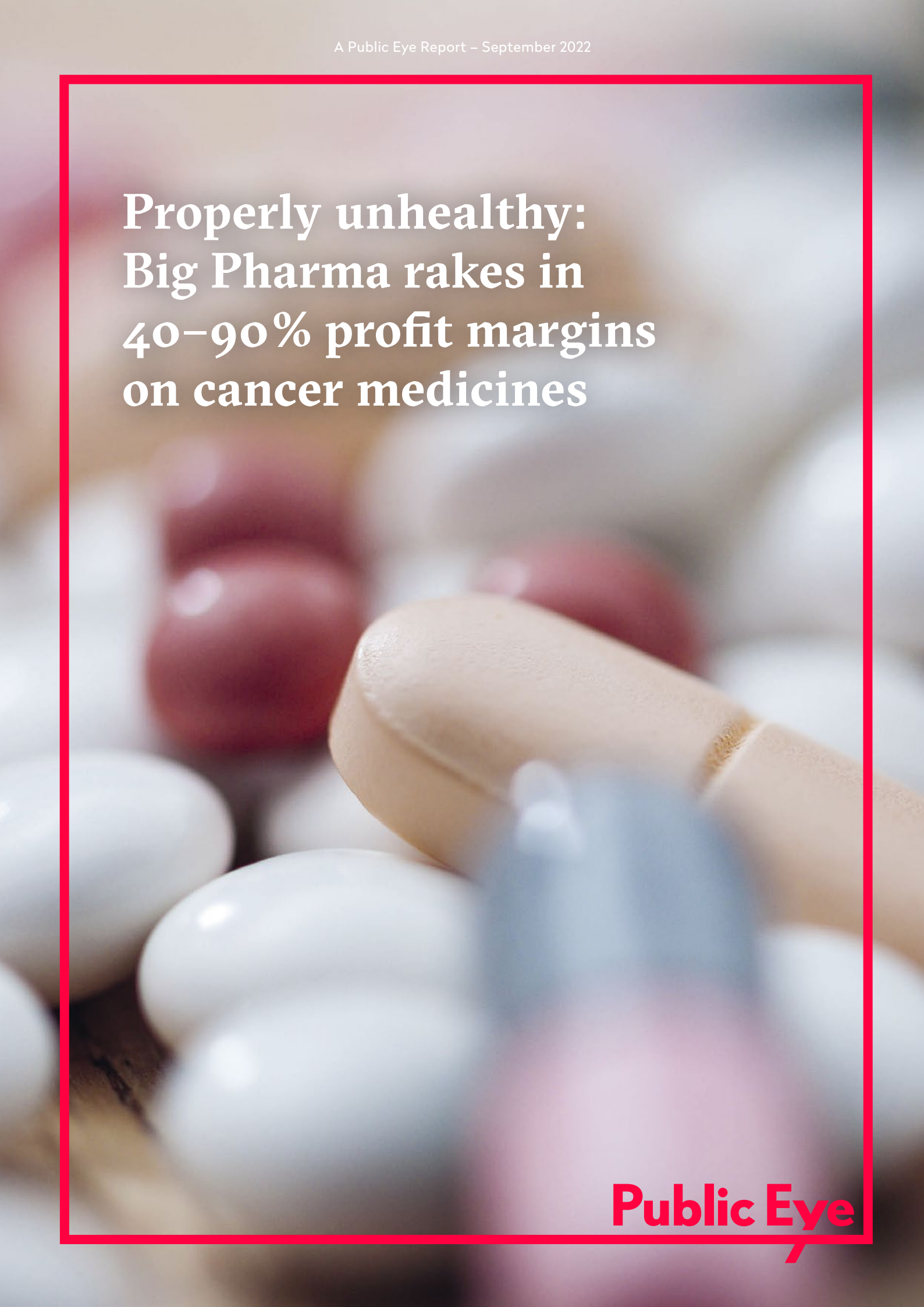
A Public Eye Report – September 2022

Properly unhealthy: Big Pharma rakes in 40–90% profit margins on cancer medicines



Public Eye

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Executive summary

Constantly rising prices mean that over two billion people lack access to drugs and the cost of healthcare in countries with public social security systems is constantly increasing. This jeopardises the right to health and risks causing two-tiered healthcare, even in wealthy countries like Switzerland. Pharmaceutical companies are able to set such high prices due to patent-based and regulatory monopolies and the ensuing pricing power they enjoy. The pharma industry argues that these high prices serve to hedge against the high risks associated with the research and development (R&D) process for new drugs. Yet it refuses to provide any transparency around actual investments made. It is challenging for researchers and specialised NGOs to estimate the amount of these investments, and both datasets and methodologies are hotly debated. For the industry and its lobbyists, this is a question of nothing less than the legitimacy of their business model.

Public Eye estimated the R&D costs for six cancer treatments marketed by Novartis, Roche, Johnson & Johnson, Bristol Myers Squibb and MSD Merck Sharp & Dohme and calculated the profit margins for the individual treatments in Switzerland. The calculations were based on the global costs of the clinical trials funded by the industry. The R&D costs were then broken down into sales in the Swiss market. The resulting profit margins of 40–90 percent are huge and far exceed those of other sectors. The lower end of this profit scale is comprised of drugs that are relatively new on the market and still have many years to benefit from patent protection and market exclusivity – meaning their profit margins will rise further.

Such margins call into question the current system – such monopolies and pricing power are theoretically supposed to guarantee that drugs are developed. However, the profit margins of cancer treatments where the high-risk R&D process has already been priced in show that pharmaceutical companies are not using high prices to hedge risks, but to make excessive profits. The high prices of cancer treatments make a significant contribution to the companies' exorbitant return on investment and to the skyrocketing costs of Swiss healthcare. Under these conditions, equitable access for all is no longer guaranteed.

Healthcare and access to drugs are a human right. The state is tasked with protecting this. Privatising services does not remove the state's primary duty to protect and guarantee human rights. It is therefore up to the state to exert effective oversight over the privatised provision of drugs. In doing so, it should retain control over the activities of pharmaceutical companies. Efforts have long been made at the international level to create transparency around prices and R&D investments, most recently through the 2019 WHO resolution on improving transparency. Switzerland is nonetheless moving in the opposite direction. In a context of cost-containment measures, managed entry agreements and secret discounts are set to make mechanisms for price setting even more opaque. This will neither provide faster access nor cut costs, but will only further strengthen pharmaceutical companies' pricing power and negotiating position. The Swiss Government must act as a matter of urgency – in favour of drug prices taking into account actual R&D investments and of the sustainability of the Swiss healthcare system.

1
Research & Development costs – a black box

Today, over two billion people, primarily in lower income countries, lack access to essential drugs. Healthcare costs are also constantly rising in wealthy countries like Switzerland – driven by high drug prices.

Intellectual property rights and the ensuing monopolies grant pharmaceutical companies huge pricing power. Market power and high prices are justified by the argument that they respond to the need to hedge against the high-risk research and development (R&D) process for treatments and at the same time serve to incentivise innovation. However, the industry refuses all transparency in relation to its own investments and the available public subsidies for its R&D work.

In short, Big Pharma R&D costs are a black box. Access to drugs is an essential element of the right to health – a right that is not guaranteed due to Big Pharma's policy of high prices. The business of medicines is very lucrative, despite the assertions around high R&D costs. This is clear from the huge profits the sector makes. The end costs for treatments are ultimately born by those who pay insurance premiums. Today, drugs account for a quarter of the costs of compulsory health care insurance (basic insurance package)[1] and are therefore an important factor in the constant increase in healthcare costs and health insurance premiums.

SIGNIFICANT VARIATION OF R&D COST ESTIMATES

The lack of transparency around real R&D expenditure has long represented a fundamental political problem for scientists, international organisations and NGOs; it also presents them with a methodological challenge. Estimates of the average costs up to the marketing authorisation of a new drug vary significantly and range between USD 67 million and 4.5 billion.[2] The development of a new active substance for the treatment of cancer carries the highest cost, namely between USD 944 million and 4.5 billion.[3] For comparison, not-for-profit organisations like the *Drugs for Neglected Disease initiative (DNDi)* and the *Global Alliance for Tuberculosis Drug Development* (or *TB Alliance)* come to much more modest costs of USD 67–345 million.[4] [5] Different datasets, calculation methodologies and political orientations are the main causes of the significant divergences. It is notable that all estimates based on the industry's non-verifiable data produce on average significantly higher R&D costs than those which draw on publicly available data.[6] [7] As a result, the debate revolves

Box 1

PRICING MODELS WITH SECRET DISCOUNTS IN SWITZERLAND

In the 2019 WHO resolution on transparency,[17] Switzerland committed to upholding transparency around the real prices of drugs. However, as part of a revision of the Health Insurance Act (KVG/LAMal) currently being discussed in the context of cost-containment measures, the Federal Council is seeking to legalise pricing models (or managed entry agreements) with secret discounts, thereby further reducing transparency.

