TAB OFFICE OF TECHNOLOGY ASSESSMENT AT THE GERMAN BUNDESTAG

NEW MEDICINES FOR NEGLECTED DISEASES

TAB-Fokus no. 11 regarding report no. 170 January 2017

Summary

- Some diseases are particularly raging in poor countries leading to a considerable burden of diseases in these countries. Besides insufficient local medical care, the innovation system of industrialised countries is held responsible for this problem.
- The diseases are considered to be neglected, because industry has little incentive to develop new medicines and medical devices due to the financially weak demand. In recent years, national and international measures have been discussed and partly been implemented in order to deliberately strengthen research and development (R&D) with regard to such diseases and to make new medicines affordable for poor countries as well.
- Germany is one of the world's leading locations for medical R&D. Yet with regard to fighting neglected diseases, Germany lags behind compared to several other industrialised countries. The TAB report gives an overview of various measures aiming at strengthening research and product development to fight against neglected diseases and identifies options for a stronger political commitment in Germany.

What is involved

Poverty-related and neglected diseases (PRND) are diseases mainly occurring in poor countries for which industry hardly develops any new products. Mostly, the so-called »big three« (tuberculosis, malaria, HIV/AIDS), most of the 17 neglected tropical diseases defined by the WHO as well as some respiratory and diarrhoeal diseases are referred to as poverty-related and neglected – all of them being infectious diseases.

Before new medicines are authorised to be used in industrialised countries, it is necessary to prove their safety, efficacy and quality. This has to be ensured by means of a structured procedure with several R&D phases. Clinical trials – first in healthy volunteers and then, step by step, in larger patient populations – are the core piece relevant for market authorisation. In the industrialised countries, the manufacturers of new medicines are responsible for these complex R&D activities and bear the costs. In return, they are granted intellectual property rights ensuring them the temporary exclusive commercial use of their developments and promising them positive R&D investment returns via monopoly prices. Thus, in the industrialised countries, it has been possible to commercialise considerable R&D activities. Public budgets are not burdened by the costs of product development, but by high product prices caused by the monopoly. International treaties increasingly secure the enforceability of these intellectual property rights worldwide. On the one hand, one of the effects of these structures is that new medicines are very expensive over several years – and thus mostly unaffordable for poor countries (access issue). On the other hand, there is a lack of sufficient product development regarding diseases almost exclusively affecting poor countries (R&D issue). In this case, another challenge has to be faced: The complex clinical trials to prove the efficacy of new medicines have to be carried out in mostly large patient populations as well as in the affected regions. For this, both clinical centers for carrying out the trials and governance structures for approving and monitoring the R&D activities are required which still need to be built up or at least further developed in poor countries.

As the established commercialised R&D structures of the pharmacological innovation system are at least not fully functional in case of a low and/or financially weak demand, additional measures are to be taken in order to provide an incentive for the necessary research and product development.

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Elements for strengthening R&D

Evidence-based medicine of industrialised countries requires various R&D activities which are assigned to different phases (from basic research and clinical trials to surveillance under conditions of use), but which are often entwined in terms of time and content (see case study in the figure below). Measures aiming at improving the situation tackle different phases of this procedure.

Public research funding: In the industrialised countries, there is a certain division of responsibilities between the public sector (funding of basic research) and industry (financing of product development). In recent years, many countries have enhanced their research funding capacities and thus have mainly strengthened basic research in their public institutions. Typically, the available public funds of individual countries are not sufficient to secure the implementation of clinical trials requiring authorisation in countries of the »Global South« as well as efficient product development so that other sources of funding (from pharmaceutical companies to philanthropic foundations) play an important role as well.

