Project Proposal	
Donor	**Government of Belgium**
Project / programme title	**Increasing Global Equitable Access to Health Products & Health Technologies**
Cluster	**Access to Medicines and Health Products (MHP)** **Universal Health Coverage/Life Course (UHC/Life Course)**
Department	**Department of Health Policy and Standards, MHP** **Department of Regulation and Prequalification, MHP** **Department of Immunization, Vaccines and Biologicals (UHC/Life Course)**
Geographical / country focus	**Global**
Total project cost	**€ 8 million**
Implementation period	**November 2021 – November 2025**
Contact details of focal point	**Dr Soumya Swaminathan** Executive Director - Chief Scientist Office of Chief Scientist (HQ/SCA) Office: +41 22 791 30 90 E-mail : swaminathans@who.int
Technical contacts	**Dr Martin Friede** Tel no. +41 22 791 4398 -Email: friedem@who.int **Dr Gilles Forte** Tel no. +41 22 791 3617 - Email: forteg@who.int

Executive summary

Given the urgency of the current pandemic, much of the attention and effort of the global health community is targeted at development or repurposing of existing vaccines, diagnostics and therapeutics for prevention, diagnosis or treatment of COVID-19. This is important because, in the absence of these health products, health systems everywhere will continue to be overstretched or unable to function, with the result that the health gains of previous years are further wiped out.

That said, figures for vaccine distribution and vaccine coverage underscore (yet further) the gross inequity that already existed in relation to access to health products.

Clearly, more than ever, effective approaches are called for, to improve access to essential medicines, vaccines, diagnostics and devices for primary health care.

This proposal therefore combines two approaches:

- increasing access to needed quality-assured health products as part of the response to the current pandemic
- maintaining and, where called for, expanding existing initiatives aimed at increasing access to quality-assured health products and health technologies.

Increasing Global Equitable Access to Health Products & Health Technologies: during COVID-19 and beyond

Challenges in parallel

Many populations worldwide do not have regular access to affordable and quality-assured health products. Gross inequity has been underscored (yet further) by COVID-19. For example, 70% of adults in the European Union but less than 3% of Africa's population are fully vaccinated against COVID-19. Much of this result is attributable to wealthy or producing countries that have prioritized securing of limited vaccine supplies for their own populations, over the need to work to ensure that all populations everywhere are vaccinated.

The continued spread of COVID-19 around the world hastens the day when new SARS-CoV-2 variants will emerge, undermining the effectiveness of vaccines, therapeutics, and diagnostics. Restrictions to contain COVID-19 will be prolonged, leading to increased human and economic suffering in every country, but hitting the poorest and most vulnerable hardest. World Bank estimates published in late 2020 suggest that, in 2020, between 88 million and 115 million people could fall back into extreme poverty as a result of the pandemic, with an additional increase of between 23 million and 35 million in 2021, potentially bringing the total number of new people living in extreme poverty to between 110 million and 150 million.[1] These figures represent the first rise in global poverty in more than two decades.

Given the current pandemic, much of the attention and effort of the global health community is directed to development or repurposing of existing vaccines, diagnostics and therapeutics for prevention, diagnosis and treatment of COVID-19. Without them, the health gains of previous years risk being further wiped out. The Global Fund has reported that the pandemic is having a serious impact on the most vulnerable communities worldwide and threatening progress on HIV, TB, malaria, vaccination and other areas of health. Comparing April to September 2020, with the same six-month period in 2019, the Global Fund has observed that in low-and middle-income countries (LMIC) in Africa and Asia in 2020: HIV testing fell by 41%; TB referrals declined by 59%; malaria diagnoses fell by 31% and antenatal visits fell by 43%.[2] The Stop TB Partnership estimates that just the first year of COVID-19 eliminated 12 years of progress against this disease.[3]

The ability of countries to address and respond to noncommunicable diseases (NCDs) has also been severely impacted by the pandemic. In the majority of countries, essential services for hypertension management, diabetes or cancer have been disrupted, and leaving millions of people unattended. The disruption of health services – not only in LMIC, but also in high-income countries – is

[1] Poverty and Shared Prosperity 2020: Reversals of Fortune
https://openknowledge.worldbank.org/bitstream/handle/10986/34496/9781464816024.pdf
[2] How COVID-19 is Affecting the Global Response to AIDS, Tuberculosis and Malaria
www.theglobalfight.org/covid-aids-tb-malaria/
[3] 12 Months of COVID-19 Eliminated 12 Years of Progress in the Global Fight Against Tuberculosis
stoptb-org/news/stories/2021/ns21.011.html

particularly problematic, for NCD patients who need regular or long-term care.[4]

In brief, although health products for COVID-19 are a priority, ongoing efforts and initiatives to increase access to health products for all conditions must be maintained or even expanded. A key outcome (1.3) under WHO's Global Programme of Work for 2020–2023, improved access is fundamental to attaining WHO's target of one billion more people benefiting from universal health coverage,[5] specifically:

- Output 1.3.2: *Improved and more equitable access to health products through global market shaping and supporting countries to monitor and ensure efficient and transparent procurement and supply systems.*
- Output 1.3.3: *Country and regional regulatory capacity strengthened, and supply of quality-assured and safe health products improved, including through prequalification service.*
- Output 1.3.4: *Research and development agenda defined and research coordinated in line with public health priorities.*

The need for a dual approach

This proposal takes into account the need for a dual approach to access to quality-assured health products:

- as part of the response to the current pandemic
- and by maintaining or expanding existing initiatives aimed at increasing access to quality-assured health products and health technologies for the treatment of communicable and non-communicable diseases, some of which also contribute to WHO's pandemic response.