Pricing models are agreements between the Federal Office of Public Health (FOPH) and pharmaceutical companies that lay out the modalities (price, discount, requirement for additional trials) for the admission of drugs onto the 'List of Pharmaceutical Specialties' (LS) so the treatment will be covered by the compulsory health insurance system (see box 3). There are different categories of agreement, whereby the focus lies on three different criteria – the price (discount per treatment granted by pharmaceutical companies), the quantity (costs covered up to a specific annual quantity) or performance (reimbursement by the producer if the drug does not achieve its expected result).

Pricing models are gaining ground in Switzerland. In January 2019, there were only 20. Today 100 managed entry agreements cover 79 products – a five-fold increase. Three years ago, all the price discounts could be seen in the public LS database. In early 2022, secret discounts apply to some 50% of these managed entry agreements. The Federal Office of Public Health is already showing a strong tendency to negotiate secret discounts

The revision of the Health Insurance Act will thus serve to retroactively legalise an existing practice. In addition, it also serves to remove the amount and methodology used to calculate the discount from the scope of the Freedom of Information Act (FoIA). It will no longer be possible to determine the net price of a drug, i.e. the price actually covered by health insurance. [18]

For pharmaceutical companies, managed entry agreements offer the advantage that, officially, a higher (fictitious) list price is disclosed. Given that Switzerland and many other states refer to the price applied in other countries when setting prices (see box 3), this further strengthens the negotiating power of pharmaceutical companies. The Federal Council promises that the move will reduce prices on the basis that pharmaceutical companies would guarantee lower secret net prices and the duration of price negotiations will be reduced.[19] This claim is however not supported by studies from neighbouring countries and the comparison of the duration of negotiations over drugs with and without discounts.[20] [21]

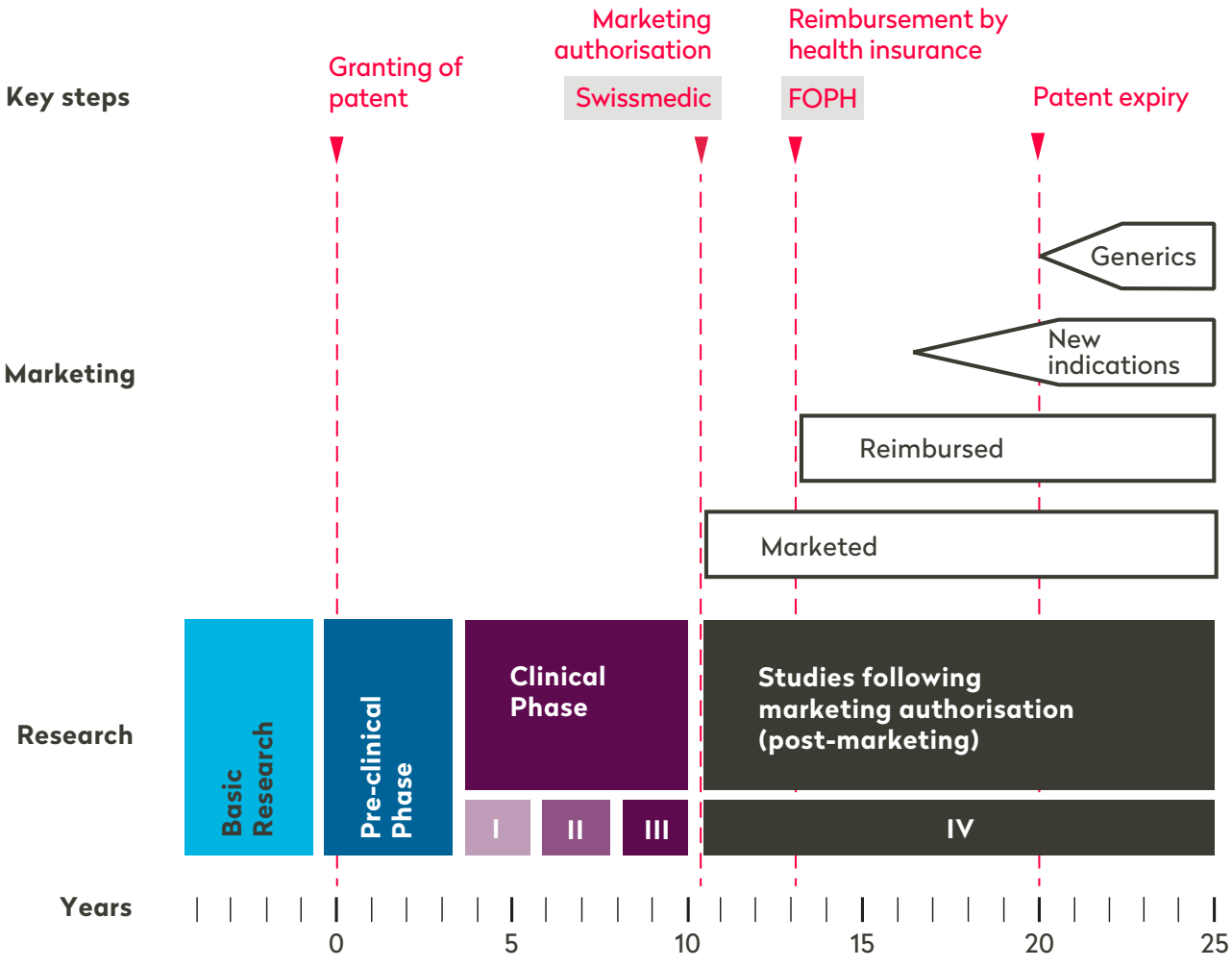
Box 2

FROM PATENT PROTECTION TO REIMBURSEMENT

This graphic shows the different stages in the development of a drug – from basic research to patent application, to the point when generics become available on the market. Patent applications for a period of 20 years are generally submitted before the start of pre-clinical studies, in order to secure the further costs through a monopoly.

Patent applications must be submitted in every country and/or to the European Union. In Switzerland, drugs are authorised by Swissmedic and can be marketed from that point on. According to the result of the negotiation between the pharmaceutical company and the Federal Office of Public Health (FOPH), the drug is then admitted onto the 'List of Specialties' (LS) (see box 3). From then, it is reimbursed through the compulsory health insurance system (possibly with restrictions). The time period after a drug is authorised for marketing or admitted onto the LS and benefits from patent protection depends on how long it took to develop the drug. Often pharmaceutical com-panies successfully apply for additional patents in order to extend their monopoly beyond the usual 20 years of patent protection. New indications are an additional possibility to apply for new patents and thereby to strengthen the monopoly.

CHART 1 – **THE DEVELOPMENT OF A DRUG OVER TIME**



around data transparency, calculation methodologies, how results are interpreted and the resulting conclusions for economic policy.

LEGITIMACY OF THE SYSTEM AT STAKE

Estimates of R&D costs question the legitimacy of an economic policy based on patents and other intellectual property rights and that grants the industry huge pricing power that leads to rising prices of healthcare. If it were to become clear that the real R&D costs are many times lower than the industry asserts, it would put at stake the legitimacy of a business model that for decades has provided the pharma industry with revenues and profit margins that far exceed those of other sectors.[8] [9] [10]

A standard argument put forward by pharmaceutical companies and their lobby associations is that it is not possible to precisely determine R&D costs. However, clinical trials, which represent the greatest cost item within the R&D process, can in fact be attributed to very specific drugs.[11] Public Eye did this and undertook a product-specific estimate of the R&D costs for all approved indications[12] of six cancer treatments produced by large pharmaceutical companies. To do so, the number of clinical trials was multiplied by the average cost per trial and then increased to take into account additional costs associated with the R&D process. R&D costs per unit sold in Switzerland were then calculated based on the proportion of sales in Switzerland in relation to global sales. Together with production and distribution costs, these costs were deducted from the sales price of the treatment in Switzerland. The results are profit margins of 40–90 percent, knowing that those treatments that have not been on the market for long and currently lie at the lower end of the profit spectrum will benefit from many years of monopoly status.

Public Eye's estimates show the urgency to act. These huge profits demonstrate that the high prices charged by the pharma industry are not justified by their own investments, but are the result of the monopoly and pricing power they enjoy. The fundamental problem with this model is that it gambles with people's lives and their fundamental right to health. These high prices mean that many people lack access to drugs. In countries like Switzerland with its compulsory health insurance, such prices significantly contribute to the skyrocketing costs of healthcare. In addition to this, reimbursement limitations or even rationing decisions of treatments covered by the compulsory health insurance system are on the rise.[13] [14]

DANGER OF TWO-TIERED HEALTHCARE

Such a situation threatens equitable access to medicines, even in Switzerland, and raises the risk of two-tiered healthcare. If there were transparency around real R&D costs, these could be taken into account for sustainable pricing. Creating a fair pricing mechanism that revolves primarily around the use for patients and society while also serving companies' investments and innovations is an important imperative for health policy that has long been discussed at the World Health Organization (WHO).[15] [16] Implementation is a political issue at the international and national level and the pharma industry and its lobby is doing everything possible to protect its profits and prevent this.

2
Approach and methods

2.1 – WHY CANCER TREATMENTS?

