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DG SANCO / C2

Development of public health performance indicators for the pharmaceutical sector

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FINAL REPORT

30/05/2006

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This document presents the results of the work by SOGETI within the frame of the contract N° SI2.404788 (SANCO/G1/2003/06) signed with the European Commission (DG SANCO). The final report regarding Phase I and II dealt with 6 main sections.

1 Executive summary

1.1 Purpose and objectives

This project aimed at developing a first set of indicators for monitoring the performance of the pharmaceutical industry in meeting public health objectives. It was driven by the G10 Medicine Group recommendation 1b "*The development by the Commission of a comprehensive set of indicators covering […] the prevention and treatment of diseases and emerging health threats with reference to data on morbidity and mortality including the performance of products…*".

The intention behind this recommendation is to develop well established methods for monitoring industry competitiveness while ensuring that social and public health objectives, at national and European levels, are also brought into the picture.

1.2 Methodology

The first stage of the project consisted in defining the objectives and identifying the main issues to be considered from the patient's perspective through consultation with public health stakeholders. The scope of the range of indicators was then identified, according to three main types:

(A) High-level indicators of pharmaceutical industry performance;
(B) Indicators for the wider pharmaceutical sector;
(C) In-depth indicators for specific disease areas: 2 case-studies were conducted for an acute and a chronic condition.

In a second stage, data availability was reviewed along with a detailed description, evaluation and recommendations for indicators covering the areas identified in the first stage. Two case-studies were also conducted for a chronic disease, diabetes mellitus, and an acute one, acute stroke. Globally, those 2 conditions account for over 7% of the EU-25 total burden of disease[1].

Throughout the project, the work was carried out in regular collaboration with public health experts from national health institutes, European and worldwide organisations.

1.3 Results

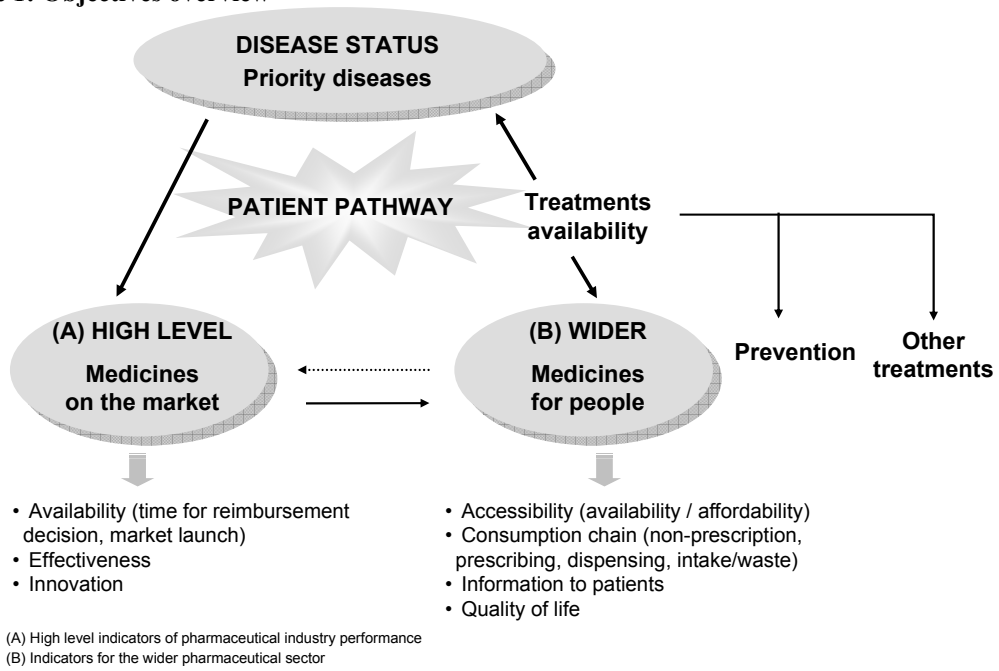
Use of medicines has an important impact on public health in at least four different ways[2]:

- The expected therapeutic benefit;
- The risk linked to medicine-related problems (i.e. adverse medicine reaction, medication errors);
- The economic implications for health systems;
- The eco-toxicological impact on the environment.

