to the standard single-dose ALB 400 mg in children attending primary schools in *T. trichiura* transmission settings.

1.6. Type of intervention (medicinal product / advanced therapy medicinal product / medical device / in vitro diagnostic medical device / surgical or other invasive procedure / other medical intervention, including, e.g., counselling)

Two interventions will be included in this study: Albendazole is the standard of treatment, recommended by WHO and used by most countries having deworming programmes, and the oro-dispersible fixed-dose formulation (experimental product), manufactured by Laboratorios Liconsa SA.

Schools participating in the study will be randomized to receive either:

1. ALB: 400 mg single dose
2. FDC: IVM/ALB single dose:
    a. 9/400 mg to subjects <45 kg body-weight
    b. 18/400 mg to subjects >= 45 kg body-weight

1.7. Description and timing of study procedures

Participants in the trial will be school-aged children more than 5 years old attending primary and secondary schools in the study area. Participants will be recruited and followed up for:

- Safety component: Study pharmacovigilance (collection of adverse events) will be active for 7 days after treatment allocation. Effectiveness component: Follow-up visits will be conducted to participants contributing to the effectiveness outcomes at month +1 and +11 post treatment allocation.

Procedures	Visit 0 Day-30 to -1	Visit 1 Baseline Day 0-7	Visit 2 Day 21-30	Visit 3 Month1	Visit 4 Month11	Withdrawal
School information and sensitization	X					
Randomization and treatment assignation	X					
Informed consent (effectiveness participants)	X					
Informed assent (effectiveness participants)	X					
Deworming campaig (study treatment administration)		X				
Pharmacovigilance (collection of Aes)		X				
Stool collection (effectiveness participants)	X		X	X	X	X
Stool analysis (effectiveness participants)	X		X	X	X	X
Dried blood spot (effectiveness participants)	X					

2. Preparedness status

2.1 Development of the clinical study protocol

2.1.1 Scientific advice from regulatory and health technology assessment bodies

A scientific advice from regulatory bodies for the coming study is not foreseen since not required for registration purposes. It was performed though for the current registration safety and efficacy ALIVE trial for the STOP and STOP2. Along the development of the FDC, we have worked hand in hand with EMA Scientific Advice.

The clinical study outlined in this proposal will provide additional evidence at larger scale to demonstrate the public health benefit from a safety and effectiveness standpoint to stakeholders and decision makers in local African communities and beyond, to advance the usage of this new, more convenient, and more efficient therapy that is as safe as current standards of care once it´s formally registered.

2.1.1 Clinical efficacy, safety, and methodological guidelines (including guidelines on statistics)

Declaration of Helsiniki, in its last version, Good Clinical Practice and applicable local law will be implemented in this study.

2.1.2 Involvement of citizens / patients, carers in drawing up the clinical study protocol

Citizens / patients or carers are not planned to participate in drawing up the clinical study protocol.

Study protocol will be prepared by ISGlobal jointly with other Consortium team members where Ministries of Health of both countries through the Ghana Health Services, in Ghana, and the Kenyan Medical Research Institute/Eastern and Southern Africa Centre of International Parasite Control (KEMRI ESACIPAC), in Kenya are involved and will support WP2, namely the Task 2.1. Trial design, implementation, and coordination.

2.2 Regulatory intelligence to ensure timely regulatory approval and ethics clearance of the clinical study in all jurisdictions where its implementation is planned.

As in GCP, the sponsor is responsible for obtaining regulatory and ethical clearance. As part of the Consortium we are working with local partners in both the countries and they can support in ensuring timely approval and clearance within the stablished timelines per country.

The Sponsor and its partner ISGlobal have a long and extensive expertise in clinical trials.

2.2.1 How the consortium will ensure access to regulatory expertise necessary to get advice on, and management of, regulatory affairs activities in all concerned jurisdictions?

This consortium integrates expertise in regulatory processes with a pharmaceutical company, namely Laboratorios Liconsa S.A. being part of the Consortium.

Laborarorios Liconsa, S.A. ("Liconsa"), part of InsudPharma Group, have access to the necessary team staff to support the STOP2030 Project, including but not limited to a regulatory affairs team that has been involved already to align the development for future filling of dossier for obtaining a Marketing Authorization. Contact with European regulatory agencies have already been initiated and in fact three Scientific Advices did happen with EMA to discuss with them about the best regulatory pathway and to discuss the clinical development of the proposed drug.

Our group has regulatory experience not only in Europe, but also in additional jurisdictions, including the United States, where we managed to register and approved Benznidazole, being the first drug ever registered by the US FDA to treat Chagas disease and also, we did achieve WHO prequalification of ivermectin, being developed and registered by Liconsa.

2.2.2. How the consortium will ensure access to ethics expertise necessary to get advice on current proceedings and documentation requirements of all concerned ethics committees?

Liconsa, as part of InsudPharma Group, has a long and extensive experience in the management of world-wide clinical trials and also ISGlobal, that as well provides significant experience in this field.
For this study, ethical clearance will be obtained from the respective institutions and national regulatory agencies as per standard procedures for each trial center in Kenya and Ghana. The ethical clearance will be also obtained from the coordinating centre: The Barcelona Institute for Global Health, that shares a joint IRB with the Hospital Clínic de Barcelona. This institution has a broad experience in proceedings and documentation requirements for international trials.

Furthermore, the scientific and technical advisory board (STAB) of the project will be composed by a small group of renowned researchers and policy-makers in the field of neglected tropical diseases. We will ensure the appointment of an Ethics Mentor in the STAB to monitor and provide advice to the project participants on ethics issues.

2.3 How the scientific and operational governance of the clinical study will be ensured?

2.3.1 Please give details about the sponsor(s) (name, type of entity, seat or country of residence).

On behalf of the consortium, the sponsor will be:
Laboratorios Liconsa SA.
Avda.Miralcampo, 7
19200 Azuqueca de Henares. (Spain)
Tel: +34 949 349 700

2.3.2 Please describe the composition, the role and the functioning of the planned board(s), governing bodies.

The team in ISGlobal will be responsible of the overall scientific leadership of the trial, coordinating and supporting the different teams involved in the study to accomplish trial activities.
The study will have:

- A Data Safety Monitoring Board (DSMB), which main responsibilities are to
  (1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, including efficacy, and
  (2) make recommendations to the investigators concerning the continuation, modification, or termination of the trial. The DSMB will consider study-specific data as well as relevant background knowledge STH, study drugs and the population under study. Members of the DSMB will include 3 independent members with expertise in the study drugs and STH. Reports to the DSMB will be performed by the trial statistician and will have an independent statistician upon request.
- A scientific and technical advisory board (STAB) to ensure the appointment of an Ethics Mentor to monitor and provide advice to the project participants on ethics and strategic issues.

3. Operational feasibility

3.1 Please describe how the availability of the intervention(s) (including comparators) is secured throughout the entire implementation phase (give details on manufacturing, packaging / labelling operations, storage, logistical, import/export issues, etc.)

Insud Pharma Group and, in particular, Laborarorios Liconsa, S.A. ("Liconsa") is especially well suited to this project due to our expertise in the development of drugs, including innovative fixed-dose combinations. As examples, in the last years the Group has developed and marketed new formulations of Ivermectin (EMA, WHO) and Benznidazol (FDA).

We have access to the necessary facilities to support the Stop Project, including:

- A pharmaceutical developing team with expertise in such type of drugs.
- A manufacturing pilot plant to develop the formulation and methods validation (including laboratory, stability, etc.).
- A manufacturing facility to manufacture the product under GMP including packaging operations.
- A QA team to assure the quality of the entire process.

Freight services, international, export, logistics, warehousing, customs services among others is guarantee through our partner Airpharm S.A.U, a freight company linked to Liconsa, specialized in the chemical-pharmaceutical sector, who can ship the product up to Kenya and Ghana.

