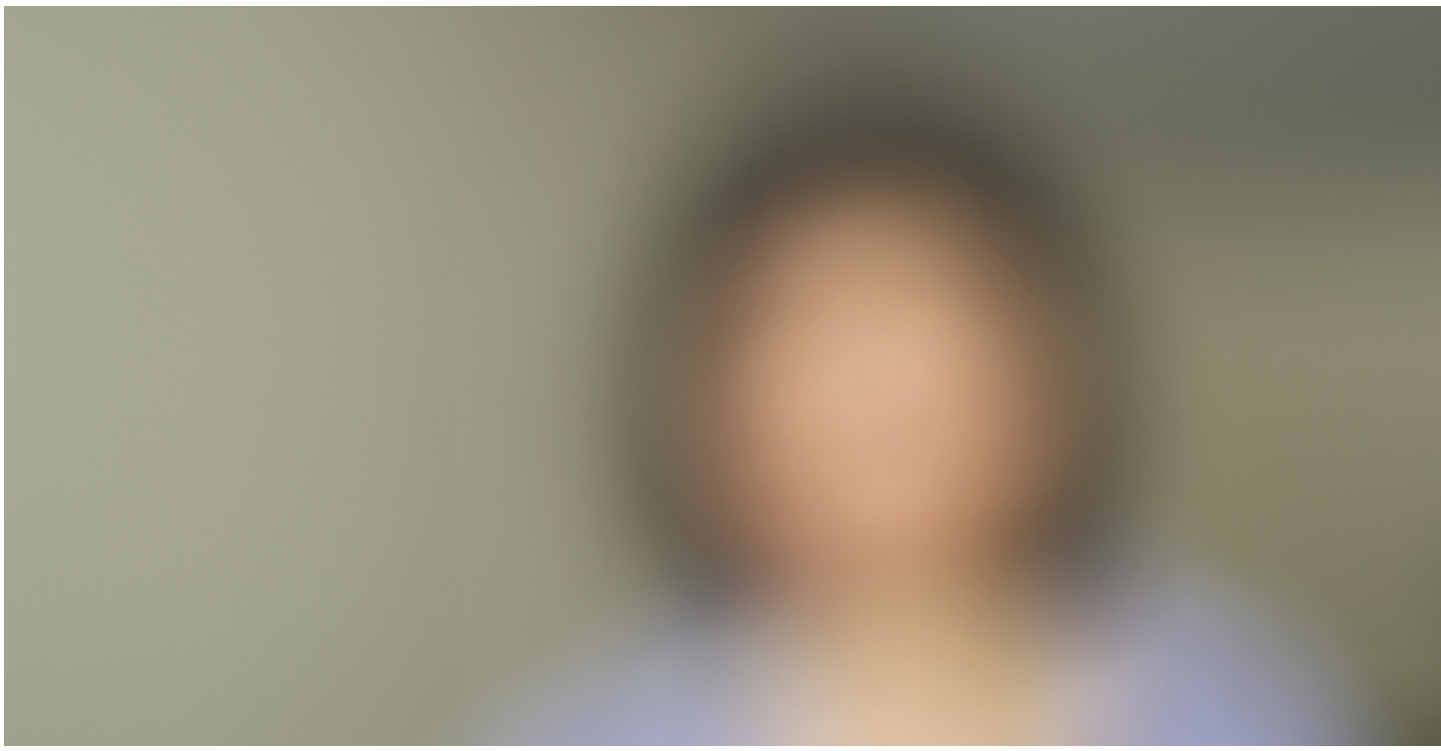
POLICY BRIEF

September 2021

THE STATE OF **TRANSPARENCY** & **MEDICINES POLICY** IN THE EU



Transparency is crucial at every step along the research and development (R&D) continuum of medicines: whether we are talking about public investment in research clinical trials data, regulatory practices, or the content of procurement negotiations. However, transparency is a means, not an end: a means to bring about change for more sustainable, patient-centred healthcare systems that ensure affordable access to safe, effective, quality-assured medicines for everyone, everywhere. This paper gives an overview of the progress that has been made towards that goal over the last two years.