Cancer is one of the main causes of death globally. It caused nearly 10 million deaths in 2020, 70% of which were in low-income countries.[22] [23] Cancer treatments are an extremely lucrative business for pharmaceutical companies – they are not only sold at high prices, but must often be taken repeatedly or over a long period.[24] The five selected pharmaceutical companies are leaders in the global market for cancer treatments: (1) Bristol Myers Squibb with USD 28.14 billion, (2) Roche with USD 26.37 billion, (3) MSD Merck Sharp & Dohme with USD 15.83 billion, (4) Novartis with USD 14.71 billion and (5) Johnson & Johnson with USD 12.36 billion in revenues in 2020.[25]

The treatments whose prices were analysed were Kisqali (ribociclib[26]) and Kymriah (tisagenlecleucel) by Novartis, Tecentriq (atezolizumab) by Roche, Darzalex (daratumumab) by Johnson & Johnson, Revlimid (lenalidomide) by Bristol Myers Squibb and Keytruda (pembrolizumab) by MSD Merck Sharp & Dohme. These are among their producers' and the world's best-selling drugs.[27]

In Switzerland, these treatments cost between CHF 2 000–6 500 per unit.[28] A year of treatment, often used as a combination therapy with other expensive patented drugs,[29] costs between CHF 43 000–370 000.[30] In Switzerland, cancer drugs account for a third of all medicines costs taken on by the compulsory health insurance system and the trend is increasing.[31] In 2020, cancer treatments increased in cost by 10.5 percent as compared to the previous year.[32] Two of the selected treatments are among the overall most expensive products for public health in Switzerland: Keytruda (3) and Revlimid (6).[33] The skyrocketing costs of cancer treatments can be primarily traced back to the development of new, high-cost biologics; classic oncology products (synthetic, small molecules drugs) play only a subordinate role in this.[34] The range of treatments analysed reflects this development in cancer treatments, i.e. both biological products (monoclonal antibodies and cellular therapies) and classic oncology products (small molecules) were included.

A further important selection criterion was the World Health Organization's (WHO) list of essential medicines – i.e. those that represent the minimum medicine needs for a basic healthcare system – and especially the justifications for the drug being included on or excluded from the list. The WHO Model List of Essential Medicines (EML)[35] is updated every two years, most recently in October 2021. At the time, the responsible WHO committee explicitly announced for the first time that there was a need to act to address the ever higher costs of essential medicines, especially for cancer.[36] [37] [38] The WHO Model List provides national authorities with a guidance to help them decide which drugs they consider to be essential and, depending on the healthcare system, which drugs they reimburse on that basis.

Box 3

LIST OF SPECIALTIES FOR REIMBURSEMENT THROUGH THE COMPULSORY HEALTH INSURANCE SYSTEM

In Switzerland, the compulsory health insurance system (or basic insurance package) only reimburses medicines that are registered on the List of Specialties (LS) and prescribed for authorised indications. The LS is established by the Federal Office of Public Health (FOPH).

To be registered on the LS, a medicine must be authorised by Swissmedic, the Swiss Agency for Therapeutic Products, and must meet legal criteria, such as efficacy, adequacy and economic efficiency (EAE evaluation).[39] Those conditions must be analysed by the FOPH for reimbursement and be reviewed every three years. The request for the admission of a medicine onto the LS is submitted to the FOPH, and each modification of a medicine or its price should be subject to a new request of admission.

In general, the FOPH decides to admit a medicine on the LS at the request of the holder of the market approval and after consultation with the Federal Commission of Medicines (FCM), which is composed of different interest groups – i.e. industry, insurers, patients, doctors, hospitals, pharmacists, federal and cantonal authorities.[40] The FCM examines whether the medicine meets the criteria of efficacy, adequacy and economic efficiency. The FCM then formulates a recommendation to the attention of the FOPH, which also assesses these criteria, especially the economic efficiency, and makes a final decision.

In principle, in order to decide on the maximum public price, the FOPH has to conduct, inter alia, two comparative assessments:

- A comparison with prices of the medicine in referenced countries (geographic comparison);
- A comparison with other medicines used to treat the same disease (therapeutic comparison).

Inclusion on the LS is thus an important step as it sets the conditions and level of reimbursement for the product under the compulsory health insurance system. Reimbursement for a medicine on the LS is guaranteed, assuming all conditions spelt out in the so-called "limitation" are met. Reimbursements for medicines not on the LS are considered under a separate legislative framework and are the sole decision of each health insurer.[41] Therefore, the decision whether to include a drug on the LS has major implications for access to medicines in Switzerland.

THE TREATMENTS SELECTED BY PUBLIC EYE

NOVARTIS

KISQALI (RIBOCICLIB)

Indication	Breast cancer (HER2-)
Type	Synthetic small molecule
Public price per unit (63 tablets, 200mg)	CHF 3 079.15
Production costs per unit	CHF 189.76
Discounts[42]	Secret (managed entry agreement)
Annual treatment cost – monotherapy[43] *Combination therapy*	 CHF 37 000 CHF 43 000
Global revenues since first marketing approval (2017)	CHF 2.2 billion
Sales in Switzerland since inclusion on LS[44] *(06/2019)*	CHF 8 million

Kisqali is a small molecule drug for the treatment of breast cancer, the most common form of cancer among women (30 percent).[45] In Switzerland, 18 percent of women's deaths from cancer are attributable to breast cancer.[46] Kisqali has been on the List of Specialties since 2019 and is indicated for cases of advanced or metastatic HER2-negative breast cancer.[47] For a patient, the drug costs up to CHF 43 000 per year as a combination therapy. Since its approval in the United States in 2017, Kisqali has generated CHF 2.2 billion[48] [49] in global sales for Novartis. Since its inclusion on the LS, the drug has cost Swiss health insurers CHF 7.9 million.[50]

Roche

TECENTRIQ (ATEZOLIZUMAB)

Indication	Lung and other forms of cancer
Type	Monoclonal antibodies
Public price per unit (1,200 mg/20ml infusion)	CHF 4 941.85
Production costs per unit	CHF 109.20
Discounts	Secret (managed entry agreement)
Annual treatment cost – monotherapy *Combination therapy*	 CHF 85 000 CHF 102 000
Global revenues since first marketing approval (2016)	CHF 6.7 billion
Sales in Switzerland since inclusion on LS (07/2017)	CHF 50 million

Tecentriq is a biological drug used to treat lung and liver cancer, specific kinds of skin and breast cancer and cancer of the renal pelvis, urinary tract and bladder. In 2020, lung cancer was the second most common form of cancer after breast cancer, and by far the most fatal.[51] [52] In Switzerland, some 11 percent of all oncological diagnoses were lung cancer. Over 20 percent of men who die from the consequences of cancer, die from lung cancer.[53] The WHO considers Tecentriq (atezolizumab) to have a clear benefit. However, it does not recommend that the drug be included on the Model List of Essential Medicines because it is far too expensive and because costly diagnostic tests are required to identify those patients that will benefit from the treatment.[54] In 2021, Tecentriq was Roche's second best-selling treatment in its oncology branch.[55] Per year and per patient it costs up to CHF 102 000 as a combination therapy. Since it was approved in the United States in 2016, Tecentriq earned the firm CHF 6.7 billion globally. Since it was included on the LS in 2017, the treatment has cost Swiss health insurers CHF 50.1 million.

Johnson & Johnson

DARZALEX (DARATUMUMAB)

Indication	Bone-marrow cancer (myeloma)
Type	Monoclonal antibodies
Public price per unit (400mg/20ml infusion)	CHF 2 052.95
Production costs per unit	CHF 36.40
Discounts	Secret (managed entry agreement)
Annual treatment cost – monotherapy *Combination therapy*	 CHF 138 000 CHF 223 000
Global revenues since first marketing approval (2015)	CHF 15.5 billion
Sales in Switzerland since inclusion on LS (06/2017)	CHF 84 million

Darzalex is a biological treatment used for bone-marrow cancer (blood cancer). As it is used to treat a rare form of leukemia, [56] [57] the drug has been designated an orphan drug by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA). In the United States, this status provides certified products with tax breaks for clinical trials, exemption from fees and marketing exclusivity[58] for seven years after it is authorised. [59] In the European Union this exclusivity period is even for 10 years.[60] The treatment was designated as an orphan drug in Switzerland and therefore benefits from simplified approval and a marketing exclusivity for 15 years.[61] [62] The WHO emphasises that, in this case too, the drug is too expensive for a small added value in comparison to already existing treatments.[63] If Darzalex is administered with Revlimid (see next box), a year of treatment for one patient costs CHF 223 000. Since it was approved in the United States, the drug has earned Johnson & Johnson a full CHF 15.5 billion. Since the drug was included on the List of Specialties (LS) in 2017 it has cost Swiss health insurers CHF 83.8 million.

Bristol Myers Squibb™

REVLIMID (LENALIDOMIDE)

Indication	Blood cancer (myeloma; lymphoma)
Type	Synthetic small molecule
Public price per unit (21 capsules, 25mg)	CHF 6 544.90
Production costs per unit	CHF 4.20
Discounts	Secret (managed entry agreement)
Annual treatment cost – monotherapy *Combination therapy*	 CHF 79 000 CHF 95 000
Global revenues since first marketing approval (2005)	CHF 81.5 billion
Sales in Switzerland since inclusion on LS (07/2008)	CHF 600 million

Revlimid is also used to treat blood cancer. The authorised treatments for multiple myeloma and non-Hodgkin's lymphoma relate to some 6 percent of new cancer cases globally and in Switzerland.[64] Revlimid has also been designated an orphan drug. The drug was developed by Celgene, a company that was acquired by Bristol Myers Squibb in 2019. Since it was first authorised in the United States in 2005, the drug has accounted for global revenues of CHF 81.5 billion. In Switzerland, since the product was accepted onto the LS in 2008, it has cost at least CHF 598.7 million. Revlimid is a global blockbuster[65] and Celgene has come under criticism, because the company increased its price numerous times[66] despite the fact that Revlimid is a follow-on from an old molecule.[67] The cost of the product for one patient currently costs up to CHF 95 000 per year as a combination therapy.