3.2 Please describe how the study population will be recruited

Recruitment: Since the interventions will be delivered by the country's national deworming programme during the annual deworming campaign in the context of a pragmatic trial, no specific strategy for recruitment will be conducted. All school aged children attending the study schools and not having contraindications will be offered treatment with one of the two study interventions, following standard procedures of the programme.

The monitoring plan of the study will be designed, organized and coordinated by the team in ISGlobal (coordinating WP2) with the participation of the teams at KEMRI (coordinating WP3) for overall Data Management and Mundo Sano, contributing with the monitoring capacity of a physician experienced in clinical studies in SSA countries. Through the leadership of Dr Jose Muñoz (leader of WP2), the team at ISGlobal is currently in charge of the monitoring plan and activities of the registrational ALIVE trial, which is the study that serves as the basis for the implementation project of the proposal and this clinical study.

The intermediate and final reports will be shared with the trial Sponsor (Liconsa).

A number of risks and mitigation measures have been described in the proposal. The major mitigation strategies

identified with this study are related with insufficient reporting and adverse events, delay in IRB approvals, and unexpected safety issues with the experimental arms. These risks have been addressed with mitigation strategies in the corresponding section of the proposal.

3.2.1 How many clinical sites will contribute to the recruitment of the study population in which countries? Are these clinical sites part of an established clinical trial network? Please also describe the selection criteria of the clinical sites.

Two countries, two clinical sites are involved in the study, Kenya and Ghana. Each will plan to involve 23 schools.

The trial will be implemented by the Ministries of Health of both countries through the Ghana Health Services, in Ghana, and the Kenyan Medical Research Institute/Eastern and Southern Africa Centre of International Parasite Control (KEMRI ESACIPAC), in Kenya. These institutions will be working closely with the research teams for the deployment and monitoring of the intervention.

The team in Kenya is part of the STOP consortium and is also contributing with the ongoing phase II/III clinical trial of STOP. The new partner in Ghana has been selected because it is a country targeted for STH control and elimination of morbidity through the Preventive Chemotherapy strategy from WHO and counts with well-established teams at the Ghana Health Services, which can follow the proposed study and benefit from its results.

3.2.2 Will recruitment of the study population be of competitive nature between the clinical sites?

Recruitment is not expected to be competitive in the trial, for the two sites. Since the interventions will be delivered by the deworming programme at school level, a similar number of participants and schools have been assigned to each of the two participating countries.

3.2.3 What evidence supports the ability of the individual clinical sites to recruit the required number of study participants within the planned timeline (e.g. documented performance in previous clinical studies of similar complexity targeting very similar study population)?

The team at KEMRI is a member of the current STOP Consortium and has recruited already 70% of the total trial target recruitment and as a research team within the MoH, participates in the logistics of MDA activities; therefore, coordinated with the organization and timing of those activities. The TUMIKIA trial is an example of trials of similar scale carried by this group (38)

The team at GHS is integrated to the deworming activities coordinated by the MoH, with a long experience in Schisto-STH MDA activities in schools in all areas in the country

3.3 Please describe what additional supply (e.g. an electronic device for remote data capture, a specific instrument for administering the investigational product, etc.) is necessary to carry out the required study procedures and how this supply will be made available to the clinical sites

Data collection will be done in an electronic data capture system on site. These specific forms will be generated by ISGlobal (WP2) and incorporated into cell phones in collaboration with KEMRI (WP3).

3.4 Please provide plans on data management aspects (data standards, type of data capture, verification of data, central data collection, cleaning, analysis, reporting, security)

The management of the clinical data generated in this clinical study will be in charge of ISGlobal (WP2) and KEMRI (WP3) to be incorporated based in electronic data capture systems that the teams in both recruitment sites are familiar with, as is Open Data Capture (ODK)

The ODK system will allow sending data from the field in real time. Additionally, barcodes will be designed using P-Touch software and printed using Brother Barcode Printer QL-800. The barcode will be used to link all the samples collected in the field and those processed in the laboratory to the respective individuals. All data will be submitted to ODK central database for safe storage. Only key study team members will be given login credentials to the database.

Different user access rights will be assigned to each user based on their perceived roles.

After the completion of the study, all the collected experimental and field observational datasets will be anonymized and deidentified before being deposited into an open access stable public repository to enable the data and all the associated research outputs to be findable, accessible, interoperable and reusable in accordance with the FAIR principles and standards (https://fairsharing.org). We will use figshare repository (https://figshare.com) to deposit all the field-based data and a subject-specific public repository for the laboratory-based sequencing data.

3.5 Please give details on how reporting obligations (regarding study initiation, safety of study participants, ethical concerns, quality issues, integrity of data, study results) to regulatory bodies and ethics committees will be met.

The safety of the FDC will be continued to be monitored as per requirements set in the pharmacovigilance regulation of marketed products. This includes collection of adverse events, periodic safety update reports (PSUR) and monitoring in accordance with any conditions set forth in a specific Risk Management Plan (RMP). Such activities are named routine pharmacovigilance activities and the marketing authorization holder is obligated to perform such surveillance.

3.6 Please list all items of the sponsor's responsibilities (e.g. monitoring clinical sites, meeting regulatory obligations, data management, etc.) that will be supported by entities that are not part of the sponsor's organisation. Please describe how the sponsor will ensure oversight of these activities.

- Ensure that comparators are sourced from the sites from an authorized and qualified source.
- The team in ISGlobal will be responsible of the overall scientific leadership of the trial, coordinating and supporting the different teams involved in the study, same as they are doing for the current ALIVE project.
- The monitoring plan of the study will be designed, organized and coordinated by the team in ISGlobal (coordinating WP2) with the participation of the teams at KEMRI (coordinating WP3) for overall Data Management and Mundo Sano contributing with the monitoring capacity of a physician experienced in clinical studies in SSA countries.
- A data management plan will be developed for each site in coordination with the coordinating center of WP3. Sponsor, being the coordinator will stablish a Data Transfer Agreement.

3.7 What are the plans for major study milestones and what evidence supports its feasibility?

Compiling the required regulatory and ethics submission package will take us 9 months, this is based on our previous and recent experience in ALIVE project for Kenya, and on previous interactions with IRBs and regulatory authorities in Ghana.

In both the African sites where the trial will be conducted, 3 months is the average time to obtain all the approvals and clearance for the study. Once approvals in place, study can be initiated based on the MDA campaigns.

Final assessment of all study participants and analysis and reporting of the study results will be completed within 6M from database lock.