TRANSPARENCY CHALLENGES

One of the most significant challenges to transparency in access to medicines of the last two years has been the European Commission's approach to COVID-19 vaccine procurement. Negotiations with pharmaceutical companies have taken place behind closed doors, and when relevant papers have been disclosed to the European Parliament Library and published more widely, they have been heavily redacted. European Commissioner for Health, Stella Kyriakides, claimed in a statement in November 2020 to 'recognise fully the importance of transparency in this process' but went on to capitulate to non-disclosure clauses and reiterate the 'business sensitive' information lines that serve only to protect pharmaceutical companies' interests. Lack of transparency in procurement means prices and terms cannot be scrutinised by external parties and leaves the bargaining power lying in pharmaceutical companies' hands, rather than providing a level playing field for countries and regions around the world watching how the deals are made in Europe.

Publication of negotiation and contractual documents has only occurred as a result of civil society and parliamentary pressure.

Organisations, such as Corporate Europe Observatory (CEO), have been working tirelessly to press the Commission to release more information on the negotiations via freedom of information (FOI) requests. Early in 2021, the European Ombudsman began investigations into the 'opaque' handling of the procurement of vaccines by the Commission—this is an indication of the seriousness of the issue and follows complaints by CEO about the Commission's reactions to their FOI requests. Health Action International (HAI) and Médecins Sans Frontières have briefed Members of the European Parliament (MEPs) on transparency and procurement issues in advance of key plenary and committee sessions. While the Commission's behaviour has caused great concern about the future of transparency in medicines, we should take comfort in the fact that MEPs and civil society organisations that don't usually focus on transparency are now banging the drum and calling for improvements to be made.

CLINICAL TRIALS

The last two years have also seen a disheartening lack of progress on transparency of clinical trial data. Not only has the implementation of the Clinical Trial Regulation been glacially slow, but universities across the European Union (EU) have been found to be consistently underreporting on trial data. TranspariMED, an organisation that works to end evidence distortion in medicine, has highlighted the 'dismal reporting of drug trial results and address widespread data inaccuracy'. The numbers show that we are a long way off transparency in trial data with over 3,800 trials results missing from the European registry. Indeed, the performance of Member States varies greatly: only 10% of Dutch single-country trials approved up to 2015 have been uploaded. A 2020 HAI/TranspariMED report on the situation in the Netherlands goes into more detail on this. The onus lies on national regulators to ensure universities and pharmaceutical companies running clinical trials make the results public on the European trial registry within 12 months of completion: we are seeing a total dereliction of this duty, putting patient interests at risk, undermining the medical evidence base and damaging efforts to develop better treatments.

With the COVID-19 pandemic, we are seeing more clearly how important it is that patients and consumers have access to accurate and timely information about how medicines are approved, from sources they trust. Without accurate and detailed information concerning the cost-benefit analysis and added therapeutic value, the media focus on potential side effects contributes to vaccine hesitancy. Other high-profile media stories—including accusations that AstraZeneca 'cherry-picked' data to artificially increase the efficacy statistics for its vaccine—could further erode public confidence in the vaccine and in trial data more broadly. A recent HAI blog has delved more deeply into the issue of media scrutiny of clinical trial data and the damaging impact this can have on independent regulation of pharmaceuticals.

If we are going to undo the damage the COVID-19 pandemic has had on transparency of and confidence in trial data, we need to:

- Urgently implement the Clinical Trial Regulation
- Ensure regulators hold trial conveners to account on submission of data
- Develop more robust ways to regulate of the information pharmaceutical companies are publishing
- See the European Commission leading by example.