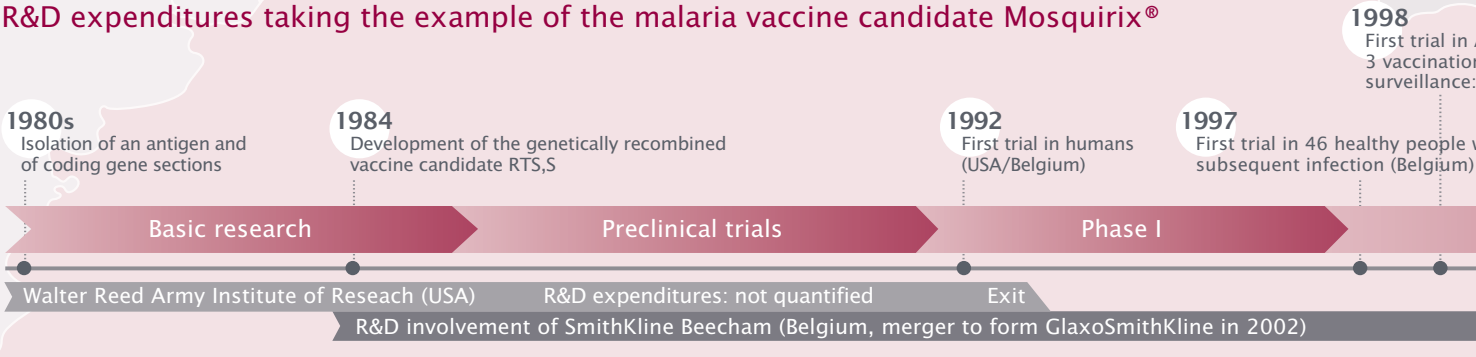
Open innovation: Some stakeholder are starting to open individual R&D instruments for PRND activities and to develop products together. Open innovation comprises the following: open access (access to publications), open data (access to R&D data) as well as the opening of R&D infrastructures for PRND activities (substance libraries, laboratory facilities) or approaches regarding the shared use of intellectual property rights for this purpose (patent pools). Beyond open access, opportunities for use for certain R&D actors and/or defined PRND activities currently are more likely to become realised than an absolutely free access.

European & Developing Countries Clinical Trials Partnership (EDCTP): The EDCTP is financed by the European Commission and several European countries on equal terms in order to increase capacities and know-how for organising and conducting clinical trials in Sub-Saharan Africa. The EDCTP comes into play where public R&D funding reaches its administrative, organisational and financial limits. Particularly activities with regard to clinical trials to prove efficacy are financed on a joint basis. So far, public institutions are participating in the partnership almost exclusively. Since it was established in 2003, the EDCTP carried out many training activities, published numerous research results and further developed several product candidates, though none of them received market authorisation so far.

Product development partnerships (PDP): Since the turn of the millennium, numerous non-profit organisations with their own financing (donations, public funding) have emerged, which at least partly take over R&D tasks in case of failing market mechanisms. With regard to PRND activities, they have become a link between public institutions and industry. In cooperation with industry, first application extensions of already available active pharmaceutical ingredients could be approved. Since the financial crisis, however, the available funds are decreasing. Currently, it is open whether PDPs will be able to provide the necessary resources in order to attain marketing authorisation for completely new active pharmaceutical ingredients, because in later clinical R&D phases there is an increase of expenditures and thus of the financial requirements involved.

Additional sources of R&D funding: In recent years, there have been discussions on whether and how new and/or additional sources of funding for R&D regarding PRND can be tapped. In 2006, some industrialised and newly industrialised countries launched an initiative to generate additional funds by means of solidarity levies on airline tickets. However, there is neither an implementation of these levies nor of any other surcharges (e. g. for financial transactions) on a global scale. So far, even ideas of setting up additional funds to finance R&D have been hardly accepted to a relevant extent. Though expert panels of the WHO have been calling for measures ranging from a global research convention to

R&D expenditures taking the example of the malaria vaccine candidate Mosquirix®



obligatory contributions to R&D regarding PRND for several years now, the suggested forms of those measures have not been supported very much by the member states so far.