ANNEX 2

ESTIMATED BUDGET FOR THE ACTION

	Estimated eligible[1] costs (per budget category)												Estimated EU contribution[2]			
	Direct costs										Indirect costs	Total costs	EU contribution to eligible costs			Maximum grant amount[6]
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories			E. Indirect costs[3]		Funding rate %[4]	Maximum EU contribution[5]	Requested EU contribution	
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	D.2 Internally invoiced goods and services	D.3 Transnational access to research infrastructure unit costs	D.4 Virtual access to research infrastructure unit costs	E. Indirect costs					
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Actual costs	Actual costs	Actual costs	Actual costs	Unit costs (usual accounting practices)	Unit costs[7]	Unit costs[7]	Flat-rate costs[8]					
	a1	a2	a3	b	c1	c2	c3	d2	d3	d4	e = 0,25 * (a1 + a2 + a3 + c1 + c2 + c3)	f = a + b + c + d + e	U	g = f * U%	h	m
1 - Liconsa	279 805.00	0.00	0.00	0.00	60 200.00	3 160.00	34 500.00	11 734.00	0.00	0.00	94 416.25	483 815.25	100	483 815.25	483 815.25	483 815.25
2 - ISGLOBAL	564 514.00	0.00	0.00	0.00	25 000.00	1 800.00	3 000.00	0.00	0.00	0.00	148 578.50	742 892.50	100	742 892.50	742 892.50	742 892.50
3 - FMS ESPANA	127 080.00	0.00	0.00	0.00	24 800.00	0.00	47 120.00	0.00	0.00	0.00	49 750.00	248 750.00	100	248 750.00	248 750.00	248 750.00
4 - KEMRI	248 103.00	0.00	0.00	0.00	75 000.00	3 000.00	331 012.00	0.00	0.00	0.00	164 278.75	821 393.75	100	821 393.75	821 393.75	821 393.75
5 - GHS	275 400.00	0.00	0.00	0.00	218 300.00	0.00	216 300.00	0.00	0.00	0.00	177 500.00	887 500.00	100	887 500.00	887 500.00	887 500.00
6 - GRL	137 594.00	0.00	0.00	0.00	21 000.00	8 412.00	53 861.00	93 067.00	0.00	0.00	55 216.75	369 150.75	100	369 150.75	369 150.75	369 150.75
7 - Bridges																
Σ consortium	1 632 496.00	0.00	0.00	0.00	424 300.00	16 372.00	685 793.00	104 801.00	0.00	0.00	689 740.25	3 553 502.25		3 553 502.25	3 553 502.25	3 553 502.25

[1] See Article 6 for the eligibility conditions. All amounts must be expressed in EUR (see Article 21 for the conversion rules).
[2] The consortium remains free to decide on a different internal distribution of the EU funding (via the consortium agreement; see Article 7).
[3] Indirect costs already covered by an operating grant (received under any EU funding programme) are ineligible (see Article 6.3). Therefore, a beneficiary/affiliated entity that receives an operating grant during the action duration cannot declare indirect costs for the year(s)/reporting period(s) covered by the operating grant, unless they can demonstrate that the operating grant does not cover any costs of the action. This requires specific accounting tools. Please immediately contact us via the EU Funding & Tenders Portal for details.
[4] See Data Sheet for the funding rate(s).
[5] This is the theoretical amount of the EU contribution to costs, if the reimbursement rate is applied to all the budgeted costs. This theoretical amount is then capped by the 'maximum grant amount'.
[6] The 'maximum grant amount' is the maximum grant amount decided by the EU. It normally corresponds to the requested grant, but may be lower.
[7] See Annex 2a 'Additional information on the estimated budget' for the details (units, cost per unit).
[8] See Data Sheet for the flat-rate.

ANNEX 2a

ADDITIONAL INFORMATION ON UNIT COSTS AND CONTRIBUTIONS

SME owners/natural person beneficiaries without salary (Decision C(2020) 7115[1])

Type: unit costs

Units: days spent working on the action (rounded up or down to the nearest half-day)

Amount per unit (daily rate): calculated according to the following formula:

{EUR 5 080 / 18 days = **282,22**}
multiplied by
{country-specific correction coefficient of the country where the beneficiary is established}

The country-specific correction coefficients used are those set out in the Horizon Europe Work Programme (section Marie Skłodowska-Curie actions) in force at the time of the call (see Portal Reference Documents).

HE and Euratom Research Infrastructure actions[2]

Type: unit costs

Units[3]: see (for each access provider and installation) the unit cost table in Annex 2b

Amount per unit*: see (for each access provider and installation) the unit cost table in Annex 2b

* Amount calculated as follows:

For trans-national access:

$$\frac{\text{average annual total access costs to the installation (over past two years[4])}}{\text{average annual total quantity of access to the installation (over past two years[5])}}$$

For virtual access:

$$\frac{\text{total virtual access costs to the installation (over the last year[6])}}{\text{total quantity of virtual access to the installation (over the last year[7])}}$$

Euratom staff mobility costs[8]

Monthly living allowance

Type: unit costs

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1 Commission Decision of 20 October 2020 authorising the use of unit costs for the personnel costs of the owners of small and medium-sized enterprises and beneficiaries that are natural persons not receiving a salary for the work carried out by themselves under an action or work programme (C(2020)7715).

2 Decision of 19 April 2021 authorising the use of unit costs for the costs of providing trans-national and virtual access in Research Infrastructure actions under the Horizon Europe Programme (2021-2027) and the Research and Training Programme of the European Atomic Energy Community (2021-2025).

3 Unit of access (e.g. beam hours, weeks of access, sample analysis) fixed by the access provider in proposal.

4 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

5 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

6 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

7 In exceptional and duly justified cases, the granting authority may agree to a different reference period.

8 Decision of 15 March 2021 authorising the use of unit costs for mobility in co-fund actions under the Research and Training Programme of the European Atomic Energy Community (2021-2025).

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit*: see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

* Amount calculated as follows from 1 January 2021:
{**EUR 4 300** multiplied by
country-specific correction coefficient** of the country where the staff member is seconded}[9]

**Country-specific correction coefficients as from 1 January 2021[10]

EU-Member States[11]

Country / Place	Coefficient (%)
Bulgaria	59,1
Czech Rep.	85,2
Denmark	131,3
Germany Bonn Karlsruhe Munich	101,9 95,8 98 113,9
Estonia	82,3
Ireland	129
Greece	81,4
Spain	94,2
France	120,5
Croatia	75,8
Italy Varese	95 90,7
Cyprus	78,2
Latvia	77,5
Lithuania	76,6
Hungary	71,9
Malta	94,7
Netherlands	113,9
Austria	107,9
Poland	70,9
Portugal	91,1
Romania	66,6
Slovenia	86,1

[9] Unit costs for living allowances are calculated by using a method of calculation similar to that applied for the secondment to the European Commission of seconded national experts (SNEs).

[10] ⚠ For the financial statements, the amount must be adjusted according to the actual place of secondment.
The revised coefficients were adopted in the Decision authorising the use of unit costs for the Fusion Programme co-fund action under the Research and training Programme of the European Atomic Energy Community 2021-2025. They are based on the 2020 Annual update of the remuneration and pensions of the officials and other servants of the European Union and the correction coefficients applied thereto (OJ C 428, 11.12.2020) to ensure purchasing power parity. The revised coefficient are applied as from 1 January 2021 through an amendment to the grant agreement.

[11] No correction coefficient shall be applicable in Belgium and Luxembourg.

Slovakia	80,6
Finland	118,4
Sweden	124,3

Third countries

Country/place	Coefficient (%)
China	82,2
India	72,3
Japan	111,8
Russia	92,7
South Korea	92,3
Switzerland	129.2
Ukraine	82.3
United Kingdom	97.6
United States	101,4 (New-York) 90,5 (Washington)

Mobility allowance

Type: Unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit: **EUR 600** per person-month; see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

Family allowance

Type: unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit: **EUR 660** per person-month; see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

Education allowance

Type: Unit costs

Units: months spent by the seconded staff member(s) on research and training in fission and fusion activities (person-month)

Amount per unit*: see (for each beneficiary/affiliated entity and secondment) the unit cost table in Annex 2b

*Amount calculated as follows from 1 January 2021:
{EUR 283.82 x number of dependent children[12]**}**

[12] For the estimated budget (Annex 2): an average should be used. (⚠ For the financial statements, the number of children (and months) must be adjusted according to the actual family status at the moment the secondment starts.)