COST OF RESEARCH AND DEVELOPMENT

The COVID-19 pandemic has also exposed the issue of transparency in pricing, and more specifically public return on public investment. Without true transparency of the costs of R&D, and the key avenues of funding pharmaceutical companies are benefitting from (i.e., taxpayer funded government grants) it is impossible to tell whether the public is getting bang for their buck in pharmaceutical development. Much was made of the government investments in the

labs that went on to produce the first COVID-19 vaccines. In particular, many would argue the UK Government heralded its investment in Oxford University to win political points, but without understanding how such investments translated into product prices and profit margins for private developers, we do not know if this was a sound investment, or indeed whether the public is paying twice, by investing in the research through taxes, and then paying through the nose for the final product. Universities Allied for Essential Medicines (UAEM) have mapped the public funding for COVID-19 vaccines, diagnostics and therapeutics, which is an impressive step towards transparency in this area. UAEM found that only 82% of funding for these products had been disclosed indicating the progress that still needs to be made.

Poor transparency of R&D costs also makes it difficult for governments and healthcare organisations to know whether they are getting a reasonable final price from the manufacturer compared to other countries. We can already see how much the price of COVID-19 vaccinations and therapeutics varies from country to country: a situation which is far from exclusive to the pandemic. Pfizer/BioNTech for example charged $28 a dose in Israel, compared to $6.75 in the African Union. While at first glance this looks positive, given how critical it is both from an ethical and a global health perspective that lower- and middle-income countries can purchase vaccines at a seemingly reasonable price, at $6.75 the African Union is still paying an estimated five times the cost of production. This situation is completely unsustainable, and with only estimated production costs to go on, and a reliance on countries to make public the final price they paid, it is difficult for civil society to advocate for change. Such disparate prices and lack of transparency also undermines efficient and thorough marketing authorisation decisions by hampering cost-benefit analyses.

Pricing transparency has been a key issue for HAI and our peers in the access to medicines field for some time. We have produced a number of publications going into detail on various aspects and have held events to discuss responsible licensing of publicly funded knowledge. Progress towards more transparent and equitable pricing information seems to be slow, but clauses to compel pharmaceutical companies and manufacturers to improve their behaviour were included in the Transparency Resolution—see below—so as and when Member States are able to fully implement this resolution, we hope to see movement on this complex issue.

TRANSPARENCY OPPORTUNITIES

Notwithstanding the above concerns, there have been moments over the last two years that have signalled progress towards greater transparency, and the potential for further developments in coming years.

A decision in early 2020 at the Court of Justice of the European Union (CJEU) saw the Court rule to reject an opinion of Advocate General Gerard Hogan (made in autumn 2019), that 'clinical trial data featured in marketing authorisation applications should be presumed to be commercially sensitive and therefore confidential.' Had the CJEU accepted this opinion, made in a case brought against the European Medicines Agency (EMA) by PTC Therapeutics, it would have been an existential blow to the EU regulations on transparency and the EMA's own access to documents policy.

In July 2021, the Heads of Medicines Agencies (HMA) in Europe outlined their plans to address the aforementioned issue of clinical trial reporting. In a letter to TranspariMED, the HMA explained that 'there is universal support from the NCAs [national competent authorities] for HMA to initiate joint actions with EMA and the

Commission to improve clinical trial sponsors' compliance with CTIMP [Clinical Trials of Investigational Medicinal Products] results reporting requirements.' Importantly, the letter also makes clear that the HMA is aware that the issue of missing data from old trials will not be resolved by the launch of the new CTIS registry. These efforts on the part of the HMA, if they come to fruition, will greatly contribute to transparency in clinical trial data. It is hoped that the new databases will also improve transparency, but it is imperative that lessons are learnt from the current EudraCT register in order to make the new CTIS more user friendly, and to ensure there are robust methods to hold trial sponsors to account on their duty to upload data.

Clinical Trial Registries in the EU

EudraCT: The European Union Drug Regulating Authorities Clinical Trials Database

The EudraCT is the existing clinical trial registry in the EU. It the 'database for all interventional clinical trials on medicinal products authorised in the European Union [and EEA]', as well as some specific paediatric trials outside the EU/EEA. Information on the database have been made public via the European Union Clinical Trials Register since September 2011.