R&D incentives for businesses: Some industrialised countries try to offer targeted incentives for private-sector commitment, i. a. with tax credits for specific R&D, performance-based rewards via vouchers for fast-track authorisation procedures or by massively strengthening and ensuring the product demand. There are different opinions whether such measures can stimulate economic commitment to PRND product development to a significant extent.

Assistance for product authorisation: European and US drug regulatory authorities have established procedures in order to ensure a fast and cost-effective assessment of the benefits and risks of new medicines to fight against PRND. Procedures by the WHO help with the quality assessment of medicines and medical devices against PRND (centralised product prequalification). These are major elements to be able to provide socially acceptable access to new products via global initiatives.

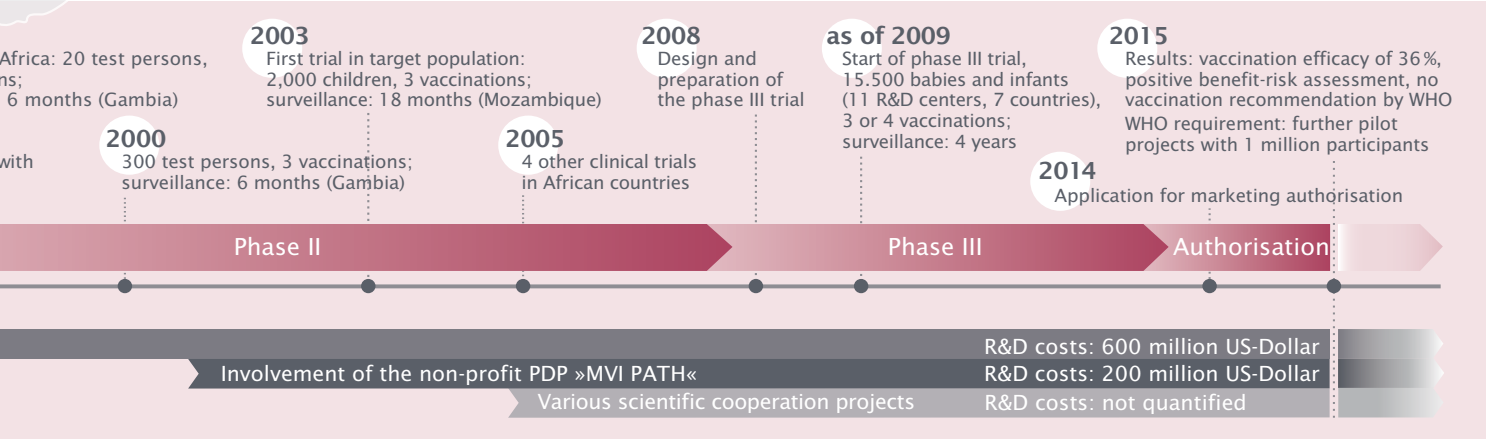
e I, II and III) Marketing authorisation Utilisation

Equitable access to products: Some bilateral and multilateral initiatives are aiming at providing medicines and medical products particularly in the least developed countries as extensively and cost-effectively as possible. So far, however, they only cover some areas of the global market. The »GAVI Alliance« pools the demand for vaccines of approx. 50 developing countries and subsidises the vaccines up to a free provision for the 20 poorest countries. The »Global Fund« supports approx. 100 countries in getting access to medicines and medical devices, but only to fight the »big three«. On the one hand, these initiatives are aiming at massively supporting mainly the poorest countries, but also at increasingly involving countries with a higher economic potential in the costs. On the other hand, bundling and boosting the demand shall strengthen market mechanisms.

Situation in Germany

Germany as a location for R&D has highly-competent public and private-sector institutions which in total cover almost the entire range of diseases and products. Particular strength with regard to fighting PRNDs can be found in tuberculosis research as well as in the development of diagnostic methods and insecticide-containing products for malaria prevention. Though it is difficult to give a detailed overview of the commitment of the public sector with regard to funding R&D of PRND, international studies conclude that Germany lags behind several other industrialised countries with regard to the public funding of R&D for PRND. When it comes to strengthen R&D with regard to PRND, German stakeholder are not among the pioneers – neither regarding open innovation activities nor regarding funding instruments for business development.