Responding to the pandemic

Work undertaken to coordinate and accelerate the development of vaccines, therapeutics and diagnostics for COVID-19 has been fruitful. New health technologies to tackle COVID-19 have been developed in record time. In addition, the establishment of the COVAX Facility of the ACT Accelerator was a landmark achievement in 2020. But in 2021, WHO and its ACT Accelerator partners have struggled for resources to meet the operational costs of vaccination, to ensure that COVID-19 vaccines reach all populations, including those that are difficult to reach, such as migrants, those affected by humanitarian crises, indigenous and afro descendant populations, and taking into account gender, human rights, and equity considerations. If extensive vaccine coverage is not achieved in all countries, the vaccine coverage achieved to date in high-income countries will be undermined. (A study commissioned by the International Chamber of Commerce concluded that insufficient vaccine coverage would result in a loss to high-income economies of an additional US$ 2.4 trillion in 2021 alone.[6])

[4] The impact of the COVID-19 pandemic on noncommunicable disease resources and services: results of a rapid assessment
www.who.int/publications/i/item/9789240010291
[5] Thirteenth general programme of work 2019-2023
www.who.int/about/what-we-do/thirteenth-general-programme-of-work-2019---2023
[6] The Economic Case for Global Vaccinations
https://iccwbo.org/publication/the-economic-case-for-global-vaccinations/

Rapid and sustainable scale-up and diversification of global manufacturing capacity — not only for vaccines but also for diagnostics and medicines — would contribute to more effective management of the current pandemic. However, reaching this goal is difficult given the different types of intellectual property (IP) rights currently applied to successful diagnostics, therapeutics and vaccines for COVID-19 and the limited global production capacity for these health products. In October 2020, South Africa and India proposed to the World Trade Organization (WTO) that TRIPs provisions on COVID-19 technologies be waived temporarily. The proposal has received the support of 100 WTO Member states, but others have opposed it. Implementation of a waiver would be binding on all WTO Member States, but even if implemented it is unlikely to occur soon enough to address the pandemic.

WHO is therefore working on an alternative approach to the waiving of IP rights, whereby appropriate technologies, technology holders and potential technology recipients are identified, and conditions for win–win partnerships created. Within this framework, WHO is working to develop the COVID-19 mRNA vaccine technology transfer hub and the COVID Technology Access Pool (C-TAP). If these responses can be tested and successfully implemented during today's pandemic, the world will be better prepared to deal with future public health crises, and to avoid the disruption of health services that typically follow. Both initiatives are founded on the premise that ending the pandemic is a benefit best realized through the voluntary contribution of knowledge, clinical trial data, manufacturing processes, and other kinds of know-how, to the public domain.

COVID-19 mRNA vaccine technology transfer hub

Under the umbrella of ACT-A and the COVAX manufacturing task-force, which also addresses upstream supply issues and the establishment of fill–finish partnerships (workstreams 1 and 2 of the COVAX manufacturing working group (WG)), WHO is establishing technology transfer hubs to expand LMIC capacity to produce COVID-19 and future pandemic-response vaccines (workstream 3 of the COVAX manufacturing WG). The hubs will serve as training centres where the full manufacturing process is established and from there transferred to manufacturers in LMIC. The public health value of a hub will extend beyond the individual countries where a hub and manufacturers are located, to all countries within that region, since it is intended that supply within a region as a whole is strengthened through creation of local and sustainable sources of supply.

WHO and its COVAX partners are working with a South African consortium comprising Biovac, Afrigen Biologics and Vaccines, a network of universities and the Africa Centres for Disease Control and Prevention, to establish the first such hub, in South Africa, which offers established manufacturing infrastructure and R&D expertise. The hub will facilitate transfer of mRNA vaccine technology, initially to a South African vaccine manufacturer and thereafter to multiple LMIC manufacturers. Selection of these manufacturers will be based on their technical capacity to receive and implement the technology, and on the contribution that the technology transfer will make to implementing the regional plan for sustainable pandemic response capacity. Rwanda and Senegal have been identified by the African Union (AU) as priority countries for establishment of mRNA production and the necessary technology transfer.[7] The hub will complement other ongoing

[7] Technology transfer organized in connection with the mRNA hub in South Africa may be supplemented by technology transfer initiated by BioNTech and Moderna.

activities aimed at ramping up vaccine production[8] and will also carry out R&D in collaboration with the South African Medical Research Council (SAMRC) to develop a second-generation mRNA vaccine that is appropriate for use in LMIC. Further technology transfer hubs for other vaccine technologies will be established in the near future.