CTIS: The Clinical Trials Information System

The CTIS, to be launched in January 2022, is intended to replace the EudraCT over time. It will be the 'single entry point for submitting clinical trial information in the EU'. Once submitted, the EMA will make this information publicly available in accordance with transparency rules. The system aims to capture all regulatory and ethical assessments from Member States, the public registration of the clinical trial and following updates. It will 'support the day-to-day business processes of Member States and sponsors throughout the life-cycle of a clinical trial in a user-friendly way [and] provide regulatory oversight of clinical trials and tools for supervision and monitoring.'

Although the CTIS is replacing the EudraCT, this will not happen instantly: the two will continue to run in parallel so that results from trials originally uploaded onto EudraCT can be collected on the original registry. New trials will only be registered on CTIS once it is launched in January 2022.

THE TRANSPARENCY RESOLUTION

A World Health Organization (WHO) Europe regional office report on mechanisms for improving transparency, published in July 2021, is another positive development. It is vital for intranational bodies to make statements about how they intend to improve transparency as it sends a signal, not only to the pharmaceutical industry, but also to the European Commission, and Member States as they implement the resolution on transparency passed at the 72nd World Health Assembly (WHA) in 2019. Resolution WHA72.8 was widely regarded as turning point that meant countries agreed to be open about net real prices of medicines, as well as support other transparency measures. The expectation of civil society is that we will see more WHO Regional offices developing specific plans for transparency mechanisms in the coming years as the Transparency Resolution's promises are enacted. The EMA has similarly made promising mentions of transparency in recent months, including in its new Network Strategy to 2025, in which transparency, innovation and collaboration were buzzwords. This, in tandem with the work with the HMA on clinical trial data, is an improvement on the EMA's former reputation for inadequate transparency policies that fail to acknowledge the changes needed to make meaningful progress on the ground. As ever, we need these supranational bodies to do more than pay lip service to transparency.

THE ITALY CASE

The last couple of years has seen some impressive steps by individual Member States towards greater transparency, most notably in the case of Italy, which was one of the key drivers of Resolution WHA72.8 on transparency. A few months later, in July 2020, Italian policy makers looked to make changes closer to home.

The Italian medicines agency and regulatory body, AIFA, issued a 'Pricing and Reimbursement' decree that asks pharmaceutical companies to provide information about R&D costs and commercial conditions agreed in other countries. This will mean that AIFA is able to fully understand the prices the company is charging elsewhere, reducing companies' ability to charge overinflated prices. Other European Member States should take inspiration from this initiative as a way of bringing Resolution WHA72.8 to fruition. At the time, the head of the regulator pointed out how the pandemic had shone a light on the importance of transparency:

'The need for more transparency in the pharmaceutical markets was already felt as a priority by all delegations at WHA72, but has become even greater during the pandemic. It's only through sharing information and data that we will collectively learn how to best fight this virus and find effective therapies and vaccines to reverse its course and save lives.'

LOOKING TO THE FUTURE

Over the remainder of 2021 and into 2022, attention will focus even more stringently on the Clinical Trial Regulation, which comes in force in January 2022, and as the final touches are made to the CTIS and EudraCT databases. This will be a big moment for progress towards a more transparent regulatory system—if the systems to enforce the new regulation are robust enough.

In terms of COVID-19 vaccines and therapeutics, the European Commission is already negotiating for delivery of vaccines to cover booster vaccinations in the autumn of this year, so there is plenty more work to be done to compel them to make key documents public. There might, too, be space to encourage a review of the EU's Transparency Directive, and the refinement and adoption of the new Pharmaceutical Strategy also leaves some room for discussions about the importance of transparency.

Transparency is a critical tenet of a just health care system, and a means to improve public health by enabling access to medicines for everyone, everywhere. The role of civil society and all those stakeholders, both in the Commission and among Member States, who agree with the importance of transparency, is to ensure that the positive steps—made in spite of the extraordinary circumstances of the last two years—are built upon.

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