JU Discharge 2019 hearing. IMI2 JU written replies

IMI would like to stress that the pharma industry contributes to half of IMI´s budget, yet the rules governing IMI funding are strictly EU rules. IMI works under the Financial Regulation, the Horizon 2020 Rules for Participation and the EU Staff Regulations. No other rules or frameworks apply. This means that we and our projects are subject to the same obligations and standards as any other EU-funded research programme. This goes for audits, IP, open access, project reporting and project financial costs, to mention but a few.

Return of EUR 139.1 million of commitment appropriations to the EU budget of 2019

The first IMI2 JU 2019 budget amendment adopted by Governing Board Decision No. 12/2019 of 21 June 2019 included the return of EUR 139 100 891 to the EU budget with a view to supporting additional collaborative health projects under Horizon 2020, where immediate absorption capacity was available due to oversubscription of excellent proposals.

This decision was reached for a number of reasons, including the capacity to absorb the funds available as major projects launched in 2018 and early 2019 drew significantly on available industry resources. The Governing Board carefully evaluated the various options available in mid-2019 and considered the risks associated with moving those commitment appropriations to the 2020 budget (2020 being the last year to commit funds under H2020). The Governing Board opted to return the commitment appropriations to the European Commission in line with the principle of sound financial management of public funds, and efficient operational budget planning from the IMI2 JU side. This decision secured the required matching of public funds against private contributions.

At that time, it seemed prudent and sound not to withhold funds that were much needed elsewhere in the EC budget. In hindsight, in light of the COVID19 pandemic and the response to IMI Call 21 (Development of therapeutics and diagnostics combatting coronavirus infections), which received the highest number of proposals in IMI JU's history, we acknowledge that these funds could indeed have been used within the IMI programme[1].

In-kind contribution validation process and figures

The IMI Programme Office implements two research framework programs under two different legal frameworks, with specific modalities affecting the reporting process of industry contributions during project implementation. It is worth noting that the in-kind contribution validation process is equally robust for both programmes.

Under the IMI1 framework, industry contributions are declared on a project basis, together with the periodic report of each project. Following the assessment performed, the Authorising Officer validates individual project reporting period-linked contributions, while the accountant records them in the accounting system (SAP). In contrast, under IMI2, in accordance with Article 4 of the Council Regulation No 557/2014, each EFPIA company and Associated Partner is required to report its contributions once a year for the totality of all the costs generated that contribute to IMI2 projects. Following the assessment performed on the audit certificates, received from individual contributors for all their participations, the Authorising Officer issues an annual validation decision which is then recorded in the accounting system.

[1] In response to Call 21 launched on 3 March 2020 144 proposals were received. Out of 120 eligible proposals, 12 were recommended for funding by the independent experts. However, due to the budget limitation only 8 were funded.

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Notably, industry Members and Associated Partners do not receive any IMI funding but rather contribute their own resources *in kind* to the projects in which they participate. The IMI legal basis allows in-kind contributions for operational activities (IKOP) while there are no in-kind contributions for additional activities (IKAA).

A rigorous control system is in place for scrutinising industry in-kind contributions all along the life cycle of a project.

Proposals for new projects are evaluated by independent high-level experts. During the evaluation, the level of estimated in-kind contributions of the companies is subject to a stringent review in order to ensure that they are appropriate in relation to the proposed work to be carried out in the project.

Reported in-kind contributions are thoroughly checked and questioned by the IMI Programme Office. Before validating any contributions, IMI carries out a series of checks to verify the eligibility of in-kind contributions i.e. that they are in line with the Grant Agreement requirements and the project's description of its work. As a precondition for the assessment, all the reported costs must be accompanied each year by a certificate from an independent external auditor, confirming that the costs are in line with the requirements of the IMI2 Regulation. For the certification to be considered, it must be based on the standard terms of reference[2] (audit procedures) provided by IMI. IMI analyses and questions the audit certificates and adjusts the amounts where necessary. EFPIA and Associated Partner contributions are only validated for inclusion in the IMI's accounts (in the form of net assets from Member contributions) after these checks and adjustments are completed.