MSD

KEYTRUDA (PEMBROLIZUMAB)

Indication	Numerous forms of cancer
Type	Monoclonal antibodies
Public price per unit (100 mg/4ml infusion)	CHF 4 893.95
Production costs per unit	CHF 18.20
Discounts	Secret (managed entry agreement)
Annual treatment cost – monotherapy	CHF 83 000 (no combination therapy)
Global revenues since first marketing approval (2014)	CHF 50.6 billion
Sales in Switzerland since inclusion on LS (10/2015)	CHF 297 million

In 2021, Keytruda was the best-selling cancer drug in the world, [68] in part because it is authorised for many forms of cancer, including skin, lung, blood, breast, liver and cervical cancer. As a result, the treatment is essential for a large number of patients. In 2019, it was accepted onto the WHO List of Essential Medicines (EML) for the treatment of skin cancer. However, in 2021 the WHO committee did not accept Keytruda for the treatment of lung cancer, once again due to the high cost and expensive diagnostic testing.[69] The WHO stated that specifically because numerous patients would benefit from the treatment, it would not be affordable for the health system and therefore would not recommend that it be designated an essential medicine. This assessment demonstrates the perverse nature of the high prices of cancer treatments and their costs to the health system. The drug, which costs up to CHF 83 000 per year, has earned CHF 50.6 billion since it was authorised in the United States in 2014. In Switzerland, since its admission onto the LS in 2015, it has cost CHF 296.6 million.

NOVARTIS

KYMRIAH (TISAGENLECLEUCEL)

Indication	Leukaemia, lymphoma
Type	Cell therapy
Public price	CHF 370 000
Production costs per unit	USD 20–60 000[70]
Discounts	Secret (managed entry agreement)
Annual treatment cost	Kymriah is a single therapy (CHF 370 000)
Global revenues since first marketing approval (2017)	CHF 1.3 billion
Sales in Switzerland since marketing approval (2018)	Unknown

Kymriah is what is known as a CAR T-cell therapy. It is not a drug, but a medical service that was essentially developed through university research and public funding. This personalised therapy by Novartis has been authorised for refractory or relapsing forms of blood cancer (specific forms of leukaemia and lymphoma) since October 2018. Lymphocytes (a type of white blood cell) are taken from the sick person and genetically modified so that they can recognise and attack cancer cells, before being re-injected into the same person. According to experts, only some 100 people could benefit from Kymriah every year in Switzerland. This kind of procedure is likely to play an important role in treating other kinds of cancer in the near future, resulting in a rapidly rising number of cases requiring such expensive therapies.[71] Kymriah costs CHF 370 000 per treatment. CAR T-cell therapies are classified as a medical service. Accordingly, they are not admitted on the LS but are regulated by the Health Care Benefits Ordinance (Krankenpflege-Leistungsverordnung KLV).[72] Consequently, they are not automatically reimbursed by the compulsory health insurance system. The costs must be negotiated in advance with and approved by every individual health insurer. This applies initially to the evaluation phase up to the end of 2022. Since Kymriah was approved in the United States in 2017, it has generated global revenues totalling approximately CHF 1.3 billion. As the treatment is not on the List of Specialties, there are no figures available on the volume of sales of Kymriah in Switzerland.

2.2 – DATA, CALCULATIONS AND ESTIMATES[73]

FROM CLINICAL TRIALS TO RESEARCH & DEVELOPMENT COSTS

There are essentially two methodologies for calculating R&D costs for specific products: a) use the company's own information, e.g. reports submitted to the US Securities and Exchange Commission (SEC) or reports published by companies[74 75], or b) by taking the number of clinical trials[76] multiplied by the average costs of clinical trials. SEC data[77] is verifiable by other researchers, as these documents are publicly available. However, they still draw on information provided by companies, which ultimately cannot be verified (see 'SEC data' in the annex). Public Eye therefore opted for the second option, with data that is independent and verifiable.

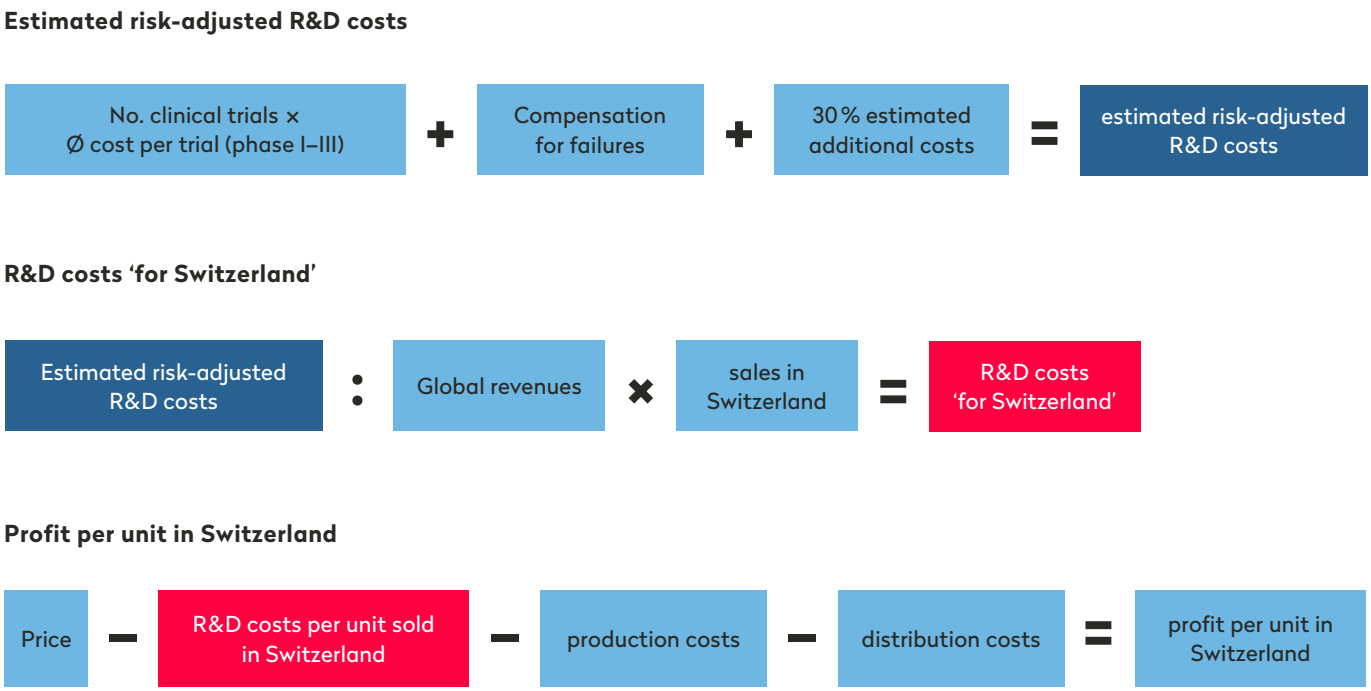
The following calculations were thus based on the clinical trials undertaken by the industry for each drug, for all approved indications until marketing approval. Numerous drugs produced by pharmaceutical companies are initially authorised for one indication (for example, a specific form of lung cancer), but subsequently undergo trials for further forms of cancer. The application for marketing approval, e.g. for other forms of lung cancer or other forms of cancer that can be treated with the same mechanism of action, is submitted in subsequent years. To find all the clinical trials that have been carried out for the six compounds analysed, Public Eye consulted the European Medicines Agency's (EMA) European Public Assessment Reports (EPAR)[78], the US approval authority's (FDA) databank Drugs@FDA[79] and the US database clinicaltrials.gov.[80 81] The end date for this was April 2022.

To calculate the cumulative costs on the basis of the data derived on clinical trials for each treatment, the number of trials per phase was multiplied by the average costs of a trial per phase (for details, see 'Average costs of clinical trials' in the annex).