According to the German Federal Government, in particular the German Federal Ministry of Education and Research (BMBF) is responsible for strengthening R&D for PRND. In 2011 for the first time, the BMBF set up a PRND research funding concept which bundles major measures (public research funding, promotion of PDPs, participation in the EDCTP) and, since 2014, is also intended to boost sustainable health research cooperation between Germany and the countries of Sub-Saharan Africa, thus complying with the Ministry's »Africa Strategy«. This was accompanied by restructuring national activities (networking between existing public research institutions within the framework of the German Center for Infection Research) and a reassignment of departmental responsibilities (originally, the Federal Ministry for Economic Cooperation and Development [BMZ] was responsible for PDP funding) which first made it necessary again to bundle resources and to gather experience. Also with regard to a financial reinforcement of some funding measures since 2014, Germany falls behind other industrialized countries. It seems to be almost impossible that the intended amounts are sufficient to rapidly push product development.



Options for action

The funding concept by the BMBF is a major step to reduce the neglect of poverty-related diseases with regard to R&D. It can help to develop, approve and provide products to fight these diseases. The impact of the funding concept can be increased by adding other **research policy elements and interlinking them with activities regarding economic, development and health policy**.

For this purpose, the established research infrastructures should be opened up for PRND activities (keyword: open innovation) and used more frequently (e. g. PRND-specific areas regarding the process, access and application as well as contact persons). Furthermore, the **documentation of national commitment regarding R&D for PRND** shall play a more important role in the future.

A significant part of the necessary R&D activities can only be carried out in countries where the respective diseases are endemic. For this reason, the required local clinical centers and supervisory institutions have to be strengthened. As, besides their research tasks, these clinics also have responsibilities regarding medical care, **measures of research funding and development cooperation should be interlinked**. So far, some regulatory authorities of industrialised countries and the WHO are bridging the gaps of incomplete local governance structures especially in Sub-Saharan Africa, are helping with approvals for trials and are particularly taking over **tasks of benefit and quality assessment** within the framework of product authorisation. Besides ensuring this bridging process organisationally and financially, the necessary structures in the »Global South« should be further developed in order to reduce the associated dependency on the industrialised countries. To achieve this, the aim is to **link scientific cooperation, technical development assistance and international health policy efforts**.

Some multilateral initiatives support **equitable access to quality-controlled medicines and medical devices** particularly for poor countries in individual areas of the global market. The health-related effects of these initiatives could be increased, if the currently highly fragmented coverage could be extended.

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Neue Arzneimittel gegen vernachlässigte armutsassoziierte Krankheiten

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www.tab-beim-bundestag.de/en/research/u10300.html

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As, in the established innovation system, product development is mostly carried out within the private sector and market authorisation is achieved there, some industrialised countries – in case of weak market mechanisms – try to offer incentives for private-sector commitment via **economic policy measures** (tax credits for R&D measures, rewards for product development, R&D funds). In Germany, at least a debate on a targeted stimulation of private-sector commitment regarding PRND should be initiated, given that the funding of public and non-profit R&D for PRND is still rather reluctant compared to other countries and that the chances of finding an international agreement regarding adequate additional forms of financing are rather small. Moreover, it should be verified whether and to what extent established measures to support private-sector commitment (e. g. **»Export Initiative for the German Health Care Industry«, »KMU-innovativ«** [national initiative promoting innovation in Small and Medium Enterpreises]) are also focusing on poverty-related diseases.

Different department-specific measures to strengthen research, product development and product provision as well as medical supply regarding poverty-related diseases should be **merged to an overall strategy of the German Federal Government** and should be further developed. **Regular progress reports** should be agreed upon.

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