In order to provide a complete picture of the process, it is important to mention that IMI has issued guidance[3] to the industry Members and Associated Partners on reporting in-kind and financial contributions[4] as well as internal guidance on acceptance and validation of in-kind contribution[5] in IMI2 JU.

Under the IMI1 legal framework, IMI has conducted ex-post reviews and financial audits on the declared in-kind contributions made by EFPIA companies participating in IMI projects. The purpose of these controls, using a risk-based approach as per IMI's audit strategy, is to independently verify that these in-kind contributions accepted by IMI have been effectively committed to the projects. By the end of 2019, IMI completed ex-post audits of 20 EFPIA companies, covering a total of EUR 617.9 million in accepted contributions to IMI1 projects, or 90 % of all EFPIA contributions.

Under the IMI2 framework, if the audit certificate provided with the cost declaration leave uncertainties as to the value of the contribution, the Programme Office may carry out an additional audit itself, before validating the EFPIA and Associated Partner contributions.

The IMI Governing Board regularly monitors the state of play on reported and validated industry contributions.

IMI annual accounts including the in-kind contributions (see Part 2.7) are prepared by the European Commission Accounting Officer acting as the appointed IMI Accounting Officer. IMI accounts are voted upon by the Governing Board where the European Commission has a controlling vote.

In accordance with Article 54 of the IMI Financial Rules, an independent external auditor[6] verifies that the annual accounts of IMI2 JU properly present the income, expenditure and financial position of IMI2 JU. The Court of Auditors considers the audit work performed by the independent external auditor and the action taken in response to the external auditor's findings. The European Court of Auditors audits IMI's accounts annually and in the last five consecutive years has issued an unqualified opinion. The Court has full access to each step of the IKC validation and accounting documentation.

[2] https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/ToR_V2017-02-14_Final.pdf
[3] IMI1 issued the Financial guidelines (IMI/INT/2013-00767) to beneficiaries and EFPIA members and defined reporting and certification obligations and modalities.
[4] IMI2 JU Guidance for reporting in kind and financial contributions by Members and Associated partners IMI2/INT/2018-00527 - https://www.imi.europa.eu/sites/default/files/uploads/documents/apply-for-funding/call-documents/imi2/IMI2_JU_Guidelines_for_reporting_in_kind_and_financial_contributions_by_%20Members_other_%20than_the_%20Union_%20and_%20Associated_Partners_0.pdf
[5] SOP on Acceptance and validation of in-kind contribution in IMI2 JU - IMI2/INT/2017-01885
[6] EY audited IMI financial statements of 2016, 2017, 2018, 2019 and issued unqualified audit opinions for the Court of Auditors considerations.

In full transparency, the in-kind contributions are reported in the annual accounts and the consolidated annual activity reports of IMI. These are published on IMI website and also transmitted to the budgetary authorities in full compliance with the regulatory requirements.

The tables below present an overview of the IMI1 commitments and validated in-kind contributions for 59 projects contracted under FP7 programme:

IMI1 IKC In million EUR	EU commitment	EFPIA commitment	EFPIA contribution validated
Up to 31.12.2018	965.7	965.0	633.4
Up to 31.12.2019	965.7	977.1	688.6
Up to 31.12.2020	965.7	975.5	737.5

The following table provides an overview of the EU, EFPIA and Associated Partner commitments and validated IKC amounts to IMI2 projects. The IMI2 portfolio was comprised of 89 projects in 2019 and 108 projects in 2020, contracted under H2020 programme:

IMI2 IKC In million EUR	EU commitment	EFPIA & Associated Partners commitment	EFPIA& Associated Partners contribution validated
Up to 31.12.2018	664.9	655.6	135.5
Up to 31.12.2019	1 062.2	1 097.3	219.7
Up to 31.12.2020	1 262.6	1 285.6	352.2

The table below provides a snapshot of the results of controls performed on audit certificates provided to support declarations on IMI2 contributions. When an audit certificate was incomplete it was rejected and, consequently, the related reported in-kind contribution was also rejected:

IMI2	No of audit certificates received	EFPIA & Associated Partners reported	Rejection rate (due to absence or incomplete audit report)
Validation 2019	46	86 288 770	6,43%
Validation 2020	60	145 892 535	17,24%

The IMI2 JU has established a rigorous control system for managing industry in-kind contributions in conformity with the relevant legislation, and diligently monitors the matching principle for public and private contributions.