The industry likes to justify the high margins it makes on individual products by stating that they need to provide commercial compensation for failures

The industry likes to justify the high margins it makes on individual products by stating that they need to provide commercial compensation for those products that do not make it to marketing approval. Yet this self-serving assertion made by the pharma industry to artificially increase estimates, as well as the figures used to do so, are contested. In reality, individual pharmaceutical companies and products can ultimately be more or less successful. In addition, large pharmaceutical companies can distribute the risks associated with a failed product across various projects.[82] The probability of success is in itself an estimate and small changes to these figures have a significant impact on the

CHART 2 – **CALCULATION STEPS FOR THE ESTIMATION OF THE PROFIT MARGINS FOR SWITZERLAND**



Researchers at the Fraunhofer Institute for Cell Therapy and Immunology (IZI) in Leipzig working on a new form of personalised cell therapy against cancer. | © Waltraud Grubitzsch/Keystone

EXPERT INPUT

Public Eye was supported in this research of databases by a research assistant. JianHui Lew is a clinical pharmacist currently working in Malaysia. He was highly qualified for the role due to his in-depth knowledge acquired as a pharmacist with experience working to treat cancer and specific expertise in the use of such databases from his Masters degree in International Health Policy at the London School of Economics.

estimated R&D costs.[83] Despite these reservations (see detailed explanation of this in 'Compensation for failures' in the annex), Public Eye decided to produce an estimate taking into account these probabilities in order to factor in the systemic risk in the pharmaceutical sector. To do so, a new independent estimate with specific data for cancer drugs[84] was used and the R&D costs were increased to account for additional costs in compensation for potential failures. At the same time, an estimate was produced without these, in order to show the huge difference in relation to estimated R&D costs and related profit margins (see chapter 3.1).

The clinical trials of phases I–III are by far the largest cost area for the entire research and development process. In addition to the costs of clinical trials, there are additional costs associated with the discovery phase, pre-clinical trials and the fees for marketing authorisation. It is estimated that the costs for clinical trials account for 60–70 percent of overall R&D costs.[85] Public Eye took this into account in the calculations

Clinical trials phases I–III are by far the largest cost area for the entire research and development process

presented here and increased the estimated costs for clinical trials by 30 percent to ultimately obtain an approximate value for the total R&D costs.

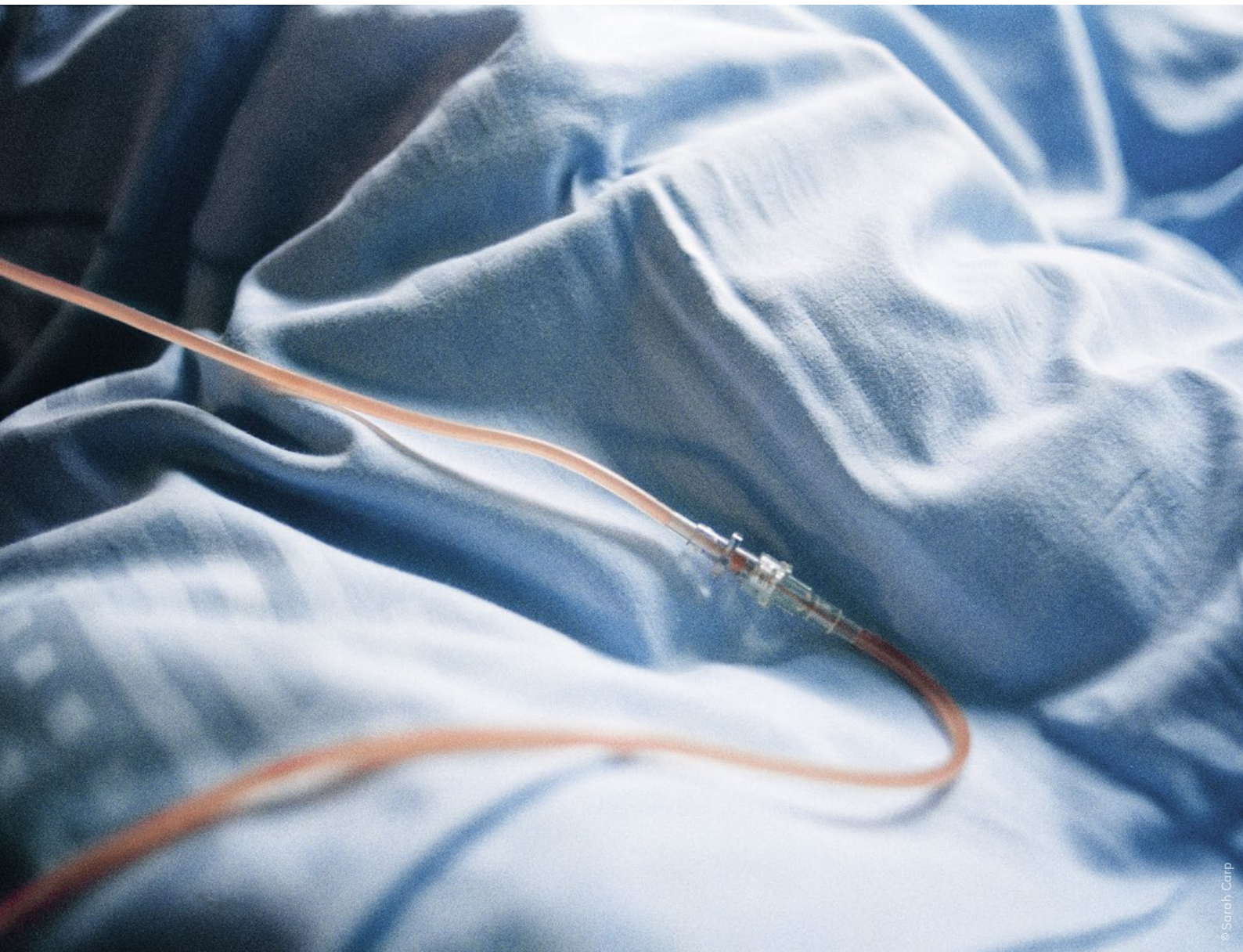
In addition, estimates of R&D costs often price in opportunity costs alongside a compensation for failed products. These 'costs' are defined as the 'cost of capital' and are also controversial. They are aimed to be compensation for foregone returns that could have been earned on the stock market if the capital invested in the R&D process had been invested there instead. In reality, this cost of capital doubles the estimated R&D costs.[86] It is not surprising that this fictitious cost area has become a favourite method used by economists since the 1970s to artificially inflate their R&D cost estimates[87]. Public Eye therefore opted to estimate R&D costs without opportunity resp. capital costs (for the detailed justification of this see 'opportunity costs' in the annex).

CALCULATION OF PROFIT MARGINS FOR SWITZERLAND

The total estimated R&D cost per drug was then put in perspective relative to the revenues earned in Switzerland with the global income generated by the drug (see 'Swiss and global revenues' in the annex). The result provides the R&D costs 'for Switzerland'.[88] To calculate profit margins, the production and distribution costs of each drug were estimated alongside the R&D costs. In the case of biological drugs, an established reference value for monoclonal antibodies was used to calculate the production costs. This includes the three drugs Tecentriq (atezolizumab) by Roche, Darzalex (daratumumab) by Johnson & Johnson and Keytruda (pembrolizumab) by MSD Merck Sharp & Dohme. For the synthetic small molecules Kisqali (ribociclib) by Novartis and Revlimid (lenalidomide) by Bristol Myers Squibb, the calculations are based on an estimate of the 'cost-based generic price' (for details see 'Production and distribution costs' in the annex). Marketing costs were not taken into account. The reason is that the cancer treatments selected for analysis are lifesaving drugs for which there is no real choice between different products and therefore they are not subject to competitive market dynamics. In order to calculate the profit margins for each of the six drugs, the R&D, production and distribution costs for Switzerland were subtracted from the official public prices.

3

Huge profit margins for cancer treatments



3.1 – RESEARCH AND DEVELOPMENT COSTS AND PROFIT MARGINS FOR SWITZERLAND

Table 1 presents the results from Public Eye's research on the number of globally undertaken clinical trials and the number of trial participants, as well as the estimated global costs for the clinical trials per drug (number of trials multiplied by average cost per trial [Sertkaya et al. 2016]).

The two following tables show the results of the R&D costs and profit margin estimates without compensation for failures (Table 2) and with compensation for failures (Table 3). The R&D costs and profit margin differences between Table 2 and 3 show the significant impact of this parameter on the estimations.

TABLE 1 – **NUMBER OF CLINICAL TRIALS AND ESTIMATED GLOCAL COSTS**

	Kisqali	Tecentriq	Darzalex	Revlimid	Keytruda	Kymriah
Number of clinical trials (phases I–III)	7	22	16	21	31	3
Number of trial participants (phases I–III)	2243	10288	3672	4706	15823	337
Global costs of clinical trials (phases I–III) in mn. CHF	99	287	164	261	442	8

TABLE 2 – **CALCULATION OF PROFIT MARGINS PER DRUG WITHOUT COMPENSATION FOR FAILURES**

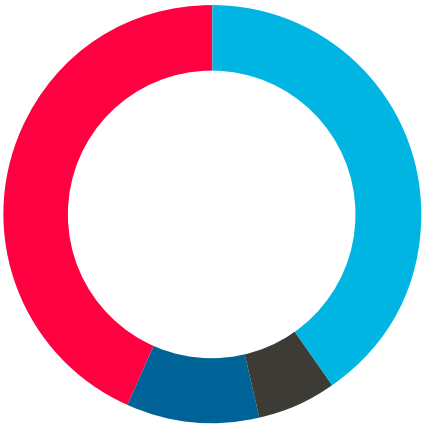
	Kisqali	Tecentriq	Darzalex	Revlimid	Keytruda	Kymriah
Global R&D costs (clinical trials + 30% additional costs) in mn CHF	141	410	234	373	631	11
R&D costs per unit for Switzerland in CHF	198	302	31	30	61	No data available. Global profit margin: 99%
Production costs per unit for Switzerland in CHF	190	109	36	4	18	
Distributions costs per unit for Switzerland in CHF	315	361	237	400	360	
Price per unit for Switzerland in CHF	3079.15	4941.85	2052.95	6544.90	4893.95	
Profit per unit for Switzerland in CHF	2376	4170	1749	6111	4455	
Profit margins for Switzerland	77%	84%	85%	93%	91%	99%[89]