[1] "Priority Medicines for Europe and the World". WHO. Kaplan W. and Laing. R., 2004.
[2] "Impact of medicines on public health: EURO-MED-STAT" Folino-Gallo P, Walley T, De Joncheere K, Vander Stichele R. Kirch W. Springer-Verlag Berlin 2003

Based on consultations conducted and from the experts' perspective, the main purpose of the indicators is to **balance how patients' health needs are met by medical treatment** -(B) Indicators for the wider pharmaceutical sector-, **including diagnosis and prevention issues,** and more specifically **medicines available on the market** -(A) High-level indicators of pharmaceutical industry performance-. Diagnosis, prevention and other forms of treatment (e.g. surgery) should not be excluded from the scope of the indicators as they are not the primary focus of the project.

Figure 1: Objectives overview



Considering that most medicines are used out of hospital and that there is a significant trend to shift care from hospital to general practice, it was decided to concentrate on out-of-hospital use (primary care). Still, hospital data may be considered upon experts' advice for specific diseases such as cancer for which the analysis may be biased or insufficiently representative if not included.

The development and use of performance indicators is a dynamic process. They should be adapted to include newly available data and to focus on more relevant issues. For example, changing the choice of priority disease (emerging health threats) or indicators according to research outcomes, such as the relative effectiveness of a medicine. A secretariat of experts would need to be set up to take forward the work carried out in the framework of this project and also to continue the benchmarking exercise once started.

An outcome of the project was that such indicators should be monitored by priority diseases separately. Two types of indicators were identified:

- The **general** ones common to all diseases (e.g. national reimbursement systems);
- The **disease-specific** ones: only for a few diseases (e.g. 5-year survival rate for cancers, prevention).

Based on extensive consultations with a wide range of experts and on the work carried out by WHO ("Priority Medicines for Europe and the World-PRIMs"), the proposal is to start the monitoring with this list of priority diseases for Europe. This list will then be regularly updated once the monitoring has been set up.

It is important that the number of indicators is kept to a minimum in the interests of management of the exercise and to maintain the focus on critical areas.

A wide range of indicators were identified and reviewed from the consultations and literature review. A selection was then made which identified two sets of indicators:

- A **core** list of 21 indicators to be regularly collected for all priority diseases:

PRIORITY AREAS	CORE INDICATORS
Disease status	Prevalence of disease Disability Adjusted Life Years (DALY) Exposure to main risk factors Therapies availability overview Main active ingredients sales and status
Accessibility to medicines	Share of non-marketed medicines in newly authorised outpatient medicines National reimbursement systems National co-payment systems Share of public expenditure on pharmaceuticals Share of reimbursed medicines on outpatient market Price of medicines in number of days wages
Consumption chain	Average number of medicines prescribed per inhabitant Utilisation in DDD/1000 inhabitants/day Share of medicines actually dispensed Adherence to treatment
Quality of life	Ease of use
Medicines' accessibility to market	Time from license to market
Medicines effectiveness	Incremental cost-effectiveness ratio (ICER) ASMR
Innovation	Uptake of new medicines Share of New Chemical Entities covering priority diseases within the last 5 years

- A **supplementary** list of 24 indicators to be collected on a less regular basis for focus on specific issues or diseases.

One of the main difficulties was to link the areas identified and find a way to evaluate the impact of medicine use on health. Availability of routine data was also a major concern. The main criteria for selecting the indicators once defined according to the needs were to have indicators that are fairly simple, routinely collectable and which are not too cumbersome to collect. The lack of aggregate data, which are comparable and valid at national and EU levels, posed a major difficulty.

Finally, proposals and recommendations are made. The sets of indicators identified include both indicators ready to be implemented and ones requiring further research or development work to complete the specification of indicators to a level appropriate for large-scale monitoring.

Data availability assessment could not be conducted in detail for all indicators reviewed, some requiring much effort at national level and being in-depth projects in themselves to be explored further, for example through feasibility studies. Such areas

include innovation from the patient's perspective, effectiveness of medicines, quality of life and information to patients. Indeed, some issues are very controversial with neither standardised nor agreed methodology to monitor them. Outcomes of several ongoing projects at EU and national level concerning these issues have been singled out for consideration.