IMI's COVID-19 response

IMI´s COVID-19 Call for faster diagnostic tools and safe and effective treatments

IMI launched a fast-track Call on 'Development of therapeutics and diagnostics combatting coronavirus infections' already on 3 March. The eight large-scale research projects selected are contributing to both the European and international response to the pandemic by addressing one of the eight immediate research actions that were agreed at the WHO global research and innovation forum held on 11-12 February 2020, and by collaborating worldwide with all relevant research initiatives, as mandated in the Call topic text.

The projects are:

1. Diagnostics projects

COVID-RED It is well known that people with COVID-19 are highly infectious in the 48 hours before they develop symptoms. A key element in COVID-RED's proposal is an Ava bracelet, a wearable device typically used by women to track their fertility. The bracelet is equipped with sensors to measure things like the user's breathing rate, pulse and skin temperature, which could change slightly before the user actually starts to feel ill. The bracelet will sync with a mobile app that will detect any unusual variation in these parameters.

DECISION is developing an easy-to-use, low-cost, disposable test for COVID-19 that can give reliable results (it works like a PCR since it is a molecular amplification of the viral genetic material), on the spot, within minutes. The idea is that it can be deployed anywhere; at drive-through testing centres, airports, physician offices, hospitals, quarantine centres, and eventually, even in people's own homes.

DRAGON is using artificial intelligence and machine learning to develop a decision support system capable of delivering a more precise coronavirus diagnosis and more accurate predictions of patient outcomes. The project will draw on new and existing data and sample collection efforts, including computed tomography scans to carry out detailed profiling of patients. They will then use AI technology to transform this information into a precision medicine approach that will help clinicians and patients with decision making around treatments.

KRONO is working to deliver an ultra-fast COVID-19 diagnostic test that will provide results within 40 minutes and is designed to work in resource and economically poor regions. It will be used to detect pre-symptomatic and asymptomatic cases, when and where it is needed, without the need for a lab or trained technicians. In the long run, the project plans to build up a generic platform technology pipeline that can be operational within weeks of the appearance of a new disease-causing agent in the population.

RAPID-COVID While the world focuses on COVID-19, other infectious diseases with similar symptoms continue to circulate. Rapidly identifying and diagnosing not only COVID-19, but other infections such as colds and the flu, will ensure that COVID-19 patients can be quickly isolated, limiting the spread of the disease. Furthermore, rapid diagnosis of infections besides COVID-19 will ensure that all patients receive the right treatments, and reduce the unnecessary use of antibiotics. RAPID-COVID is developing a diagnostic kit capable of simultaneously detecting SARS-CoV-2 (the virus that causes COVID-19) plus 30 other common respiratory bacteria and viruses. The consortium already has a prototype technology called MPA (Multiplex Probe Amplification), and the goal of the project is to validate this and get a CE mark for both point of care (PoC) and high throughput laboratory testing.

2. Treatment projects

CARE is working to come up with better treatments against COVID-19 mainly through (i) the discovery of small molecule treatments directed against viral proteases, and (ii) the discovery of antibodies directed against the spike protein. Antibodies have become the main focus of the project because they have not just the potential to treat the disease, but also to prevent it, since antibodies could be given to family members or peers of people who have tested positive in order to prevent infection, or to elderly people who may not be able to achieve sufficient vaccine immune responses. They could also play a role if vaccines are not as effective as hoped. In the long-term, CARE is also working on preparing for a better response to future coronaviral threats.