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FUNDACION PRIVADA INSTITUTO DE SALUD GLOBAL BARCELONA (ISGLOBAL), PIC 951414122, established in C ROSSELLO 132 PLANTA 05, BARCELONA 08036, Spain,

hereby agrees

to become beneficiary

in Agreement No 101103089 — STOP2030 ('the Agreement')

between LABORATORIOS LICONSA SA (Liconsa) **and** the **European Union** ('EU'), represented by the European Commission ('European Commission' or 'granting authority'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FUNDACION MUNDO SANO ESPANA (FMS ESPANA), PIC 885624551, established in GRAN VIA CARLOS III, 98, BARCELONA 08028, Spain,

hereby agrees

to become beneficiary

in Agreement No 101103089 — STOP2030 ('the Agreement')

between LABORATORIOS LICONSA SA (Liconsa) **and** the **European Union** ('EU'), represented by the European Commission ('European Commission' or 'granting authority'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

KENYA MEDICAL RESEARCH INSTITUTE (KEMRI), PIC 997741225, established in Off Mbagathi Way, Nairobi 00200, Kenya,

hereby agrees

to become beneficiary

in Agreement No 101103089 — STOP2030 ('the Agreement')

between LABORATORIOS LICONSA SA (Liconsa) **and** the **European Union** ('EU'), represented by the European Commission ('European Commission' or 'granting authority'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

GHANA HEALTH SERVICE (GHS), PIC 894057343, established in PRIVATE MAIL BAG MINISTRIES ACCRA, Accra, Ghana,

hereby agrees

to become beneficiary

in Agreement No 101103089 — STOP2030 ('the Agreement')

between LABORATORIOS LICONSA SA (Liconsa) **and** the **European Union** ('EU'), represented by the European Commission ('European Commission' or 'granting authority'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

GENOME RESEARCH LIMITED (GRL), PIC 999981343, established in THE GIBBS BUILDING, EUSTON ROAD 215, LONDON NW1 2BE, United Kingdom,

hereby agrees

to become beneficiary

in Agreement No 101103089 — STOP2030 ('the Agreement')

between LABORATORIOS LICONSA SA (Liconsa) **and** the **European Union** ('EU'), represented by the European Commission ('European Commission' or 'granting authority'),

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 39.

By signing this accession form, the beneficiary accepts the grant and agrees to implement it in accordance with the Agreement, with all the obligations and terms and conditions it sets out.

SIGNATURE

For the beneficiary

FINANCIAL STATEMENT FOR [PARTICIPANT NAME] FOR REPORTING PERIOD [NUMBER]

	Eligible[1] costs (per budget category)																EU contribution[2]				Revenues
	Direct costs															Indirect costs	Total costs	EU contribution to eligible costs			Total requested EU contribution	Income generated by the action
	A. Personnel costs			B. Subcontracting costs	C. Purchase costs			D. Other cost categories								E. Indirect costs[2]		Funding rate %[3]	Maximum EU contribution[4]	Requested EU contribution		
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons		A.4 SME owners and natural person beneficiaries	B. Subcontracting	C.1 Travel and subsistence	C.2 Equipment	C.3 Other goods, works and services	[D.1 Financial support to third parties]	D.2 Internally invoiced goods and services	[D.3 Transnational access to research infrastructure unit costs]	[D.4 Virtual access to research infrastructure unit costs]	*[OPTION for HE PCP/PPI:* D.5 PCP/PPI procurement costs*]*	*[OPTION for Euratom Programme Cofund Actions:* D.6 Euratom Cofund staff mobility costs*]*	*[OPTION for HE ERC Grants:* D.7 ERC additional funding*]*	*[OPTION for HE ERC Grants:* D.8 ERC additional funding (subcontracting, FSTP and internally invoiced goods and services)*]*	E. Indirect costs						
Forms of funding	Actual costs	Unit costs (usual accounting practices)	Unit costs[5]	Actual costs	Actual costs	Actual costs	Actual costs	[Actual costs]	Unit costs (usual accounting practices)	[Unit costs[5]]	[Unit costs[5]]	[Actual costs]	[Unit costs[5]]	[Actual costs]	[Actual costs]	Flat-rate costs[6]						
	a1	a2	a3	b	c1	c2	c3	[d1a]	d2	[d3]	[d4]	[d5]	[d6]	[d7]	[d8]	e = 0,25 * (a1 + a2 + a3 ~~+b+~~ c1 +c2 + c3 ~~+d1a + d2 + d3 + d4 (+ d5][+ d6]~~ [+d7] ~~[+ d8]~~)	f = a+b+c+d+e	U	g = f*U%	h	m	n
XX – [short name beneficiary/affiliated entity]																						

The beneficiary/affiliated entity hereby confirms that:

The information provided is complete, reliable and true.

The costs and contributions declared are eligible (see Article 6).

The costs and contributions can be substantiated by adequate records and supporting documentation that will be produced upon request or in the context of checks, reviews, audits and investigations (see Articles 19, 20 and 25).

For the last reporting period: that all the revenues have been declared (see Article 22).

① Please declare all eligible costs and contributions, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Only amounts that were declared in your individual financial statements can be taken into account lateron, in order to replace costs/contributions that are found to be ineligible.

[1] See Article 6 for the eligibility conditions. All amounts must be expressed in EUR (see Article 21 for the conversion rules).

[2] If you have also received an EU operating grant during this reporting period, you cannot claim indirect costs - unless you can demonstrate that the operating grant does not cover any costs of the action. This requires specific accounting tools. Please contact us immediately via the Funding & Tenders Portal for details.

[3] See Data Sheet for the reimbursement rate(s).

[4] This is the *theoretical* amount of EU contribution to costs that the system calculates automatically (by multiplying the reimbursement rates by the costs declared). The amount you request (in the column 'requested EU contribution') may be less.

[5] See Annex 2a 'Additional information on the estimated budget' for the details (units, cost per unit).

[6] See Data Sheet for the flat-rate.

ANNEX 5

SPECIFIC RULES

CONFIDENTIALITY AND SECURITY (— ARTICLE 13)

Sensitive information with security recommendation

Sensitive information with a security recommendation must comply with the additional requirements imposed by the granting authority.

Before starting the action tasks concerned, the beneficiaries must have obtained all approvals or other mandatory documents needed for implementing the task. The documents must be kept on file and be submitted upon request by the coordinator to the granting authority. If they are not in English, they must be submitted together with an English summary.

For requirements restricting disclosure or dissemination, the information must be handled in accordance with the recommendation and may be disclosed or disseminated only after written approval from the granting authority.

EU classified information

If EU classified information is used or generated by the action, it must be treated in accordance with the security classification guide (SCG) and security aspect letter (SAL) set out in Annex 1 and Decision 2015/444[1] and its implementing rules — until it is declassified.

Deliverables which contain EU classified information must be submitted according to special procedures agreed with the granting authority.

Action tasks involving EU classified information may be subcontracted only with prior explicit written approval from the granting authority and only to entities established in an EU Member State or in a non-EU country with a security of information agreement with the EU (or an administrative arrangement with the Commission).

EU classified information may not be disclosed to any third party (including participants involved in the action implementation) without prior explicit written approval from the granting authority.

ETHICS (— ARTICLE 14)

Ethics and research integrity

The beneficiaries must carry out the action in compliance with:

- ethical principles (including the highest standards of research integrity)

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[1] Commission Decision 2015/444/EC, Euratom of 13 March 2015 on the security rules for protecting EU classified information (OJ L 72, 17.3.2015, p. 53).

and

- applicable EU, international and national law, including the EU Charter of Fundamental Rights and the European Convention for the Protection of Human Rights and Fundamental Freedoms and its Supplementary Protocols.

No funding can be granted, within or outside the EU, for activities that are prohibited in all Member States. No funding can be granted in a Member State for an activity which is forbidden in that Member State.

The beneficiaries must pay particular attention to the principle of proportionality, the right to privacy, the right to the protection of personal data, the right to the physical and mental integrity of persons, the right to non-discrimination, the need to ensure protection of the environment and high levels of human health protection.

The beneficiaries must ensure that the activities under the action have an exclusive focus on civil applications.

The beneficiaries must ensure that the activities under the action do not:

- aim at human cloning for reproductive purposes
- intend to modify the genetic heritage of human beings which could make such modifications heritable (with the exception of research relating to cancer treatment of the gonads, which may be financed)
- intend to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer, or
- lead to the destruction of human embryos (for example, for obtaining stem cells).