TABLE 3 – **CALCULATION OF PROFIT MARGINS INCLUDING COMPENSATION FOR FAILURES**

	Kisqali	Tecentriq	Darzalex	Revlimid	Keytruda	Kymriah
Global risk-adjusted R&D costs (clinical trials + 30% additional costs) in mn CHF	885	3146	2433	3655	4101	162
R&D costs per unit for Switzerland in CHF	1240	2319	322	293	396	No data available. Global profit margin: 88%
Production costs per unit for Switzerland in CHF	190	109	36	4	18	
Distribution costs per unit for Switzerland in CHF	315	361	237	400	360	
Price per unit for Switzerland in CHF	3079.15	4941.85	2052.95	6544.90	4893.95	
Profit per unit for Switzerland in CHF	1334	2153	1458	5848	4120	
Profit margin for Switzerland[90]	43%	44%	71%	89%	84%	88%

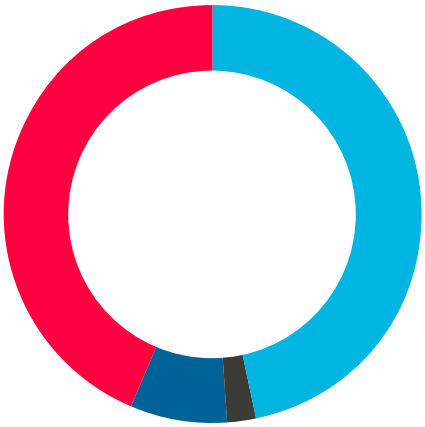
CHART 3 – BREAKDOWN OF THE SALES PRICE OF THE SELECTED CANCER DRUGS IN SWITZERLAND

The pie charts show the proportion of risk-adjusted R&D costs, production costs, distribution costs and the profit on the sales prices in Switzerland. It is not possible to outline these costs for Kymriah, because no information is available on sales in Switzerland.



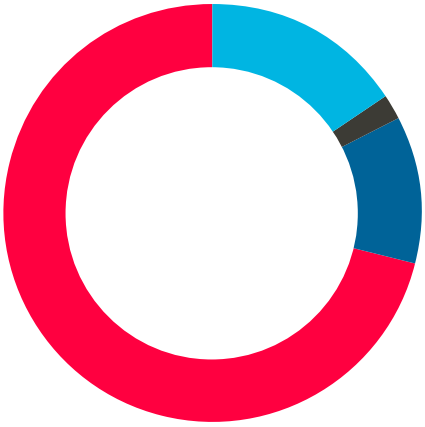
KISQALI

- R&D-Share 40,3 %
- Production 6,2 %
- Distribution 10,2 %
- Profit margin 43,3 %



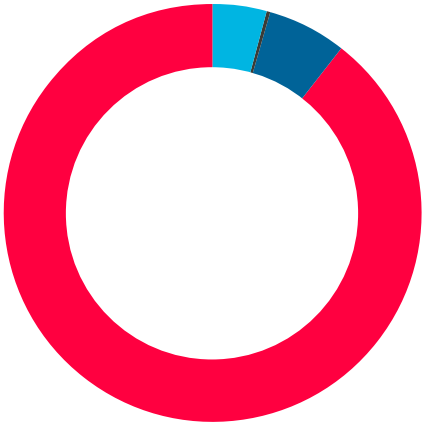
TECENTRIQ

- R&D-Share 46,9 %
- Production 2,2 %
- Distribution 7,3 %
- Profit margin 43,6 %



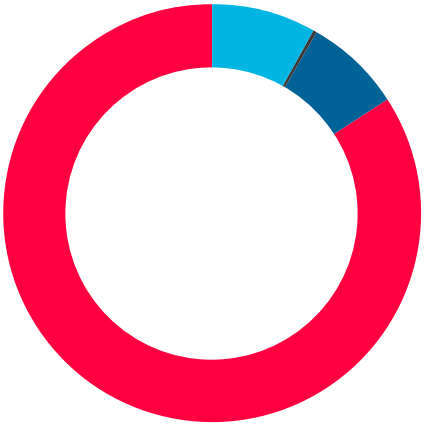
DARZALEX

- R&D-Share 15,7 %
- Production 1,8 %
- Distribution 11,5 %
- Profit margin 71,0 %



REVLIMID

- R&D-Share 4,4 %
- Production 0,1 %
- Distribution 6,1 %
- Profit margin 89,4 %



KEYTRUDA

- R&D-Share 8,1 %
- Produktion 0,4 %
- Distribution 7,4 %
- Profit margin 84,1 %

3.2 – ANALYSIS OF RESULTS

APPRECIATION OF THE RESEARCH AND DEVELOPMENT COSTS

It is challenging to compare Public Eye's estimated R&D costs with other estimates, because they are based on different data sets and calculation methodologies. Often there is no disaggregated data available; particularly not for individual cancer treatments, which are generally more expensive to develop.[91] Public Eye's estimates calculate the cost per drug on the basis of the number of clinical trials for all authorised indications, whereas other estimates only calculate average costs for the initial marketing approval of a new drug (new active substance, NAS[92] [93]). In addition, estimates are calculated using different success/failure rates as well as costs of capital. In an attempt to obtain an overview despite these constraints, the estimated R&D costs of the six drugs were compared with those of four recent international estimates (for further details see 'Comparison with other R&D estimates' in the annex).

In the case of Public Eye's estimates, it is noticeable that globally risk-adjusted R&D costs increase massively (cf. 'table 2 variant without' with 'table 3 variant with compensation for failures'). Public Eye has estimated the risk-adjusted costs for all approved indications with the aim of calculating profit margins (all revenues minus all costs, including systemic risk). Therefore, these results cannot be compared with other risk-adjusted average R&D costs for the initial marketing approval of a new drug only.

Subject to reservation it is possible to compare estimated global costs of clinical trials and additional costs (without success/failure rate, see second column in the table 'Comparison with other R&D estimates' in the annex). It is particularly noteworthy that, although clinical trial costs for all indication extensions have been factored in, the estimated R&D costs of all treatments selected by Public Eye are on a similar level to comparable figures from the four international studies based on average costs for an initial marketing approval of a new drug.

APPRECIATION OF THE PROFIT MARGINS

Public Eye calculated a profit margin based on the sales of the product since its inclusion on the List of Specialties (LS) in Switzerland, global revenues generated by the product since it was initially authorised in the US and the estimated risk-adjusted R&D costs of all clinical trials that led to marketing approval or indication extensions.

The profit margins for 2022 were between 40–90 percent. At the lower end of this range are margins for products that have only been reimbursed in Switzerland for three years, at the upper end, there are products that have been authorised (and reimbursed) for longer and at the same time have received numerous indication extensions. The highest revenues are generated, with R&D costs correspondingly recouped, when a product has been on the market for longer and is authorised for a range of forms of cancer. This is particularly because such drugs are often sold at the same price, but the development phase for indication extensions is less expensive.[94] It is astounding that the profit margin, including a fictitious compensation for failure, for a product like Kisqali is already 40 percent three years after inclusion on the LS in Switzerland (2019; FDA authorisation 2017). In the coming years the profit margin will increase significantly, as can be seen from products like Revlimid or Keytruda, which earn their companies fabulous profit margins of 80–90 percent seven to 16 years after their authorisation and admission onto the LS.

According to Public Eye's estimates, the profit margins of the selected cancer treatments in 2022 are between 40–90%

These results counter the usual argument by companies generally that such high prices and profits have to compensate for the R&D costs of all those products that never make it to the market, because (as outlined above) this commercial risk has already been factored into the calculation. In contrast to the other five drugs, it was not possible to calculate the profit margin of Kymriah in Switzerland, since only the total R&D costs and global revenues are known. It is however noticeable that the costs for the producer are really low. The lion's share of the development was funded by the University of Pennsylvania.[95] Novartis only undertook three clinical trials and only a few years after obtaining marketing approval (2017) it had already achieved a huge profit margin of some 90 percent globally. This is despite the industry's assertions that the development of cell therapies is extremely expensive, the price correspondingly high and therefore the drug is not (yet) systematically reimbursed.

LIMITATIONS OF THE ESTIMATES

Public Eye's estimates are advantageous for the industry, because failed drugs are priced in and accounted for. The fact that clinical trials comprise the lion's share, though not the entirety, of R&D costs has also been considered. These estimates however do not take into account the huge public subsidies for R&D and the numerous tax breaks that the pharma industry usually receives.[96] [97] [98] The result is nevertheless a well-substantiated, replicable study using the data that is available despite the lack of industry transparency.