Impentri Many people with severe COVID-19 infection experience a build-up of fluid in the lungs, making it hard to breathe and, in the worst cases, contributing to the death of the patient. The body's own immune response is partly responsible for this build-up of fluid. There are signs that the generic drug imatinib, which is used to treat certain cancers including some forms of leukaemia, could address the problem. Impentri is carrying out clinical trials to get solid data on its efficacy and safety as a treatment for COVID-19 patients with a build-up of fluid on the lungs.

MAD-CoV 2 The protein ACE2 (angiotensin converting enzyme 2), found on the surface of cells in the lungs and other organs, has been confirmed to play an important role in SARS-CoV-2 infections. Based on this knowledge, the team behind MAD-CoV 2 is investigating the use of recombinant ACE2 as an antiviral treatment, and further possible new targets and treatments, through a clinical trial sponsored by MAD-CoV 2 partner APEIRON Biologics AG. The team involves partners that have experience on the ground during earlier SARS and Ebola outbreaks.

ELF - and its successor, ESCulab - Beyond the COVID-19 Call, an existing IMI project is also making a valuable contribution in the search for better treatments for COVID-19. Early on in the COVID-19 outbreak, the European Lead Factory team decided to fast-track screening proposals relating to the coronavirus -the ELF combines a large compound collection and high throughput screening centre that scientists can access to advance their own research projects. In July 2020, the project announced that it had selected its first proposal, which aims to identify small molecules that could stop the virus from getting into human cells.

Early building blocks for the development of a vaccine

ZAPI Infectious diseases and vaccines have been a priority for IMI since the beginning, and we launched a project specifically on bio-preparedness, ZAPI, in 2015. The project has demonstrated that certain antibodies can stop the MERS (Middle East respiratory syndrome) coronavirus from infecting new cells and is now assessing whether the antibodies could also be effective against SARS-CoV-2. Its findings are further feeding into research on COVID-19 through two new projects, the EU-funded MANCO project and the IMI-funded CARE project. A second project with a huge impact in preparing for a speedier regulatory approval of a potential vaccine against the SARS-CoV-v2 is EBOVAC, based on their recent experience in developing the Ebola vaccine.

More broadly, other IMI projects that are relevant to bio-preparedness and vaccines include BioVacSafe, which is developing tools to speed up and improve the testing and monitoring of vaccine safety; ADVANCE, which focuses on facilitating the rapid delivery of clinical data on vaccines to help public health authorities make decisions on vaccination strategies; VAC2VAC, which is working on developing alternative *in vitro*, non-animal tests for vaccines; and VITAL, which is performing a clinical vaccine study to understand the mechanisms underlying vaccine response in different age groups.

Learning about COVID-19 and assessing its impact on patients

EHDEN is currently developing a federated network of data partners with the goal of allowing access to the anonymised health data of 150 million citizens in Europe. The data will remain at all times under the complete control of the original data owner, thereby ensuring ethical and local data privacy rules are respected. At the heart of the project is a community of SMEs selected through open calls and trained and certified by EHDEN, who are responsible for harmonising the data owned by the partners according to a common data model. The COVID-19 pandemic has confronted the project with its first real-life test.

- The project has been working since May 2020 with 25 data partners across Europe to help them map their COVID-19 clinical data to the standardised common data model. Its goal is to help clinicians, scientists, governments and the public to know more about characterising patients with COVID-19, how best to manage their care, and whether certain treatments are safe and effective.
- EHDEN partners have played a leading role in organising the OHDSI (Observational Health Data Sciences and Informatics) COVID-19 virtual study-a-thon held on 26-29 March. Five preprints have already been published as a result of this study-a-thon, directly impacting patient care. One of them is a very large study on the safety profile of hydroxychloroquine using data comprised of 14 sources of claims data or electronic medical records from Germany, Japan, Netherlands, Spain, UK, and USA. This study demonstrated that there was a striking >2-fold increase in sudden cardiovascular mortality

when hydroxychloroquine is taken concomitantly with azithromycin. The FDA, EMA, and MHRA have evaluated this data, and the EMA issued a warning that explicitly mentions the project's preprint.