Activities involving research on human embryos or human embryonic stem cells may be carried out only if:

- they are set out in Annex 1 or
- the coordinator has obtained explicit approval (in writing) from the granting authority.

In addition, the beneficiaries must respect the fundamental principle of research integrity — as set out in the European Code of Conduct for Research Integrity[2].

This implies compliance with the following principles:

- reliability in ensuring the quality of research reflected in the design, the methodology, the analysis and the use of resources
- honesty in developing, undertaking, reviewing, reporting and communicating research in a transparent, fair and unbiased way

[2] European Code of Conduct for Research Integrity of ALLEA (All European Academies).

- respect for colleagues, research participants, society, ecosystems, cultural heritage and the environment

- accountability for the research from idea to publication, for its management and organisation, for training, supervision and mentoring, and for its wider impacts

and means that beneficiaries must ensure that persons carrying out research tasks follow the good research practices including ensuring, where possible, openness, reproducibility and traceability and refrain from the research integrity violations described in the Code.

Activities raising ethical issues must comply with the additional requirements formulated by the ethics panels (including after checks, reviews or audits; see Article 25).

Before starting an action task raising ethical issues, the beneficiaries must have obtained all approvals or other mandatory documents needed for implementing the task, notably from any (national or local) ethics committee or other bodies such as data protection authorities.

The documents must be kept on file and be submitted upon request by the coordinator to the granting authority. If they are not in English, they must be submitted together with an English summary, which shows that the documents cover the action tasks in question and includes the conclusions of the committee or authority concerned (if any).

VALUES (— ARTICLE 14)

Gender mainstreaming

The beneficiaries must take all measures to promote equal opportunities between men and women in the implementation of the action and, where applicable, in line with the gender equality plan. They must aim, to the extent possible, for a gender balance at all levels of personnel assigned to the action, including at supervisory and managerial level.

INTELLECTUAL PROPERTY RIGHTS (IPR) — BACKGROUND AND RESULTS — ACCESS RIGHTS AND RIGHTS OF USE (— ARTICLE 16)

Definitions

Access rights — Rights to use results or background.

Dissemination — The public disclosure of the results by appropriate means, other than resulting from protecting or exploiting the results, including by scientific publications in any medium.

Exploit(ation) — The use of results in further research and innovation activities other than those covered by the action concerned, including among other things, commercial exploitation such as developing, creating, manufacturing and marketing a product or process, creating and providing a service, or in standardisation activities.

Fair and reasonable conditions — Appropriate conditions, including possible financial terms or royalty-free conditions, taking into account the specific circumstances of the request for access, for example the actual or potential value of the results or background to which access is requested and/or the scope, duration or other characteristics of the exploitation envisaged.

FAIR principles — ‘findability’, ‘accessibility’, ‘interoperability’ and ‘reusability’.

Open access — Online access to research outputs provided free of charge to the end-user.

Open science — An approach to the scientific process based on open cooperative work, tools and diffusing knowledge.

Research data management — The process within the research lifecycle that includes the organisation, storage, preservation, security, quality assurance, allocation of persistent identifiers (PIDs) and rules and procedures for sharing of data including licensing.

Research outputs — Results to which access can be given in the form of scientific publications, data or other engineered results and processes such as software, algorithms, protocols, models, workflows and electronic notebooks.

Scope of the obligations

For this section, references to ‘beneficiary’ or ‘beneficiaries’ do not include affiliated entities (if any).

Agreement on background — Background free from restrictions

The beneficiaries must identify in a written agreement the background as needed for implementing the action or for exploiting its results.

Where the call conditions restrict control due to strategic interests reasons, background that is subject to control or other restrictions by a country (or entity from a country) which is not one of the eligible countries or target countries set out in the call conditions and that impact the exploitation of the results (i.e. would make the exploitation of the results subject to control or restrictions) must not be used and must be explicitly excluded in the agreement on background — unless otherwise agreed with the granting authority.

Results free from restrictions

Where the call conditions restrict control due to strategic interests reasons, the beneficiaries must ensure that the results of the action are not subject to control or other restrictions by a country (or entity from a country) which is not one of the eligible countries or target countries set out in the call conditions — unless otherwise agreed with the granting authority.

Ownership of results

Results are owned by the beneficiaries that generate them.

However, two or more beneficiaries own results jointly if:

- they have jointly generated them and
- it is not possible to:
    - establish the respective contribution of each beneficiary, or
    - separate them for the purpose of applying for, obtaining or maintaining their protection.

The joint owners must agree — in writing — on the allocation and terms of exercise of their joint ownership ('joint ownership agreement'), to ensure compliance with their obligations under this Agreement.

Unless otherwise agreed in the joint ownership agreement or consortium agreement, each joint owner may grant non-exclusive licences to third parties to exploit the jointly-owned results (without any right to sub-license), if the other joint owners are given:

- at least 45 days advance notice and
- fair and reasonable compensation.

The joint owners may agree — in writing — to apply another regime than joint ownership.

If third parties (including employees and other personnel) may claim rights to the results, the beneficiary concerned must ensure that those rights can be exercised in a manner compatible with its obligations under the Agreement.

The beneficiaries must indicate the owner(s) of the results (results ownership list) in the final periodic report.

Protection of results

Beneficiaries which have received funding under the grant must adequately protect their results — for an appropriate period and with appropriate territorial coverage — if protection is possible and justified, taking into account all relevant considerations, including the prospects for commercial exploitation, the legitimate interests of the other beneficiaries and any other legitimate interests.

Exploitation of results

Beneficiaries which have received funding under the grant must — up to four years after the end of the action (see Data Sheet, Point 1) — use their best efforts to exploit their results directly or to have them exploited indirectly by another entity, in particular through transfer or licensing.

If, despite a beneficiary's best efforts, the results are not exploited within one year after the end of the action, the beneficiaries must (unless otherwise agreed in writing with the granting authority) use the Horizon Results Platform to find interested parties to exploit the results.

If results are incorporated in a standard, the beneficiaries must (unless otherwise agreed with the granting authority or unless it is impossible) ask the standardisation body to include the funding statement (see Article 17) in (information related to) the standard.

Additional exploitation obligations

Where the call conditions impose additional exploitation obligations (including obligations linked to the restriction of participation or control due to strategic assets, interests, autonomy or security reasons), the beneficiaries must comply with them — up to four years after the end of the action (see Data Sheet, Point 1).

Where the call conditions impose additional exploitation obligations in case of a public emergency, the beneficiaries must (if requested by the granting authority) grant for a limited period of time specified in the request, non-exclusive licences — under fair and reasonable

conditions — to their results to legal entities that need the results to address the public emergency and commit to rapidly and broadly exploit the resulting products and services at fair and reasonable conditions. This provision applies up to four years after the end of the action (see Data Sheet, Point 1).

Additional information obligation relating to standards

Where the call conditions impose additional information obligations relating to possible standardisation, the beneficiaries must — up to four years after the end of the action (see Data Sheet, Point 1) — inform the granting authority, if the results could reasonably be expected to contribute to European or international standards.

Transfer and licensing of results

Transfer of ownership

The beneficiaries may transfer ownership of their results, provided this does not affect compliance with their obligations under the Agreement.

The beneficiaries must ensure that their obligations under the Agreement regarding their results are passed on to the new owner and that this new owner has the obligation to pass them on in any subsequent transfer.

Moreover, they must inform the other beneficiaries with access rights of the transfer at least 45 days in advance (or less if agreed in writing), unless agreed otherwise in writing for specifically identified third parties including affiliated entities or unless impossible under the applicable law. This notification must include sufficient information on the new owner to enable the beneficiaries concerned to assess the effects on their access rights. The beneficiaries may object within 30 days of receiving notification (or less if agreed in writing), if they can show that the transfer would adversely affect their access rights. In this case, the transfer may not take place until agreement has been reached between the beneficiaries concerned.