WHO's role in establishing the hubs includes:

- management of the competitive process for identifying additional hubs
- identification of the technologies to be established
- provision of technical support to the hubs by product experts
- coordination of the transfer of technology to manufacturers and securing of their commitment to provide the vaccines to their region.

A steering committee, which incorporates WHO Member States, oversees overall hub coordination, the support to South Africa to establish the mRNA hub, and selection of technology recipients and the technologies to be licensed. The steering committee is supported by the WHO Product Development for Vaccines Advisory Committee, and reports on a regular basis to the COVAX manufacturing taskforce and the ACT-A Facilitation Council, which can assist with resolving bottlenecks. Donors can participate in steering committee meetings, as observers, rather than as voting members, so as to minimize conflict of interest.

In addition, together with GAVI, UNICEF and other stakeholders, WHO is developing business plans and financial sustainability models for hub and technology recipients, to help ensure that new capacity continues to operate between pandemics. It is foreseen that locally-produced health products will (at least initially) be more expensive than those procured on the international market. Procurement at a premium price will be one means of sustaining local production. The size of the premium to be applied, and the duration of its application, must be identified early in the establishment of any facility or plan for technology transfer, in consultation with procurement agencies. Vaccine production is more likely to meet the requirements of today's pandemic and future outbreaks if these market considerations are fully taken into account now.

IP concerns have not been neglected. Where necessary, the Medicines Patent Pool (see also page 9) will work with WHO on the granting of licenses to those individual manufacturers to whom technology will be transferred and who are not located in South Africa. This will include with respect to any IP — for example, for a second-generation mRNA vaccine. In this particular case, the IP would be owned by SAMRC. SAMRC would provide a worldwide non-exclusive license to WHO and MPP, to facilitate production of the new vaccine and ensure global access to it.

Many of the existing activities of the Department of Regulation and Prequalification (RPQ), will complement efforts to create hubs. These activities include: regulatory strengthening; support to local production; and prequalification of in vitro diagnostics (IVDs), medicines and vaccines. In other

[8] For example, Biovac is involved in multiple initiatives, including "fill and finish" activities for Pfizer and cooperation with producers from other countries. It should be noted that, unlike production of mRNA vaccines, these are not intensive activities. Biovac's infrastructure and staffing were established for the production of Haemophilus influenzae type b vaccine. The vaccine was not produced but the infrastructure and staffing remain in place and will be used for mRNA vaccine production, representing the first time that Biovac has produced a drug substance.

words, considerable infrastructure and activities, and expertise, are already in place and will serve to increase the potential for successful implementation of the mRNA hub concept.

Regulatory strengthening

Evidently, in identifying hubs and manufacturers, attention must also be paid to the surrounding "enabling" environment, in particular the capacity of the relevant national regulatory agencies (NRAs) to oversee quality of production and regulate the market (including for export) over which they have jurisdiction. RPQ's Regulation and Safety Unit (REG) has developed the WHO Global Benchmarking Tool (GBT) for evaluating the level at which a regulatory authority is functioning. An NRA that is benchmarked and operating at maturity level (ML3) has a stable, well-functioning and integrated regulatory system; ML3 is the minimum level of maturity that an NRA should aspire to. For those NRAs that are benchmarked and found not to have attained ML3, RPQ offers support and guidance for implementation of an institutional development plan, to enable the NRA in question to improve its regulatory performance and attain ML3. Only NRAs operating at ML3, or ML4 (which signifies an advanced level of performance and continuous improvement), can be considered eligible for participation in regulatory reliance activities.

Formal benchmarking using GBT of the South African Health Products Regulatory Authority will be completed in November 2021. Self-benchmarking of Rwanda's Food and Drug Authority and Senegal's was completed — also using GBT — in September 2021 and October 2021 respectively. Both NRAs will implement recommendations resulting from the self-benchmarking, ahead of formal benchmarking, which should be conducted for both NRAs in 2022. Thus in all three countries, the regulatory maturity level is being actively monitored and action initiated to close any gaps.

Since products produced by a hub and the manufacturers to whom technology has been transferred will be circulating across more than one national market, regulatory harmonization will be important. REG has considerable experience in promoting this aspect of regulation, including through benchmarking of the progress of regulatory harmonization initiatives. It is therefore an ideal partner for NRAs and regional regulatory authorities involved in the mRNA hub and can work with them to enhance regulatory reliance — to eliminate regulatory duplication — and promote sharing of lessons learned. REG has long worked with the African Medicines Regulatory Harmonisation (AMRH) programme (of the African Union Development Agency) to support its work with different regional blocks in Africa: for example, by organizing joint assessment activities and NRA participation in WHO's Collaborative Registration Procedure. REG also supports AMRH's technical committees that focus on areas, such as clinical trials and quality control, for which harmonization and reliance at continental level can be especially beneficial. The African Medicines Agency (AMA), establishment of which is anticipated soon, will be another major partner for harmonization and reliance activities.