RADAR-CNS project is using wearable devices and mobile phones to monitor people with epilepsy, multiple sclerosis, and major depressive disorder. The hope is that by gathering data continuously via these devices, relapses in a patient's condition could be predicted or even avoided. As countries across Europe shut down in response to the COVID-19 pandemic, RADAR-CNS was able to use its systems to assess how people's behaviour changed during and after lockdown. While mobility markers fell, virtual sociability rose, with participants spending more time active on their phones and using social media apps. Participants also had a lower heart rate, went to bed later, and slept more. 'This ability to monitor response to interventions, in near real time, will be particularly important in understanding behaviour as social distancing measures are relaxed as part of any COVID-19 exit strategy,' the researchers note.

SOPHIA Obesity has been identified as a risk factor for COVID-19 disease, but how do people living with obesity feel about the pandemic? IMI's SOPHIA project aims to understand who is at greatest risk of health problems associated with obesity. The team interviewed 23 people undergoing diverse obesity treatments about their experience of living through the pandemic. Their findings, published in the journal Clinical Obesity, revealed that the pandemic affected both diets and physical activity. It also impacted on people's psychosocial wellbeing, as people worried about what would happen if they caught the disease. At the same time, some patients were not aware of the link between obesity and COVID-19. Looking to the future, the researchers call for more research into the links between obesity and COVID-19, and note that this should be communicated in a way that does not stigmatise people with obesity.

Infrastructure and tools for COVID-19 clinical research

COMBACTE-NET With more than 1000 hospitals, the COMBACTE network is currently being used in identifying and activating sites that can participate in COVID-19 clinical trials, next to the regular COMBACTE clinical trials focusing on antimicrobial resistance. COMBACTE is part of the Horizon2020 RECOVER project contributing to the observational study to identify the prevalence, disease spectrum and severity, risk factors, spread and outcomes of COVID-19 in patients in hospital care (the emergency room and respiratory ward) and to the REMAP-CAP adaptive platform trial focused on determining the optimal set of treatments for patients with severe community-acquired pneumonia, which has extended its domains to investigate new treatments specifically for COVID-19 patients on the ICU and the ward; COMBACTE was also used to select the sites for the the European part of the Australian BRACE multi-centre randomised clinical trial designed to test whether the BCG vaccine (Bacillus Calmette–Guérin), which boosts humans' 'frontline' immunity, can protect healthcare workers exposed to SARS-CoV-2 from developing severe symptoms.

The outbreak also has an impact on COMBACTE's LAB-Net activities. Supported by its state-of-the-art laboratory expertise and 800 laboratories in its network, LAB-Net has stepped up to support COVID-19 clinical trials by assessing the routine clinical laboratory practices for COVID-19. Among COMBACTE's laboratory network a survey on the level of preparedness of diagnostic laboratories for the detection of SARS-CoV-2 has been sent.

DO->IT Clinical research participants have to sign an informed consent form (ICF). IMI's DO>IT project has developed templates and guidance on how to prepare informed consent forms that enable the use of study participants' health data and biosamples while respecting their rights as data subjects. The templates are referenced in the European Commission's open access guidelines for projects working on COVID-19 and related topics.

eTRIKS Data standards are vital tools in data management, as they make it easier to load data into knowledge management platforms and compare it to other datasets that have applied the same standards. IMI's eTRIKS project created a 'standards starter pack' to raise awareness of, and provide guidance on, data standards in clinical, genomic and translational data management. The starter pack is referenced in the European Commission's open access guidelines for projects working on COVID-19 and related topics.

Contributing to a collaborative EU ecosystem to support the monitoring of COVID-19 treatments and vaccines

As treatments and vaccines get regulatory approval, it will be crucial to keep monitoring the safety and efficacy of these products in the real world setting. The EHDEN and ConcePTION projects plus the ADVANCE/VAC4EU initiative are helping the European Medicines Agency (EMA) to gather real world data on COVID-19 vaccines and treatments.