Granting licences

The beneficiaries may grant licences to their results (or otherwise give the right to exploit them), including on an exclusive basis, provided this does not affect compliance with their obligations.

Exclusive licences for results may be granted only if all the other beneficiaries concerned have waived their access rights.

Granting authority right to object to transfers or licensing — Horizon Europe actions

Where the call conditions in Horizon Europe actions provide for the right to object to transfers or licensing, the granting authority may — up to four years after the end of the action (see Data Sheet, Point 1) — object to a transfer of ownership or the exclusive licensing of results, if:

- the beneficiaries which generated the results have received funding under the grant
- it is to a legal entity established in a non-EU country not associated with Horizon Europe, and

- the granting authority considers that the transfer or licence is not in line with EU interests.

Beneficiaries that intend to transfer ownership or grant an exclusive licence must formally notify the granting authority before the intended transfer or licensing takes place and:

- identify the specific results concerned
- describe in detail the new owner or licensee and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or licence on EU interests, in particular regarding competitiveness as well as consistency with ethical principles and security considerations.

The granting authority may request additional information.

If the granting authority decides to object to a transfer or exclusive licence, it must formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information it has requested).

No transfer or licensing may take place in the following cases:

- pending the granting authority decision, within the period set out above
- if the granting authority objects
- until the conditions are complied with, if the granting authority objection comes with conditions.

A beneficiary may formally notify a request to waive the right to object regarding intended transfers or grants to a specifically identified third party, if measures safeguarding EU interests are in place. If the granting authority agrees, it will formally notify the beneficiary concerned within 60 days of receiving notification (or any additional information requested).

Limitations to transfers and licensing due to strategic assets, interests, autonomy or security reasons of the EU and its Member States

Where the call conditions restrict participation or control due to strategic assets, interests, autonomy or security reasons, the beneficiaries may not transfer ownership of their results or grant licences to third parties which are established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) — unless they have requested and received prior approval by the granting authority.

The request must:

- identify the specific results concerned
- describe in detail the new owner and the planned or potential exploitation of the results, and
- include a reasoned assessment of the likely impact of the transfer or license on the strategic assets, interests, autonomy or security of the EU and its Member States.

The granting authority may request additional information.

Access rights to results and background

Exercise of access rights — Waiving of access rights — No sub-licensing

Requests to exercise access rights and the waiver of access rights must be in writing.

Unless agreed otherwise in writing with the beneficiary granting access, access rights do not include the right to sub-license.

If a beneficiary is no longer involved in the action, this does not affect its obligations to grant access.

If a beneficiary defaults on its obligations, the beneficiaries may agree that that beneficiary no longer has access rights.

Access rights for implementing the action

The beneficiaries must grant each other access — on a royalty-free basis — to background needed to implement their own tasks under the action, unless the beneficiary that holds the background has — before acceding to the Agreement —:

- informed the other beneficiaries that access to its background is subject to restrictions, or

- agreed with the other beneficiaries that access would not be on a royalty-free basis.

The beneficiaries must grant each other access — on a royalty-free basis — to results needed for implementing their own tasks under the action.

Access rights for exploiting the results

The beneficiaries must grant each other access — under fair and reasonable conditions — to results needed for exploiting their results.

The beneficiaries must grant each other access — under fair and reasonable conditions — to background needed for exploiting their results, unless the beneficiary that holds the background has — before acceding to the Agreement — informed the other beneficiaries that access to its background is subject to restrictions.

Requests for access must be made — unless agreed otherwise in writing — up to one year after the end of the action (see Data Sheet, Point 1).

Access rights for entities under the same control

Unless agreed otherwise in writing by the beneficiaries, access to results and, subject to the restrictions referred to above (if any), background must also be granted — under fair and reasonable conditions — to entities that:

- are established in an EU Member State or Horizon Europe associated country

- are under the direct or indirect control of another beneficiary, or under the same direct or indirect control as that beneficiary, or directly or indirectly controlling that beneficiary and

- need the access to exploit the results of that beneficiary.

Unless agreed otherwise in writing, such requests for access must be made by the entity directly to the beneficiary concerned.

Requests for access must be made — unless agreed otherwise in writing — up to one year after the end of the action (see Data Sheet, Point 1).

Access rights for the granting authority, EU institutions, bodies, offices or agencies and national authorities to results for policy purposes — Horizon Europe actions

In Horizon Europe actions, the beneficiaries which have received funding under the grant must grant access to their results — on a royalty-free basis — to the granting authority, EU institutions, bodies, offices or agencies for developing, implementing and monitoring EU policies or programmes. Such access rights do not extend to beneficiaries' background.

Such access rights are limited to non-commercial and non-competitive use.

For actions under the cluster 'Civil Security for Society', such access rights also extend to national authorities of EU Member States for developing, implementing and monitoring their policies or programmes in this area. In this case, access is subject to a bilateral agreement to define specific conditions ensuring that:

- the access rights will be used only for the intended purpose and
- appropriate confidentiality obligations are in place.

Moreover, the requesting national authority or EU institution, body, office or agency (including the granting authority) must inform all other national authorities of such a request.

Additional access rights

Where the call conditions impose additional access rights, the beneficiaries must comply with them.

COMMUNICATION, DISSEMINATION, OPEN SCIENCE AND VISIBILITY (— ARTICLE 17)

Dissemination

Dissemination of results

The beneficiaries must disseminate their results as soon as feasible, in a publicly available format, subject to any restrictions due to the protection of intellectual property, security rules or legitimate interests.

A beneficiary that intends to disseminate its results must give at least 15 days advance notice to the other beneficiaries (unless agreed otherwise), together with sufficient information on the results it will disseminate.

Any other beneficiary may object within (unless agreed otherwise) 15 days of receiving notification, if it can show that its legitimate interests in relation to the results or background would be significantly harmed. In such cases, the results may not be disseminated unless appropriate steps are taken to safeguard those interests.

Additional dissemination obligations

Where the call conditions impose additional dissemination obligations, the beneficiaries must also comply with those.

Open Science

Open science: open access to scientific publications

The beneficiaries must ensure open access to peer-reviewed scientific publications relating to their results. In particular, they must ensure that:

- at the latest at the time of publication, a machine-readable electronic copy of the published version or the final peer-reviewed manuscript accepted for publication, is deposited in a trusted repository for scientific publications

- immediate open access is provided to the deposited publication via the repository, under the latest available version of the Creative Commons Attribution International Public Licence (CC BY) or a licence with equivalent rights; for monographs and other long-text formats, the licence may exclude commercial uses and derivative works (e.g. CC BY-NC, CC BY-ND) and

- information is given via the repository about any research output or any other tools and instruments needed to validate the conclusions of the scientific publication.

Beneficiaries (or authors) must retain sufficient intellectual property rights to comply with the open access requirements.

Metadata of deposited publications must be open under a Creative Common Public Domain Dedication (CC 0) or equivalent, in line with the FAIR principles (in particular machine-actionable) and provide information at least about the following: publication (author(s), title, date of publication, publication venue); Horizon Europe or Euratom funding; grant project name, acronym and number; licensing terms; persistent identifiers for the publication, the authors involved in the action and, if possible, for their organisations and the grant. Where applicable, the metadata must include persistent identifiers for any research output or any other tools and instruments needed to validate the conclusions of the publication.

Only publication fees in full open access venues for peer-reviewed scientific publications are eligible for reimbursement.