Mention must also be made of REG's support to the work of national quality control laboratories (QCLs) for medicines and national control laboratories (NCLs) for vaccines. These play a vital role in monitoring the quality of products circulating on their markets, and in the case of NCLs, performing lot release of vaccines. REG helps to increases the capacity and expertise of these laboratories through peer audits for QCLs and audits for NCLs. Through its National Control Laboratory Network for Biologicals, REG also provides support on vaccine control methods and harmonization of vaccine test methods. NCLs are very likely to be involved in monitoring the quality of any vaccines produced through the first mRNA hub and any additional hubs, and by manufacturers to whom mRNA technology has been transferred.

Local production

Local production has been discussed at World Health Assemblies since the 1970s. But in May 2021, adoption of Resolution WHA74.6 brought a renewed focus on strengthening local production of medicines and other health technologies to improve access.[9] In June 2021, organized by RPQ's Local Production and Assistance Unit (LPA), the first WHO Local Production Forum was held. It will serve as a mechanism for promoting dialogue and decision-making, aimed at strengthening local manufacturing capacity and accelerating progress towards attainment of the goal of universal access to health technologies. It is sorely needed: the current pandemic has demonstrated that global manufacturing capacity for health products is insufficient for meeting global health needs. Moreover, many LMIC had already expressed their wish to move away from dependency on imports to supplement local supply of health products, recognizing that expanded local production could improve timely access and safeguard health security.

LPA has a range of expertise that it will make available in support of the aforementioned hubs (and which it is currently making available to Algeria, Egypt, Ethiopia, India, Indonesia, Iran, Kenya, Nigeria, Senegal and Sudan). This expertise covers: situational analyses for sustainable quality local production; development of guidance tools; capacity building and specialized technical assistance to achieve quality assurance; and facilitation of technology transfer for prioritized products and technologies. In September 2021, for example, LPA organized a "Virtual cGMP Training Marathon for Vaccine Manufacturing".

Prequalification

WHO prequalification works to ensure that key health products meet global standards of quality, safety and efficacy, to help optimize use of health resources and improve health outcomes. It is a trusted and reputed symbol for safety, quality and efficacy. Currently it prequalifies: IVDs; medicines (finished pharmaceutical products but also active pharmaceutical ingredients); vaccines and immunization devices, and vector control products. Criteria for eligibility for prequalification vary according to product stream but focus on products needed by LMIC. For example for IVDs, this signifies IVDs needed for a specified disease or disease state, that are appropriate for use in resource-limited settings, requested by a WHO Member State(s) and recommended for use by WHO disease-specific testing guidelines.

The prequalification process for each product stream consists of a transparent, scientifically sound assessment, which may include dossier review, product testing, performance evaluation, and inspection of manufacturing sites and contract research organizations. Prequalification outputs — including the lists of prequalified products, and WHO Public Assessment and Inspection Reports — are used by UN and other procurement agencies to inform their purchase of health products. Medicines QCLs are also prequalified and have increased country capacity to monitor medicines circulating on their markets.

WHO prequalification is managed by the Prequalification Unit (PQT). PQT not only verifies the quality of products but also contributes significantly to building the capacity and expertise of

[9] WHA Resolution 74.6. Strengthening local production of medicines and other health technologies to improve access
www.who.int/publications/m/item/resolution-strengthening-local-production-of-medicines-and-other-health-technologies-to-improve-access

manufacturers and regulators to regulate health products. Increased capacity is sometimes a by-product of prequalification activities. For example, assessors and inspectors who take up a temporary assignment at WHO Headquarters, increase their regulatory skills and experience, to the benefit of their agencies when they return home. For many manufacturers, the experience of undergoing prequalification has enabled them to increase quality across the range of their products, and not only products submitted for prequalification. PQT itself has amassed considerable knowledge and understanding of the challenges faced by LMIC manufacturers when seeking to produce quality-assured products.

PQT works closely with other units in RPQ and other WHO departments on regulatory system strengthening and development of safety monitoring and vigilance. This may consist of participating in training activities, advising on development of activities aimed at regulators or manufacturers, or advising how the WHO Collaborative Procedure for Accelerated Registration can speed up access to prequalified products.

PQT also manages implementation of the WHO Emergency Use Listing (EUL) procedure which is expediting availability (following rigorous risk–benefit assessment) of unlicensed IVDs and vaccines for emergency use for COVID-19.

Products produced by the hub and associated manufacturers can be expected to be submitted for EUL and/or prequalification.

COVID Technology Access Pool (C-TAP)

Launched in May 2020, C-TAP is a WHO-led, innovative, more comprehensive and more recent approach to scaling up production of health products for tackling COVID-19. Built on the principle of sharing, C-TAP offers technology holders a technology pool platform (overseen by WHO) to voluntarily make available their IP, know-how and data which qualified manufacturers everywhere can access and use to produce COVID-19 health technologies.