EHDEN is collaborating with the EMA on the creation of a framework for multicentre cohort studies on the use of medicines in COVID-19 patients. The work includes the identification of large national cohorts of COVID-19 patients and appropriate comparator groups, the development of a study protocol template for multinational studies as well as the establishment of a collaborative framework for researchers.

ConcePTION A high number of women are likely to be exposed to SARS-COV-2 at some point during their pregnancy. For the time being, they have to make a personal choice, on a case by case basis, about their treatment. This includes the question whether to get vaccinated or not. To make sure doctors and women have access to reliable information to support decision making, CONCEPTION will collect data on the impact of COVID-19 in pregnancy. The project will later follow up to monitor long-term outcomes of the offspring. This work will contribute to guide decision-making about vaccine indications, vaccination policies and treatment options for COVID-19 in pregnant women.

ADVANCE The international association VAC4EU (Vaccine Monitoring Collaboration for Europe) has been working with the EMA to prepare a European infrastructure for the monitoring of the benefits and risks of the COVID-19 vaccines and for conducting specific studies in a collaborative manner across EU countries. VAC4EU was born out of IMI's ADVANCE project, which drew on lessons learnt from the 2009 swine flu pandemic to create an ecosystem for monitoring vaccine benefits and risks.

The outcomes of the three projects will feed into the work of EMA's COVID-19 pandemic Task Force (COVID-ETF) and EMA's scientific committees to ensure that the evidence is translated into scientific opinions on the optimal use of the medicines and vaccines concerned.

Providing reliable guidance to vulnerable groups

EUPATI has compiled a list of content and resources that provide reliable information on COVID-19 and other topics relating to medicines research and development and patient education.

c4c is one of IMI's projects in the paediatric field, and now the team has compiled a set of trustworthy resources on the coronavirus for children and families. The resources come in a range of languages and formats and target different age ranges.

IMI's results and their application in the market.

In general terms, IMI projects are not designed to directly bring new medicines to market. Rather, they will have an impact on new product development and product safety by:

i. advancing the scientific knowledge that will underpin the development of a range of protocols, standards, technologies and medicines. For instance, the BEAT-DKD and RHAPSODY projects have identified five subtypes of diabetes. e.g. patients in group 2 ('severe insulin-deficient diabetes') are at greatest risk of eye disease, while patients in group 3 ('severe insulin-resistant diabetes') had the highest incidence of kidney damage. In 2019, the projects validated these initial findings in additional patient populations and uncovered new clues as to the best treatment options for the different groups. For example, one study demonstrated that patients with 'severe insulin resistant diabetes' (SIRD) who undergo bariatric surgery show the best recovery from diabetes and the greatest improvement in kidney function. This is important as kidney disease is a common complication in diabetes. Now, BEAT-DKD is working on a software package that would allow doctors to identify which diabetes subtype a patient has. The doctor would simply have to enter information on the six variables used for clustering. As well as indicating the subtype that is the best match for the patient,

the tool would generate information on the best choice of treatment. The tool is under development and will be formally tested as a medical device for use in clinics.

ii. improving the efficiency and productivity of the medicines development process (usually in particular disease areas), delivering future cost savings, time savings, reductions in risk or reductions in attrition rate. For instance, in the MARCAR project, researchers discovered early biological indicators that could help detect some of the more indirect ways in which drugs cause tumour formation, while the MIP-DILI project improved laboratory tests used to predict drug-induced liver injury in the early stages of drug development.

When IMI projects have been directly targeted to develop treatments or diagnostics, they have succeeded. Some examples are:

- The recent EC marketing authorisation granted to the IMI co-funded Janssen vaccine to prevent the Ebola virus disease in people one year and older (IMI EBOVAC1 and EBOVAC2 and EBOVAC3 projects);
- The two rapid diagnostic tests that were field-trialled in the Democratic Republic of the Congo during the recent Ebola outbreak, together with an iris-scanning technology which is now being adapted for use in the COVID-19 context. These products have been developed by several Ebola+ projects
- The Med Safety mobile app for smartphone users to report side effects of medicines directly to the regulatory authorities developed by the WEB-RADR project. Facilitated through a collaboration with the WHO and local regulatory authorities, the app was launched in 2019 in Armenia, Botswana, Cote d'Ivoire, Ethiopia and Ghana, bringing the number of countries using the app to 11. The UK regulator, the MHRA, has recently funded adaptation of the platform to help with the reporting of medicines used to treat coronavirus symptoms in the UK.