Open science: research data management

The beneficiaries must manage the digital research data generated in the action ('data') responsibly, in line with the FAIR principles and by taking all of the following actions:

- establish a data management plan ('DMP') (and regularly update it)

- as soon as possible and within the deadlines set out in the DMP, deposit the data in a trusted repository; if required in the call conditions, this repository must be federated in the EOSC in compliance with EOSC requirements

- as soon as possible and within the deadlines set out in the DMP, ensure open access — via the repository — to the deposited data, under the latest available version of the Creative Commons Attribution International Public License (CC BY) or Creative

Commons Public Domain Dedication (CC 0) or a licence with equivalent rights, following the principle 'as open as possible as closed as necessary', unless providing open access would in particular:

- be against the beneficiary's legitimate interests, including regarding commercial exploitation, or
- be contrary to any other constraints, in particular the EU competitive interests or the beneficiary's obligations under this Agreement; if open access is not provided (to some or all data), this must be justified in the DMP

- provide information via the repository about any research output or any other tools and instruments needed to re-use or validate the data.

Metadata of deposited data must be open under a Creative Common Public Domain Dedication (CC 0) or equivalent (to the extent legitimate interests or constraints are safeguarded), in line with the FAIR principles (in particular machine-actionable) and provide information at least about the following: datasets (description, date of deposit, author(s), venue and embargo); Horizon Europe or Euratom funding; grant project name, acronym and number; licensing terms; persistent identifiers for the dataset, the authors involved in the action, and, if possible, for their organisations and the grant. Where applicable, the metadata must include persistent identifiers for related publications and other research outputs.

Open science: additional practices

Where the call conditions impose additional obligations regarding open science practices, the beneficiaries must also comply with those.

Where the call conditions impose additional obligations regarding the validation of scientific publications, the beneficiaries must provide (digital or physical) access to data or other results needed for validation of the conclusions of scientific publications, to the extent that their legitimate interests or constraints are safeguarded (and unless they already provided the (open) access at publication).

Where the call conditions impose additional open science obligations in case of a public emergency, the beneficiaries must (if requested by the granting authority) immediately deposit any research output in a repository and provide open access to it under a CC BY licence, a Public Domain Dedication (CC 0) or equivalent. As an exception, if the access would be against the beneficiaries' legitimate interests, the beneficiaries must grant non-exclusive licenses — under fair and reasonable conditions — to legal entities that need the research output to address the public emergency and commit to rapidly and broadly exploit the resulting products and services at fair and reasonable conditions. This provision applies up to four years after the end of the action (see Data Sheet, Point 1).

Plan for the exploitation and dissemination of results including communication activities

Unless excluded by the call conditions, the beneficiaries must provide and regularly update a plan for the exploitation and dissemination of results including communication activities.

SPECIFIC RULES FOR CARRYING OUT THE ACTION (— ARTICLE 18)

Implementation in case of restrictions due to strategic assets, interests, autonomy or security of the EU and its Member States

Where the call conditions restrict participation or control due to strategic assets, interests, autonomy or security, the beneficiaries must ensure that none of the entities that participate as affiliated entities, associated partners, third parties giving in-kind contributions, subcontractors or recipients of financial support to third parties are established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) — unless otherwise agreed with the granting authority.

The beneficiaries must moreover ensure that any cooperation with entities established in countries which are not eligible countries or target countries set out in the call conditions (or, if applicable, are controlled by such countries or entities from such countries) does not affect the strategic assets, interests, autonomy or security of the EU and its Member States.

Recruitment and working conditions for researchers

The beneficiaries must take all measures to implement the principles set out in the Commission Recommendation on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers[3], in particular regarding:

- working conditions
- transparent recruitment processes based on merit, and
- career development.

The beneficiaries must ensure that researchers and all participants involved in the action are aware of them.

Specific rules for access to research infrastructure activities

Definitions

Research Infrastructures — Facilities that provide resources and services for the research communities to conduct research and foster innovation in their fields. This definition includes the associated human resources, and it covers major equipment or sets of instruments; knowledge-related facilities such as collections, archives or scientific data infrastructures; computing systems, communication networks, and any other infrastructure, of a unique nature and open to external users, essential to achieve excellence in research and innovation. Where relevant, they may be used beyond research, for example for education or public services, and they may be 'single-sited', 'virtual' or 'distributed'[4]:

When implementing access to research infrastructure activities, the beneficiaries must respect the following conditions:

- for transnational access:

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[3] Commission Recommendation 2005/251/EC of 11 March 2005 on the European Charter for Researchers and on a Code of Conduct for the Recruitment of Researchers (OJ L 75, 22.3.2005, p. 67).

[4] See Article 2(1) of the Horizon Europe Framework Programme Regulation 2021/695.

- access which must be provided:

  The access must be free of charge, transnational access to research infrastructure or installations for selected user-groups.

  The access must include the logistical, technological and scientific support and the specific training that is usually provided to external researchers using the infrastructure. Transnational access can be either in person (hands-on), provided to selected users that visit the installation to make use of it, or remote, through the provision to selected user-groups of remote scientific services (e.g. provision of reference materials or samples, remote access to a high-performance computing facility).

- categories of users that may have access:

  Transnational access must be provided to selected user-groups, i.e. teams of one or more researchers (users).

  The majority of the users must work in a country other than the country(ies) where the installation is located (unless access is provided by an international organisation, the Joint Research Centre (JRC), an ERIC or similar legal entity).

  Only user groups that are allowed to disseminate the results they have generated under the action may benefit from the access (unless the users are working for SMEs).

  Access for user groups with a majority of users not working in a EU Member State or Horizon Europe associated country is limited to 20% of the total amount of units of access provided under the grant (unless a higher percentage is foreseen in Annex 1).

- procedure and criteria for selecting user groups:

  The user groups must request access by submitting (in writing) a description of the work that they wish to carry out and the names, nationalities and home institutions of the users.

  The user groups must be selected by (one or more) selection panels set up by the consortium.

  The selection panels must be composed of international experts in the field, at least half of them independent from the consortium (unless otherwise specified in Annex 1).

  The selection panels must assess all proposals received and recommend a short-list of the user groups that should benefit from access.

  The selection panels must base their selection on scientific merit, taking into account that priority should be given to user groups composed of users who:

  - have not previously used the installation and
  - are working in countries where no equivalent research infrastructure exist.

It will apply the principles of transparency, fairness and impartiality.

Where the call conditions impose additional rules for the selection of user groups, the beneficiaries must also comply with those.

- other conditions:

  The beneficiaries must request written approval from the granting authority for the selection of user groups requiring visits to the installations exceeding 3 months (unless such visits are foreseen in Annex 1).

  In addition, the beneficiaries must:

  - advertise widely, including on a their websites, the access offered under the Agreement
  - promote equal opportunities in advertising the access and take into account the gender dimension when defining the support provided to users
  - ensure that users comply with the terms and conditions of the Agreement
  - ensure that its obligations under Articles 12, 13, 17 and 33 also apply to the users
  - keep records of the names, nationalities, and home institutions of users, as well as the nature and quantity of access provided to them

- for virtual access:

  - access which must be provided:

    The access must be free of charge, virtual access to research infrastructure or installations.

    'Virtual access' means open and free access through communication networks to digital resources and services needed for research, without selecting the users to whom access is provided.

    The access must include the support that is usually provided to external users.

    Where allowed by the call conditions, beneficiaries may in justified cases define objective eligibility criteria (e.g. affiliation to a research or academic institution) for specific users.

  - other conditions:

    The beneficiaries must have the virtual access services assessed periodically by a board composed of international experts in the field, at least half of whom must be independent from the consortium (unless otherwise specified in Annex 1). For this purpose, information and statistics on the users and the nature and quantity of the access provided, must be made available to the board.

    The beneficiaries must advertise widely, including on a dedicated website, the access offered under the grant and the eligibility criteria, if any.

Where the call conditions impose additional traceability[5] obligations, information on the traceability of the users and the nature and quantity of access must be provided by the beneficiaries.

These obligations apply regardless of the form of funding or budget categories used to declare the costs (unit costs or actual costs or a combination of the two).