The role of the C-TAP Secretariat includes:

- advocating to Member States, manufacturers, IP holders and other stakeholders for voluntary sharing with C-TAP of know-how and licenses for COVID-19 products
- rigorous assessment of the efficacy and safety of COVID-19 products
- developing a strategy to incentivize IP holders to share their technologies with C-TAP
- working with the Medicines Patent Pool on negotiation of transparent licensing agreements with manufacturers/holders of IP: licensing agreements have been finalized for some health technologies and others are about to be completed
- engaging with selected manufacturers to plan and implement technology transfer
- creating a C-TAP database to bring together and enable open access to data, know-how and licensing information for COVID-19 products
- developing communication materials to promote understanding of C-TAP objectives, deliverables and targeted impact on the COVID-19 pandemic, and of C-TAP positioning vis-à-vis related access initiatives, including the aforementioned mRNA Hub.

C-TAP is now receiving many offers to share data, know-how and licenses. For example, in November 2021, announcement will be made of the first C-TAP licensing agreement for a COVID-19 test developed by CSIC (Consejo Superior de Investigationes) in Spain. The agreement will enable manufacturers that have manufacturing capacity (including in LMIC) to produce these diagnostic

tests and contribute to scaling up global production, thereby facilitating better prevention, detection and treatment for COVID-19. Licenses for other products such as innovative vaccines including intra-nasal vaccines, and diagnostics using the very promising CRIPSR technology (clustered regularly interspaced short palindromic repeats), have also been offered to C-TAP. Licenses processes are ongoing.

Medicines Patent Pool: a proven approach

WHO has overall responsibility for C-TAP. Its C-TAP Secretariat undertakes upfront work with WHO's Member States, and with health product manufacturers, to identify potential products for which know-how could be shared and licenses negotiated. An important element of the Secretariat's work is assessment of the appropriateness of a product or technology for its inclusion in the "pool". This is essential for determining the public health value — including its safety and effectiveness — of a product or technology. For this activity, the Secretariat can tap into WHO's considerable expertise in evaluating diagnostic, medicine and vaccine products, especially those intended for use in LMIC.

However, WHO does not have a mechanism for issuing licenses to manufacturers. It therefore works with the Medicines Patent Pool (MPP). MPP's success in negotiating agreements with patent holders for HIV antivirals, and HIV technology platform, hepatitis C direct-acting antivirals and a TB treatment, has demonstrated that voluntary approaches to increasing access to health products are effective. Now, through its collaboration with C-TAP, MPP's role is expanding, and it is contributing to the development of licenses for vaccines and diagnostics.

MPP is C-TAP's core partner for overseeing negotiations for licensing agreements. MPP also gathers information on the patent, market exclusivities and the existing licensing status of vaccines, diagnostics, therapeutics and other health technologies for COVID-19. It will assist with patent landscaping if needed by the South African mRNA hub and any additional hubs that may be created. It is important to underscore that the activities of C-TAP and MPP are complementary (not duplicative). Both entities are working to expand global manufacturing capacity, but each are doing so through the application of specific and very different expertise.

The C-TAP Secretariat carries out regular consultations with Member States and Civil Society organizations to ensure good understanding of C-TAP objectives and to share information on progress in C-TAP implementation. A co-sponsors group of Member States has been established and is currently led by Costa Rica, whose president Carlos Alvarado has been together with WHO DG at the forefront of the C-TAP initiative.[10] This group carries out advocacy to explain C-TAP benefits, is encouraging additional Member States to support C-TAP, and provides feed-back on and advice to the C-TAP Secretariat on C-TAP strategy and positioning. Belgium's leadership and contribution to the co-sponsors group will be instrumental for raising C-TAP's profile.

However, in order to fully achieve C-TAP's objectives, additional work to create a critical mass of support needs to be undertaken. Unlike the mRNA hub and technology transfer which are partly based on existing concepts, C-TAP is a new concept and as such is yet to be fully understood and

[10] The relevant Member States are: Argentina; Bangladesh; Barbados; Belize; Bhutan; Bolivia; Brazil; Chile; Dominican Republic; Ecuador; Egypt; El Salvador; Guatemala; Honduras; Indonesia; Kenya; Lebanon; Luxembourg; Malaysia; Maldives; Mexico; Mongolia; Mozambique; Norway; Oman; Pakistan; Palau; Panama; Paraguay; Peru; Portugal; Saint Vincent and Grenadines; South Africa; Spain; Sri Lanka; Sudan; The Netherlands; Timor-Leste; Tunisia; Turkmenistan; Uruguay; Zimbabwe.

appreciated. C-TAP needs to establish for itself a “definitive position” in the minds of its key stakeholders. This position should be based on identification and optimizing of C-TAP’s difference and benefits relative to available alternatives (if these do indeed exist). Additionally, the Secretariat needs strengthening so that it can increase advocacy aimed at Member States, ensure availability of sufficient expertise for identifying and assessing products, and initiate and manage negotiations with individual manufacturers.