In the field of AMR, several IMI projects are working towards a more rapid and efficient development and commercialisation of much-needed new antibacterial treatments. These are a few of the ongoing trials supporting the development of novel compounds.

- COMBACTE-NET has completed the SAATELLITE study, a phase II trial of suvratoxumab, a novel monoclonal antibody (mAb) targeting Staphylococcus aureus;
- COMBACTE-CARE has now initiated the REVISIT trial, a phase III trial of aztreonam-avibactam (ATM-AVI) for treating serious infections caused by Gram-negative, carbapenem-resistant, bacteria, for which there are limited or no treatment options.
- ENABLE has selected Apramycin as phase I clinical candidate for the treatment of critical systemic infections caused by Gram-negative bacteria. These include carbapenem-resistant Enterobacteriaceae and Acinetobacter baumannii – both listed as Priority 1 on the WHO priority pathogens list;
- ENABLE has also selected Mutabilis's oral combination including MUT485 as a candidate drug. This means that if the results of the final pre-clinical tests are positive, it can be advanced to a phase I clinical trial. This drug candidate could be used to treat urinary tract and kidney infections caused by bacteria that are resistant to other antibiotics.
- TRIC-TB phase I testing in healthy volunteers for BVL-GSK098, a novel compound potentiating and overcoming resistance against ethionamide for treatment of tuberculosis (TB), is underway. BVLGSK098 targets bacterial transcriptional regulators, a ground-breaking approach that is being assessed globally for the first time in a clinical trial. Moreover, the US Food and Drug Administration (FDA) has given Qualified Infectious Disease Product (QIDP) designation to one of the compounds (BVL-GSK098) in a fixed combination with Ethionamide for the treatment of pulmonary TB. QIDP designation is given to antibacterial or antifungal drugs designed to treat serious or life-threatening infections. Crucially, QIDPs are eligible for priority and fast track review by the FDA. This will therefore help TRIC-TB to speed up the development of the compound.

IMI's research priorities

In compliance with the regulations that govern IMI, the Strategic Research Agenda (SRA) is fully aligned with the EU health research priorities, which were decided by the European Parliament and the Council during the negotiation of Horizon 2020.

Prioritisation of research areas also takes into account the *Priority Medicines Report of 2013* by the World Health Organisation (WHO), from which the SRA takes on those that (i) are most relevant for a public-private partnership; and (ii) consider IMI's remit to support pre-competitive research and innovation activities with the aim of improving European citizens' health and well-being. These are: antimicrobial resistance, osteoarthritis, cardiovascular diseases, diabetes, neurodegenerative diseases, psychiatric diseases, respiratory diseases, immune-mediated diseases, ageing-associated diseases, cancer, rare/orphan diseases and vaccines. The total IMI2 budget committed (coming from IMI, EFPIA and Associated Partners) to these priorities by the end of 2019 was EUR 1 846 613 930.

The table below illustrates current IMI2 investment in major disease/research areas – WHO and H2020 research priorities - with a cut-off date of August 2020.

	IMI2 contribution EUR	EFPIA contribution EUR	Associated Partners contribution EUR	Total contribution EUR	% Total	Number of projects
Immunology	106 472 508	103 785 890	105 000	210 363 398	9%	7
Diabetes/metabolic disorders	91 093 930	84 071 454	18 911 020	194 076 404	8%	8
Neurodegeneration	135 098 435	83 086 823	56 049 619	274 234 877	12%	15
Translational safety	74 630 989	70 907 584	0	145 538 573	6%	6
Digital health and patient-centric evidence generation	222 089 523	234 429 664	2 696 394	459 215 581	19%	18
Infections control	411 750 695	309 027 416	80 935 277	801 713 388	34%	31
Oncology	58 115 625	59 096 673	0	117 212 298	5%	5
Drug discovery	18 249 993	17 669 327	810 000	36 729 320	2%	1
Other*	59 648 531	55 436 126	6 445 380	121 530 037	5%	8
Total	**1 177 150 228**	**1 017 510 957**	**165 952 690**	**2 360 613 874**	**100%**	**99**

*Under "other", IMI has funded projects in areas such as the environmental aspects of pharmaceutical products, drug delivery or manufacturing processes improvement.