Specific rules for JU actions

JU actions must contribute to the long-term implementation of the JU partnership, including the JU Strategic Research and Innovation Agenda, the JU objectives and the exploitation of research and innovation results.

Moreover, when implementing JU actions, the members and contributing partners of the Joint Undertaking must fulfil their obligations regarding contributions to the Joint Undertaking:

- the description of the action in Annex 1 must include, for beneficiaries, affiliated entities, associated partners or other participants or third parties which are members or contributing partners, the estimated contributions to the action, i.e.:
    - in-kind contributions to operational activities ('IKOP'; if applicable)
    - in-kind contributions to additional activities linked to the action ('IKAA'; if applicable)
    - financial contributions ('FC'; if applicable)
- the contributions must be reported during the implementation of the action in the Portal Continuous Reporting tool
- at the end of the action, the members and contributing partners that have not received funding under the grant must ensure that financial and in-kind contributions of EUR 430 000 or more (see Article 21) are supported by statements of contributions (CS) and certificates on the statements of contributions (CCS) which fulfil the following conditions:
    - be provided by a qualified approved external auditor which is independent and complies with Directive 2006/43/EC (or for public bodies: by a competent independent public officer)
    - the verification must be carried out according to the highest professional standards to ensure that the statements of contributions comply with the provisions under the Agreement and the applicable JU Regulation, that the contributions cover activities that are part of the action and that they have not been reimbursed by the grant
- contributions must comply with the following conditions:

[5] According to the definition given in ISO 9000, i.e.: "Traceability is the ability to trace the history, application, use and location of an item or its characteristics through recorded identification data." The users can be traced, for example, by authentication and/or by authorization or by other means that allows for analysis of the type of users and the nature and quantity of access provided.

- costs covered by financial contributions cannot be claimed for reimbursement under the JU grant

- for Clean Aviation JU, SNS JU, Europe's Rail JU, CBE JU grants: if provided in the call conditions, a certain percentage of the total costs of the action must be covered by contributions (IKOP, IKAA or FC)

- for IHI JU grants: at least 45% (or another amount set out in the call conditions) of the total costs of the action and of the related IKAA must be covered by contributions (IKOP, IKAA or FC)

- for IHI JU grants: non-EU costs must not exceed 20% (or other percentage set out in the call conditions) of IKOP provided by members and contributing partners.

The beneficiaries must comply with the additional IPR, dissemination and exploitation obligations set out in the call conditions (Article 16 and Annex 5), in particular:

- for all JU grants: the granting authority right to object to transfers or licensing also applies to results generated by beneficiaries not having received funding under the grant

- for SESAR 3 JU and Clean Aviation JU grants: in view of the long innovation cycles:

    - the granting authority right to object to transfers or licensing (if any) can be exercised for up to 10 years after the end of the action (see Data Sheet, Point 1)

    - the beneficiaries must comply with their best effort obligation to exploit the results and any additional exploitation obligations imposed by the call conditions for up to 10 years after the end of the action (see Data Sheet, Point 1)

- for IHI JU and Global Health EDCTP3 JU grants (if applicable): the beneficiaries must ensure that the products and services that they develop based or partially based on the results of clinical studies undertaken as part of the grant are affordable, available and accessible to the public at fair and reasonable conditions.

In addition to the obligations set out in Article 17, communication and dissemination activities as well as infrastructure, equipment or major results funded under JU actions must moreover display the Joint Undertaking's special logo:

and the following text:

> "The project is supported by the [insert JU name] and its members *[OPTION for actions with national contribution top-ups:* (including top-up funding by [name of the national funding authority])*]*."

For EuroHPC JU and KDT JU grants, the beneficiaries must respect the following conditions when implementing actions with national contribution top-ups from Participating States:

- the beneficiaries must ensure visibility of the national contributions (see below)
- the payment deadlines for prefinancing, interim or final payments are automatically suspended if a national funding authority is late with its payments to the Joint Undertaking for the national contribution top-up
- the European Anti-Fraud Office (OLAF), European Public Prosecutor's Office (EPPO), European Court of Auditors (ECA), the National Court of Auditors and other

national authorities can exercise their control rights on the project implementation and costs declared, including for the national contribution top-up.

For SNS JU grants, where imposed by the call conditions for digital infrastructure projects the beneficiaries must ensure that the network technologies and equipment (including software and services) funded by the action comply with the security requirements and assessments as reflected in the applicable EU, international and national law on cybersecurity and on data protection.

Moreover, where the call conditions impose wholesale access obligations, the beneficiaries must provide wholesale access to the digital infrastructure funded by the action, under fair and reasonable conditions, in a non-discriminatory manner and in accordance with the call conditions.

For Global Health EDCTP3 JU fellowship grants, the beneficiaries must respect the following conditions when implementing them through financial support to third parties:

- avoid any conflict of interest and comply with the principles of transparency, non-discrimination and sound financial management
- take all measures to implement the principles set out in the Commission Recommendation on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers[6] and ensure that the researchers and all participants involved in the action are aware of them
- ensure that the researchers enjoy at the place of the implementation at least the same standards and working conditions as those applicable to local researchers holding a similar position
- ensure that the other direct contract or fixed-amount-fellowship agreement specifies:
    - the name of the supervisor(s) and/or mentor(s) for the research and training activities
    - the starting date and duration of the research and training activities
    - the monthly support for the researcher under this Agreement (in euro and, if relevant, in the currency in which the remuneration is paid)
    - the obligation of the researcher to work exclusively for the action, unless part-time has been approved and not to receive, for activities carried out in the frame of the action, other incomes than those received from the beneficiary or other entities mentioned in Annex 1)
    - the working pattern of the researcher
    - the arrangements related to the intellectual property rights (during implementation of the action and afterwards), in particular full access — on

[6] Commission Recommendation 2005/251/EC of 11 March 2005 on the European Charter for Researchers and on a Code of Conduct for the Recruitment of Researchers (OJ L 75, 22.3.2005, p. 67).

a royalty-free basis — for the researcher to background and results needed for their activities under the action

- the obligation of the researcher to inform as soon as possible about events or circumstances likely to affect the implementation of the action or the compliance with requirements under the Agreement (see Article 19)
- the obligation of the researcher to maintain confidentiality (see Article 13)
- the obligation of the researcher to ensure the visibility of the EDCTP Association and EU funding in communications or publications and in applications for the protection of results (see Articles 17)
- where set out in the call conditions, the obligation of the researcher to carry out a mandatory return period of 12 months

- assist the researchers in the administrative procedures related to the recruitment
- inform the researchers about:
    - the description, conditions, location and timetable for the implementation of the research and training activities
    - the rights and obligations toward the researchers under this Agreement
    - the obligation of the researchers to complete and submit — at the end of the research training activities — the evaluation questionnaire and — two years later — follow-up questionnaire provided by the granting authority
- ensure full access — on a royalty-free basis — for the researchers to background and results needed for their activities under the action
- ensure that the researchers do not have to bear any costs for the implementation of the action as described in Annex 1
- provide training, infrastructure and the necessary means for implementing the action (or ensure that such training and means are provided by other participants in the action)
- ensure that the researchers are adequately supervised and receive appropriate career guidance
- ensure that personalised career development plans are established, support their implementation and update in view of the needs of the researchers
- ensure an appropriate exposure to the non-academic sector (if applicable)
- respect the maximum limit for secondments set out in the call conditions (if applicable)
- respect the conditions for the outgoing and return phases set out in the call conditions (if any)
- ensure that the researchers are informed that they are ‘Global Health EDCTP3 JU fellows’

- ensure that the researchers do not receive, for activities carried out in the frame of the action, other incomes than those received from the beneficiaries (or other entities mentioned in Annex 1)
- host the researchers at their premises (or at the premises of other participants in the action).