4

The need for transparency for affordable drugs

Public Eye estimated the R&D costs for six cancer treatments and used these estimates to calculate the profit margins earned in Switzerland for these products. The result: profits of 40–90 percent, whereby newer drugs lie at the lower end and those on sale for longer are at the upper end of the scale. A 40 percent profit margin is already huge for a drug, and this will increase further because the company will still benefit from patent protection for numerous years and thus further enjoys pricing power. Our estimate of R&D costs is generous to the industry – the figures have been increased by costs for failures and additional costs. The profit margins would be even higher if public subsidies and the numerous applicable tax breaks were also taken into account.

Against the background of earlier scientific estimates, the results presented here constitute a well-founded and replicable estimate of what individual pharmaceutical companies will be earning from cancer treatments in Switzerland over the course of 2022. Public Eye is presenting an estimate of the global R&D costs of individual cancer treatments for all approved indications and of the R&D costs and profit margins per unit sold in Switzerland. In contrast to this, earlier studies show on average costs for the development of a new drug. The data from the number of clinical trials undertaken by the industry globally, the number of trial participants for each drug and the classification of the methodologies used for estimates and of the various applicable parameters provide a basis for further expert discussion and political action. A further key finding from analysing the literature is the huge resource investment required to compensate for the lack of transparent government regulations and unverifiable nature of information disclosed by the industry. Not only does it reveal the hotly contested space between institutions with close links to the pharma industry and independent scientists, but it shows that academics and expert organisations are forced to make particular efforts in order to generate well-founded and plausible estimates. Many of these efforts made by universities and not-for-profit organisations are funded by public funds and voluntary donations.

The findings of 40–90 percent profit margins call into question the legitimacy of the current system and show that there is an urgent need for action. Monopolies and pricing power are supposedly necessary to insure against the high-risk R&D phase. However, the profit margins on cancer treatments, where the risk of failure has already been priced in, show that pharmaceutical companies are benefitting disproportionately from their monopolies and pricing power. The high prices of cancer treatments significantly contribute to the astronomical yields of companies and the explosion of Swiss healthcare costs – costs that are born by insurance holders. At the same time, they threaten the universal access to drugs, and raise the risk of a two-tiered healthcare in which ever-increasing rationing or limitations on insurance coverage mean only some patients receive coverage.[99]

It is a question of how profit-focused companies set their prices. There are numerous indications that companies simply ignore their actual R&D costs when setting prices, but use these with authorities and the public when they need an unverifiable pretext for exaggerated price demands. Pharmaceutical companies demand what they can skim from the market.[100] However, the privatisation of services does not relieve the state of its primary duty to protect and guarantee human rights.[101] It is therefore the task of the state to safeguard effective oversight over the privatised provision of drugs and thereby to retain control over the activities of pharmaceutical companies in order to guarantee the human right to health and to implement a coherent human rights-based policy. Even if private companies do not want to set their prices in line with their R&D costs, it is essential for the state to know them. As this research demonstrates, even in today's opaque context it is possible to calculate an approximation of the R&D costs and allocate them to individual drugs. The Federal Office for Public Health (FOPH) can only strengthen its negotiating position and set sustainable drug prices if the actual R&D costs are known.

The pharma industry argues that transparency in this field would create an incentive to intentionally inflate costs and would be detrimental to the efficiency of research and development, because inefficient companies would benefit and efficient companies with innovative products would be disadvantaged. The question of a fair pricing mechanism that primarily focuses on benefits to patients and society while at the same time honouring the investments and innovations of companies is an important question for health and economic policy. Various solutions exist at the international level and within the World Health Organization (WHO).[102] [103] WHO resolution of May 2019[104] also recommends transparency of R&D costs. In Italy[105] and France[106] pharmaceutical companies must disclose public subsidies and, in cases where no comparable products are on the market, additionally private investments when applying for the cost of a treatment to be covered by the state.

In contrast to neighbouring countries, Switzerland has spoken out against such disclosure of R&D costs.[107] Instead of creating more transparency, the Federal Council is currently proposing, in the context of cost-containment measures in the area of healthcare, an amendment to the Health Insurance Act that will further exacerbate the current power imbalance in favour of the pharma industry. In particular in relation to cancer treatments, these measures will not prevent costs from skyrocketing.[108] On the contrary, pharmaceutical companies could impose their prices and excessive margins in an even more direct and uncontrolled manner, despite the fact that the use of managed entry agreements and secret discounts have not actually been proven as effective instruments to accelerate patients' access.[109] In order to ensure the government and Federal Office for Public Health (FOPH) can fulfil their duty to protect and safeguard the right to health for all and their accountability over healthcare spending, there is a need for transparency around pricing. Transparency around research and development costs is definitely part of this.

Annex

CRITERIA FOR INCLUSION OF TRIALS

The criteria for the inclusion of clinical trials from the European Public Assessment Reports (EPAR), Drugs@FDA, clinicaltrials.gov were: (i) the main sponsor was the pharmaceutical company holding the marketing authorisation or the company acquired by it[110]; (ii) the trials tested combinations that obtained authorisation; (iii) the trials tested patient groups relevant to indication extensions; (iv) the trials had a primary completion date before marketing authorisation was awarded for the treatment and indication. Decisions over marketing approval are made on the basis of these primary results, whereas further results are measured as the ongoing trial progresses. Authorisation dates were based on when marketing approval was granted by the European Medicines Agency (EMA) and, in cases where indications are only authorised in the United States, the date when the US approval authorities (FDA) granted authorisation. For the number of trial participants, entries varied between the European and US approval authorities. In this case, the figures from the EMA were decisive, because they aligned more closely with those of the Swiss approval authority Swissmedic.

SEC DATA

SEC data aims to provide investors with information on the price of a security. This information is not standardised and there are significant divergences between the nature and level of detail of the information provided by companies on their R&D costs. In particular, in the case of small companies this information is far more detailed and easier to disaggregate or view according to product, while for large companies only aggregated contributions on all R&D costs is available. This is explained by the fact that it can be essential for start-ups and small companies to provide their investors with detailed information on the expenditure incurred for one or a few products. In addition, a complicating factor is that large companies often count the cost of licenses for drugs from smaller companies as R&D expenditure.[111] This strategy is primarily suited to calculating the average costs for the research and development of drugs,[112] [113] but is not suited to calculating an estimate of the R&D costs of specific products of large pharmaceutical companies.

AVERAGE COSTS FOR CLINICAL TRIALS

The average costs per phase for a study are only rarely available in disaggregated form in literature. Disaggregated data was taken from a study by the Eastern Research Group (on behalf of the U.S. Department of Health and Human Services). It was particularly decisive that the authors Sertkaya et al. (2014, 2016) (i) provide disaggregated data per study and phase for the development of cancer treatments; (ii) for clinical trials undertaken by the industry; (iii) they are the latest available; (iv) they do not come directly from the pharma industry. These average costs per trial and phase are based on data from Medidata Solutions[114] and 31 000 entries for direct and indirect costs for the development of new active substances that were funded by the global pharma and biotech industry from 2004 – 2012 in the US.[115] For the purposes of interpretation, it is important to note that these are average costs for new drugs (the costs of studies for new indications can vary) with clinical studies being conducted in the US; outsourcing studies to cheaper countries reduces these costs.[116] Knowledge Ecology International's database [117] was used to obtain an approximation of the average costs per study and phase for the development of cell therapies (CAR-T, Kymriah).

COMPENSATION FOR FAILURES

There are important reservations around the use of success or failure rates: (i) it is hugely in pharmaceutical companies' interest to artificially maximise the figures for R&D in order to strengthen the narrative that lower prices would lead to insufficient invest-

ment in R&D, thereby conjuring up images of death and suffering; (ii) there are important considerations around the development process for drugs; (iii) the reliability of estimating success or failure rates is controversial.

Many active substances do not go through the cumbersome and expensive process of clinical trials, but are discounted through high-speed screenings. Only a small percentage are further developed and tested.[118] In addition, many active substances are declared a 'failure' when it would be more appropriate to describe them as 'withdrawn'. In some cases, treatments are not pursued for commercial reasons, while in other cases active substances undergo further testing and are authorised despite significant risks.[119] Ultimately, the use of biomarkers for the selection of trial participants, for safety and as 'surrogate endpoints' is important to increase the likelihood of marketing approval. These biomarkers are used primarily for oncology products.[120]

Alongside these considerations around the development process for drugs, there are also reservations regarding the estimates used for success or failure risks themselves. In contrast to earlier estimates on success rates, the authors of the study used by Public Eye have no ties to the pharma industry. In addition, they used a larger sample.[121] [122] Wong et al. (2019) provide disaggregated data for the various therapeutic fields. For cancer treatments these fall significantly below average.[123]

OPPORTUNITY COSTS

Factoring opportunity or capital costs into R&D estimates is highly controversial. From a company's perspective, it makes sense to assess the opportunity costs of a new project. The argument that these costs should be borne by the public however is absurd, for the following reasons[124]: (i) investments in new products, such as for example a new chip by Intel, do not lead the company to argue for state protected prices on the basis that these need to compensate for all foregone income of alternative investments. (ii) investments in stocks and shares are in no way devoid of risk. (iii) the pharma industry is seeking to portray R&D costs as long-term capital investments on the one hand, while wanting simultaneously that these expenditures be tax deductible on an annual basis.