Some voices have questioned IMI's research priorities, arguing that funding has gone to research topics "with a pre-existing private sector high interest" over areas such as poverty-related and neglected diseases. However, IMI's focus on areas such as cancer, Alzheimer's disease and diabetes is particularly relevant since, according to the WHO's report *The World Health Statistics 2020*, "compared with the advances against communicable diseases, there has been inadequate progress in preventing and controlling premature death from non-communicable diseases (NCDs)". The report warns that an estimated 41 million people worldwide died of NCDs in 2016, equivalent to 71% of all deaths, listing cancer (9 million deaths) and diabetes (1.6 million deaths) among the four biggest culprits. The main reason for the lack of significant scientific progress is that these are extremely complex diseases, and, as such, they are the ones with the most acute need for a collaborative, multidisciplinary approach of the kind facilitated by IMI.

A further assumption is that IMI does not address the diseases that affect middle- and low-income countries when, in fact, non-communicable diseases such as diabetes, depicted as only relevant to developed countries' health systems, is increasingly straining the health systems of low- and middle-income countries. According to the International Diabetes Federation, 79% of diabetes patients live in low- and middle-income countries. Therefore, the significant work done by IMI projects in these areas will be of value not only to European patients but to non-European patients too.

In a different order of variables, IMI's portfolio also addresses rare diseases, which are often chronic, progressive, degenerative and often life-threatening diseases. The most common cause (80%) of rare diseases are genetic variations and 98% of rare diseases currently lack effective treatments. As an example, fibrodysplasia ossificans progressiva (FOP) is a rare disease in which the muscles and connective tissues (e.g. tendons and ligaments) slowly turn into bone. There is no treatment; as the disease progresses, the build-up of bone material around the joints gradually limits patients' mobility, and can also result in difficulties eating, speaking and even breathing. By running a clinical trial of a drug call AZD0530 in 16 adults with FOP, the aim of the STOPFOP project is to see if it reduces the formation of new bone.

Should IMI focus on neglected infectious diseases?

In the period from 2007 to 2014, the EU was one of the world's largest funders of neglected infectious diseases (NIDs) research through the Seventh Framework Programme (FP7)[7]. NID research has remained a priority in Horizon 2020, principally (though not only), through EDCTP2, whose original remit has been extended to include NIDs in addition to its focus on HIV/AIDS, malaria and tuberculosis.

Although IMI was not specifically designed to focus on NIDs, some IMI projects do. For instance, the VHFMoDRAD project, building on the EbolaMoDRAD project's Ebola diagnostic testing technology, is developing a test that can diagnose, in a single blood sample, other viral haemorrhagic fevers like Lassa fever, Crimean Congo Haemorrhagic fever, Rift Valley fever, Marburg, Yellow fever, Dengue fever and Zika. The tests will also be validated in the field, and training courses will be set up in western Africa to teach locals how to use the tools. The project intends to partner with an African manufacturer so that the tests can be produced locally.

Some other IMI projects are developing tools that have relevant implications for NID diseases. For instance, ELF - and its successor, ESCulab - provides researchers with the opportunity to have their drug target screened free of charge against the project's compound collection. It has already run a screening programme on Dengue fever.

The European Commission has already indicated that support to these areas is planned to continue in the future through the EDCTP's successor, the EU-Africa Global Health Partnership, and other Horizon Europe initiatives.

[7] During FP7, the EU provided EUR 169 million for 65 NID research projects; these projects involved research teams from 331 different institutions in 72 countries on 6 continents.