Assessing and managing risk for mRNA hub and C-TAP

The proposed mRNA hub and technology transfer, and C-TAP, are not long-established initiatives. They do not benefit from the awareness and recognition afforded, for example, to WHO’s regulatory activities or WHO prequalification. WHO recognizes that providing funding for them is therefore not without risk for donors. The table below enumerates potential risks, the likelihood of their occurrence, and planned or in-progress mitigating action.

Risks for mRNA hub	**Potential impact**	**Probability**	**Mitigating action**
Other vaccine manufacturers establish mRNA vaccine manufacturing in South Africa /other African countries	National/regional: reduced demand from Africa countries for training from the hub	Low	The extent of LMIC need in terms of local production is significant. Initiatives such as those of BioNtech and Moderna can be seen as complementary rather than as in competition. Also, WHO is negotiating with Moderna to align its proposed construction of a manufacturing site in South Africa with those of the hub and Biovac. Open access clauses should be advocated for as more empowering for countries than establishment of facilities wholly owned by foreign pharma.
IP creates an insurmountable barrier	Product development at national/regional/ global levels cannot take place without infringing IP	Low	Arbutus/University of Pennsylvania has not filed regarding mRNA technology in African states; Moderna has some IP in South Africa but has announced that it will not enforce it, and negotiation for licenses for broader use are under negotiation.

National regulatory capacity is not adequate for ensuring adherence to GMP, or for appropriate and prompt licensing of products (be these for national or export markets)	Inadequate regulatory environment undermines confidence of procurers in quality of products manufactured by the hub	Medium	RPQ/REG seek to ensure that plans for increasing regulatory capacity and expertise to ML3 (if not already attained) advance within the necessary timeframe.
Locally-produced products (a) are priced at the same level as products on the international market or (b) they are priced at a premium (higher than on the international market) and procurers continue to procure on the international market	(a) Sustainability of manufacture is not ensured over the longer term (b) Low volumes of products procured renders production financially unviable	Medium	WHO, GAVI, UNICEF and other stakeholders are preparing business plans and financial sustainability models for hub and technology recipients. It is vital to identify the premium prices to be applied to products, and for how long, early in the establishment of any facility or plan for technology transfer, and in consultation with procurement agencies.
Risks for C-TAP	**Potential impact**	**Probability**	**Mitigating action**
Manufacturers do not perceive the benefits of C-TAP	Manufacturers do not propose their products for inclusion in the pool	High	Independent research to explore stakeholder awareness and views and attitudes towards C-TAP, with the aim of identifying and optimizing C-TAP's unique differences and benefits, relative to available alternatives.
Change in leadership and management of IP holders or manufacturers with whom negotiations for sharing licenses with C-TAP are ongoing or planned	Effort expended so far does not deliver anticipated result, and may serve to discourage other IP holders already in negotiation with C-TAP and/or additional IP holders from participating	Low–medium	Sustained advocacy for C-TAP among all stakeholders, but especially targeting the pharmaceutical and health products industry.

Change in government of Member States that have been strong advocates for C-TAP, and supported and facilitated sharing with C-TAP of patents of manufacturers in their countries	Additional IP holders discouraged from participating	Low–medium	Monitoring of political situation in relevant countries to anticipate need for additional advocacy.
Due to increasing number of requests for licensing, need for substantial, multifaceted and highly specialized technical expertise exceeds Secretariat capacity and slows its response timelines and organization of negotiations with manufacturers	Manufacturers proposing their products for inclusion do not consider additional products for inclusion or advocate to other manufacturers to participate in C-TAP	Medium	Ongoing advocacy with WHO Member States and other potential sources, to request financial and/or in-kind support.

The access "ecosystem"

While RPQ is responsible for regulatory activities focused primarily on ensuring the quality and effective regulation of health products, the Department for Health Product and Policy Standards (HPS) focuses on policy issues relating to access to health products. Some key, ongoing HPS access initiatives, for which work needs to be expanded, are outlined below. These initiatives will support both the mNRA hub and C-TAP: for example, in terms of setting prices, or selecting needed and appropriate products for technology transfer.

HPS is also responsible for development of norms and standards for medicines, and norms and standards for biologicals. These norms and standards underpin much of the work of RPQ, in particular that relating to prequalification of IVDs, medicines and vaccines.

Fair pricing

The high price of many health products is a major barrier to attainment of the goal of universal health coverage and primary health care. The poor bear a disproportionate portion of this burden. For example, it is common in LMIC for medicines to be the highest out-of-pocket expense after food. Even before the advent of COVID-19, it was estimated that each year, 100 million people fall into poverty because they have to pay for medicines out-of-pocket. Even in high-income countries, health authorities are increasingly having to ration newer, highly priced medicines for cancer, hepatitis C and rare diseases. But older medicines whose patents have expired, such as insulin for diabetes, can also be very expensive; high prices are thought to be a key contributor to poor insulin access. Yet the cost of production of most medicines on WHO's Essential Medicines List has been shown to be just a small fraction of the final price paid by governments, patients or insurance

schemes.[11] Even worse, a lack of transparency around prices paid by governments means that many LMIC pay higher prices for certain medicines than wealthier countries do.