PRODUCTION AND DISTRIBUTION COSTS

PRODUCTION COSTS

Monoclonal antibodies (mAb): the pharma industry holds that monoclonal antibodies are very expensive to produce. Improvements and economies of scale in productions methods have however drastically reduced production costs, meaning that this is no longer the case.[125] Numerous studies have shown that from a specific production capacity, the production costs can be estimated at some USD 100 per gram mAb.[126] [127] [128] [129] The costs applicable after manufacture, such as storage and distribution, are not taken into account. Further costs such as formulation of the product and packaging are estimated at approximately USD 5 per vial.[130]

Synthetic small molecules: estimated cost-based generic prices for both synthetic small molecules Kisqali (ribociclib) and Revlimid (lenalidomide) were produced for Public Eye by Melissa Barber (Department of Global Health and Population, Harvard T.H. Chan School of Public Health).[131] [132] [133] [134] [135] [136]

The formula used for the estimates takes into account capital and operating costs, including labour, land and utilities, costs associated with running facilities, costs in connection with environmental protection and compliance with the current Good Manufacturing Practice (cGMP) standards, taxes and a profit margin. On the basis of export and import data from 2019 to 2020, the costs for the active pharmaceutical ingredients (API) were calculated first, on the assumption they were produced in India. Costs of excipients come on top of this. The assumed costs for processing active substances and excipients into a tablet (conversion costs to finished pharmaceutical product, FPP) were based on reports of capital and operating costs for pharmaceutical tablet formulation facilities as well as discussions with large producers of generics. Based on these data, an estimate was calculated for the cost-based generic price for a tablet, including tax on profits (approx. 26.6% in India) and a profit margin (10%).

Lenalidomide: the estimated cost-based generic price for a 25 mg lenalidomide capsule is USD 0.22. The cost of a pack of 21 capsules containing 25 mg is USD 4.62.

Ribociclib: the estimated cost-based generic price for a 200 mg ribociclib tablet is USD 3.31. The cost of a pack of 63 tablets containing 200 mg is USD 208.53.

DISTRIBUTION COSTS

The List of Specialties (LS) contains the public price (the maximum price) charged for sales by pharmacists, doctors, hospitals and care homes. This is comprised of the ex-factory price, the distribution share and VAT. The ex-factory price is the price that the FOPH sets at the point when the drug was admitted for reimbursement or when the price was later adapted and that served as the basis on which the LS maximum price was calculated.[137] The distribution share for a prescription drug is the difference between the public price and the ex-factory price. It is comprised of a price-based surcharge and a packaging-based surcharge. This excludes 2.5% VAT.[138]

SWISS AND GLOBAL REVENUES

A drug authorised by Swissmedic is added onto the List of Specialties (LS) if the FOPH and the pharmaceutical company can agree on a price. It will then by reimbursed by the compulsory health insurance system. In cooperation with Basel University and University Hospital, the Swiss insurer Helsana has published since 2014 an annual drugs report with calculated costs for all of Switzerland, based on its own data. Helsana's data does not take into account possible managed entry agreements and secret discounts, i.e. refunds made by pharmaceutical compa-

nies to insurers. Global revenues since authorisation by the FDA were taken from companies' annual reports and compared with Statista.[139]

COMPARISON WITH OTHER R&D COST ESTIMATES

In summary, the differences between existing estimates are due to the following factors: (i) the dates used as a basis for the estimates; (ii) the extent to which new drugs (new active substances, NAS) or the authorisation of new indications were taken into account; (iii) which research and development phases were examined (discovery, preclinical, clinical phases I–III, post-approval); (iv) whether the treatment had obtained a special status (orphan drug) or fast-track approval, which hugely reduces the number of studies and time required; (v) the therapeutic field; decisive factors are also the assumptions used in the calculation method (vi) for the success/failure rate and (vii) whether to take into account opportunity costs and what 'price' is used to factor these in.[140]

The four studies that were selected as a comparison:

- A heavily criticised study by DiMasi et al. (2016)[141] at Tufts University. The institution has close links to the pharma industry and, moreover, its estimates are based on confidential, self-selected data of the pharma industry. This study has estimated some of the highest R&D costs in recent years. As a result, it is often cited and circulated by the pharma industry and its lobbyists. The comparative values in this case refer to the average value per new active substance (NAS) and are not specific to oncology.
- The study by Prasad and Mailankody (2017)[142] estimates R&D costs based on SEC data for oncology treatments – again, however, only on the basis of average costs per NAS; 9/10 treatments are drugs that have obtained orphan drug status.
- The estimates of Jayasundara et al. (2019)[143] are based on clinical trials that, like in Public Eye's estimate, were multiplied by the average costs per trial participant. The authors compare 100 drugs with, and 100 drugs without, orphan drug status. They calculate an average value for all drugs, not only NAS; as a sensitivity analysis, results for NAS were also calculated.
- The latest estimate by Wouters et al. (2020)[144]. This calculates average R&D costs for bringing a new drug (NAS) to market. With resulting costs of USD 1,360 mn, it calculates costs that are half those of DiMasi et al. at USD 2,824 mn (including pre-clinical trials, clinical trials, rate of success/failures, opportunity costs).

COMPARISON OF PUBLIC EYE'S AND FOUR INTERNATIONAL ESTIMATES

	DESCRIPTION	RESULTS		IN MILLION CHF[145]
		CLINICAL TRIALS (PHASES I–III)	R&D COSTS[146]	RISK-ADJUSTED R&D COSTS
Public Eye 2022	• Cancer treatments • All authorised indications for 6 treatments by 5 large multinational companies • Number of clinical trials and data on average costs per trial (Sertkaya et al. 2016)	Kisqali: **99** Tecentriq **287** Darzalex: **164** Revlimid **261** Keytruda **442** Kymriah **8**	Kisqali: **141** Tecentriq: **410** Darzalex: **234** Revlimid **373** Keytruda **631** Kymriah: **11**	Kisqali: **885** Tecentriq: **3146** Darzalex: **2433** Revlimid **3655** Keytruda **4101** Kymriah: **162** (Rate of success: 3.4%, 6.7%, 35.5%[147], see Wong et al. 2019, oncology[148])
Di Masi et al. 2016	• Different therapeutic fields • 106 NAS by 10 multinational companies of different sizes • Pharmaceutical companies' own data	**310**	No information	**1402** (Rate of success: 12%[149]) With opportunity costs: 2570 (10.5%[150])
Prasad and Mailankody 2017	• Cancer treatments • 10 NAS; 9/10 with orphan drug status • SEC Data	No information	**683**	No information (without rate of success/failure) With opportunity costs: 860 (7%)
Jayasundara et al. 2019	• Different therapeutic fields • 100 with, and 100 without, orphan drug status NAS or new indication • FDA authorisation between 2000–2015 multiplied by average costs per patients	Orphan: **70** Non-orphan: **105**	No additional costs	Orphan: **167** Non-orphan: **293** (Rate of success: orphan 33%, non-orphan 10%[151]) With opportunity costs: Orphan: 292 Non-orphan: 414 (10.5%)
Jayasundara et al. 2019	• NAS: 74 with 54 without orphan drug status	No information	No additional costs	Orphan: **125** Non-orphan: **310** (Rate of success: orphan 33%, non-Orphan 10%[152]) With opportunity costs: Orphan: 243 Non-orphan: 490 (10.5%)
Wouters et al. 2020	• Different therapeutic fields • 63 NAS • FDA authorisation from 2009 to 2018 • SEC data	No information	**340**	**805** (Rate of success: 13.8%, 35.1%, 59.0%, see Wong et al. 2019[153]) With opportunity costs: 1237 (10.5%) With opportunity costs for oncology products: 4130 (10.5%)

Endnotes

1 25% in 2021. Source: Federal Office of Public Health of the Swiss Confederation (FOPH), 2022, "Statistics on compulsory health insurance 2021"; [details not available in English], Formular T 2.17, 16/06/2022 (accessed 17/08/2022)

2 Schlander, M. et al., 2021, "How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment", PharmacoEconomics 39: 1243, 09/08/2021; Vieira, M., 2020 "Research Synthesis: Costs of Pharmaceutical R&D", Global Health Center, The Graduate Institute, January 2020

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Pharmaceutical companies enjoy huge pricing power due to patent-based and regulatory monopolies. The pharma industry argues that these high prices serve to hedge against the high risks associated with the research and development (R & D) process for new drugs. Yet it refuses to provide any transparency around actual investments made.

It is challenging for researchers and specialised NGOs to estimate the amount of these investments, and both datasets and methodologies are hotly debated. For the industry and its lobbyists, this is a question of nothing less than the legitimacy of their business model.

Public Eye estimated the R & D costs for six cancer treatments marketed by Novartis, Roche, Johnson & Johnson, Bristol Myers Squibb and MSD Merck Sharp & Dohme and calculated the profit margins for the individual treatments in Switzerland. The resulting profit margins of 40–90 percent are huge and far exceed those of other sectors.

The high prices of cancer treatments make a significant contribution to the companies' exorbitant return on investment and to the skyrocketing costs of Swiss healthcare. Under these conditions, equitable access for all is no longer guaranteed.

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