The call for transparency

Resolution WHA 72.8 on Improving the transparency of markets for medicines, vaccines and other health products[12] underscores that high prices for some health products, and inequitable access to such products within and among Member States, as well as the financial hardships associated with high prices, seriously impede progress towards achieving universal health coverage. It recognizes that that the types of information publicly available on data across the value chain of health products, including prices effectively paid by different actors and costs, vary among Member States and that the availability of comparable price information may facilitate efforts towards affordable and equitable access to health products.

HPS promotes programmes and policies that tackle the aforementioned issues and aim at making medicines affordable and accessible to all who need them. This includes collecting data on medicines pricing and convening the biannual WHO Fair Pricing Forum to bring stakeholders — governments, civil society organizations and the pharmaceutical industry — together for discussion of options for fairer pharmaceutical pricing. At the 2021 Forum, many participants emphasized the need for a stronger government role in medicines pricing, and that governments should have a stake in setting the innovation agenda and engage more closely with all stakeholders, including the private sector, to align incentives for access at fairer prices throughout the full innovation cycle. Many participants noted that this need has become acutely relevant during the COVID-19 pandemic. The third WHO Fair Pricing Forum will take place in 2023.

In view of the momentum in this complex area, HPA needs to intensify its actions on health technology pricing, including to:

- promote and encourage application of its electronic open-access tool, MEDMON, designed to monitor availability and prices of health products in countries
- support countries in their development of national or regional price monitoring systems
- host webinars and trainings to strengthen policy-makers' capacity to determine fair medicines pricing
- advocate for more affordable prices of health technologies by advising on policies and approaches to transform markets.

Essential Medicines List

The WHO Essential Medicines List (EML)[13] combines detailed pharmaceutical data relating to individual medicines, or categories of medicine, with information summarizing evaluation of their benefits, harms and costs. Most importantly it provides the data related to the status of a medicine as an essential medicine. Because of its well-defined scope (identifying those medicines that everyone should have access to at all times, and that all governments should ensure are available

[11] Hill A., Barber M & Gotham D. Estimated costs of production and potential prices for the WHO Essential Medicines List. *BMJ Global Health*, 2019;**4:**e001410. https://gh.bmj.com/content/4/3/e001410

[12] https://apps.who.int/iris/handle/10665/329301

[13] https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists

and affordable for their populations), the EML provides a blueprint on which countries can base their own national lists. As such, it is a key tool for achieving universal health coverage. More than 150 countries are using the EML to work out which medicines best meet their national health contexts and priorities, so that they can compile their own national essential medicines lists.

Since 1977, the EML has been revised every two years by a group of experts and published in print or PDF formats. In 2021, it was also made available in digital format.[14] The Model List issued in 2021 is also notable because the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines, which reviewed and updated the EML (and the WHO Model List of Essential Medicines for Children (EMLc)), recommended establishing a standing EML Working Group to support the Expert Committee, to provide advice to WHO on policies and rules to make highly-priced essential medicines more affordable and accessible. The Committee was especially concerned by the trend of continually increasing prices of new medicines over time, particularly in the areas of cancer, autoimmune diseases, infectious diseases and rare diseases.

Essential Diagnostics List

To address the lack of access to tests and testing services in multiple countries, the first WHO Essential Diagnostics List (EDL) was issued in 2018. The third list was published in 2021.[15] The list consists of recommended IVDs that should be available at point-of-care and in laboratories in all countries if timely and life-saving diagnoses are to be assured. The third EDL includes WHO-recommended COVID-19 tests (PCR and antigen), expands the suite of tests for vaccine-preventable and infectious diseases and NCDs (such as cancer and diabetes), and introduces a section on endocrinology, which is of particular relevance to reproductive and women's health. For the first time, it also includes tests that should not be supplied in countries, either because they are not cost-effective, or are unreliable or have been surpassed by newer, easier-to-use technologies.

As well as tests intended for use in laboratories, the EDL recommends numerous diagnostics that should be available at primary care or community level. These are of especial relevance for rural areas in LMIC, where medical facilities and equipment may be lacking, and health providers are often obliged to make treatment decisions based solely on patient symptoms.

List of Priority Medical Devices cardiovascular diseases and diabetes

The first List of Priority Medical Devices for management of cardiovascular diseases and diabetes,[16] including more than 500 devices that are required at all levels of the health system, from primary care facilities to highly specialized hospitals, and devices needed for health emergencies such as cardiac arrest, stroke and hypo or hyperglycaemic emergencies, was released in June 2021. Its aim is to assist health-care providers, particularly in LMIC, to implement interventions for the detection and management of heart conditions and diabetes across the continuum of care, to reduce the number of hospitalizations and deaths. Along with the List, WHO has developed MeDevIS, a medical devices information system and clearing house where biomedical engineers, public policymakers and hospital managers can find more information on 1500 specific medical devices, their use and how to

[14] https://list.essentialmeds.org
[15] See Annex 1 of The Selection and Use of Essential In Vitro Diagnostics, WHO Technical Report Series, No. 1031.
https://www.who.int/publications/i/item/9789240019102
[16] https://apps.who.int/iris/bitstream/handle/10665/341967/9789240027978-eng.pdf

maintain them.

The list is part of a series of lists prioritizing devices for high-burden diseases, including cancer and COVID-19.

Controlled medicines

Controlled medicines may be used for palliative care, for emergency and essential surgical care and anaesthesia, and for epilepsy. (Those used for the management of pain and palliative care are greatly needed by intensive care units when treating severely ill COVID-19 patients.*)* Yet in many countries, the availability of internationally controlled drugs for medical and scientific purposes remains low to non-existent. The Lancet Commission on Palliative Care and Pain Relief has noted that "people living in low-income and middle-income countries (LMICs) have little or no access to pain relief or palliative care".[17]

WHO and its UN partners are therefore working together to ensures the adequate availability of controlled substances for medical and scientific purposes, and the prevention of substance abuse, diversion and trafficking. WHO plays a pivotal and unique role in addressing the public health and human rights dimensions of this global issue by:

- working with Member States and partners to ensure appropriate access to necessary pharmaceuticals for issues such as pain management and developing guidelines for health care professionals and policy makers on the supply and use of controlled substances, based on research and consideration of local contexts
- strengthening the collaboration with interested nongovernmental organizations
- considering relevant resolutions of governing bodies such as the WHA and the Commission on Narcotic Drugs in Vienna.

Completion of the revision of the *WHO Guideline for Ensuring Balanced National Policies for Access to and Safe Use of Controlled Medicine* is anticipated for the end of 2021 and will represent a significant milestone. The need for revision was triggered in large part by the global burden of health-related suffering from serious life-threatening and life-limiting illnesses, which is projected to almost double by 2060, and effective treatment of which will requiremuch greater access to appropriate palliative care, including access to controlled medicines.

With respect to increasing access to controlled medicines at country level, WHO collaborates with the United Nations Office on Drugs and Crime (UNODC), the Union for International Cancer Control, and with the African Palliative Care Association on a programme to: build the capacity of healthcare professionals in countries in Africa to understand the importance of controlled medicines for medical purposes; to effectively order, prescribe and monitor their use; and to increase awareness and advocacy efforts related to pain management and palliative care. Many more programmes of this type are needed in LMIC, but tend not to be a priority for donor funding. Belgium should be commended for its global leadership for improving access to controlled medicines for the management of pain and for its support to WHO and UNODC collaboration in the Democratic Republic of the Congo.

[17] Knaul FM et al. Alleviating the access abyss in palliative care and pain relief-an imperative of universal health coverage: The Lancet Commission report. *The Lancet*, 2018; 391(10128):1391–1454.

Proposed budget

The Government of Belgium has made a provisional commitment to provide € 8 million over four years to WHO, to fund activities to increase access to health products.

	Proposed overall budget (€), including programme support cost (13%)			
	November 2021 – November 2022	**November 2022 – November 2023**	**November 2023 – November 2024**	**November 2024 – November 2025**
TOTAL	**2,000,000**	**2,000,000**	**2,000,000**	**2,000,000**

The proposed budget allocation for the duration of the agreement is presented below. Details of the budget allocation for the different components and activity outputs will be subject to yearly discussion between the Government of Belgium and WHO, and fully take into account the priorities of the Belgian Government and WHO. It is foreseen that greater allocation of funds would be made to the mRNA hub and technology transfer and to C-TAP in the first two funding periods. Depending on the progress in the different areas of activity and in line with the priorities of the Belgian Government, adjustments in the foreseen allocation of funds may be addressed and agreed upon in the context of these yearly discussions.

Area of activity	**Proposed funding allocation (€), including programme support cost (13%) – November 2021 – November 2022 and November 22 – November 2025 (indicative)**			
	November 2021 – November 2022	**November 2022 – November 2023 (indicative)**	**November 2023 – November 2024 (indicative)**	**November 2024 – November 2025 (indicative)**
mRNA hub & technology transfer	1,061,947	1,061,947	884,956	884,956
C-TAP	442,478	442,478	619,469	619,469
Regulation & LPA	132,743	132,743	132,743	132,743
Fair pricing and other access to health products work streams, e.g. EML, EDL, controlled medicines	132,743	132,743	132,743	132,743
Total	1,769,912	1,769,912	1,769,912	1,769,912
13% programme support cost[18]	230,088	230,088	230,088	230,088
GRAND TOTAL	**2,000,000**	**2,000,000**	**2,000,000**	**2,000,000**

[18] This indirect cost is not intended to cover secretarial/support costs. It is based on the principle that standard general costs (such as buildings, offices, equipment, security, electricity, heating, general services), estimated at 26% of any project, should be divided equally between WHO and the funding agency.

Reporting

It is proposed that in addition to annual technical reports, based on relevant extracts from WHO corporate Results Reports, and highlighting Belgian's support to activities to increase access to health products, WHO provide:

- yearly certified financial statements of income and expenditure
- yearly plans of activities supported with Belgian funds
- technical updates on activity implementation to be provided at in-person or virtual meetings.