From the core set of indicators, a stringent selection of **8 key indicators -** considering that two of them are already collected in the framework of the competitiveness indicators[3] but cover the whole market only - was also proposed as follows:

Table 1: Final key set of indicators proposal

PRIORITY AREAS	INDICATOR	COMMENTS
Disease status	DALY	Available every 2 years in average
Accessibility to medicines	Share of non-marketed medicines in newly authorised outpatient medicines	Access to data on payment
	Share of reimbursed medicines on outpatient market	*Further work required: data source or "Price of medicines in number of days wages" indicator, if feasibility study conclusive*
Consumption chain	*Utilisation in DDD/1000 inhabitant/day*	*Further work required: partial geographical coverage and future availability to be confirmed*
	Adherence to treatment	*Further work required*
Information to patients	_	*Further work required*
Quality of life	*Ease of use*	*Further work required, 5-year periodicity enough*
Medicines accessibility to market	Time from license to market*	
Medicines effectiveness	_	*Further work required*
Innovation	Uptake of new medicines*	*Further work required: adapt it so it covers some priority therapeutic areas*

* Already considered in the framework of the Commission response to G10 recommendations: development of 9 indicators, http://pharmacos.eudra.org/F2/register/index.htm

Finally, this report represents a first start with, in some cases, raw data that need further refinement. The real benefit of these indicators will only be realised as the Commission develops data over a number of years, which would allow for a proper analysis.

[3]from the Commission response to G10 recommendations: development of 9 indicators, http://pharmacos.eudra.org/F2/register/index.htm

2 Context

The pharmaceutical sector is a growing area of European Commission public health policy. In 2000, the EU Commission issued a report on "Global Competitiveness in Pharmaceuticals: A European Perspective" (also known as the Pammolli Report after one of its authors). This report signalled a major slowdown in the competitiveness of the European pharmaceutical industry compared with the USA, and by the rising costs of pharmaceuticals to the health care systems of Europe. For instance, eight of the top 10 best-selling medicines originated from the USA, compared with only one from Europe. The pharmaceutical industry in Europe generates wealth and high quality employment while playing a central role in the development of public health with millions of people using medicines each day to protect and improve their health. Research also plays a central role in the sector both to sustain and develop competitiveness through the identification of innovation, but also in the constant search to improve the quality, safety and efficacy of medicines to the public.

It prompted the launch of the G10 Medicines group in 2001 in order to bring together a small group of stakeholders from both industry and public health spheres to discuss the future of the pharmaceutical sector in Europe. The result was the G10 Medicines Report (May 2002) which set out 14 agreed recommendations. The first one relates to the benchmarking and development of a set of agreed indicators to monitor and measure the performance of the pharmaceutical sector in meeting public health and social objectives. The second component out of three of this recommendation forms the basis for this contract and it states:

"The development by the Commission of a comprehensive set of indicators covering…..the prevention and treatment of diseases and emerging health threats with reference to data on morbidity and mortality including the performance of products…"

The intention behind this recommendation is to balance well established methods to monitor industry competitiveness with a way to ensure that social and public health objectives, at national and European level, are also brought into the picture.

On the 1 June 2005, the European Commission has developed a strategy, which has three central features: innovation, pricing and patients. This strategy was driven by the Pharmaceutical Review adopted in 2004. This major reform of the EU's pharmaceutical legislation strengthens public health, while supporting a competitive European pharmaceutical industry.

Regarding innovation, the long term well-being of the sector of industry depends on support for science base. In April 2005, the Commission presented two proposals: the 7th Research framework Programme (FP7) and the Competitiveness and Innovation programme (CIP). The CIP complements the research-oriented activities promoted by the FP7. This will provide greater coherence and synergy in the Community instruments in support of competitiveness and innovation. These programmes not yet approved would run from 2007 to 2013. It would include a doubling of the Research

and Development budget to €70 billion and financial support of over €4 billion for innovation.

Moreover, the objective of the Commission is also to examine the benefits of giving industry more flexibility in establishing prices without sacrificing health care budgets of Member States. In addition, the reflection should look at the access speed of medicines to the market.

Finally, there are two core issues that need to be addressed: information to patients and their safety. Improving the quality of information to patients is still an ongoing issue. Also, one Commission objective is to get a public debate to consider options for improving the safe use of medicines at both the national and European level.

To evaluate progress speed, the Commission plan to establish a High Level Pharmaceutical Forum.

This project involves the review and identification of pharmaceutical indicators, which itself implies a review of the quality and availability of relevant data at European level, and recommendations for further data development work.

3 Project objectives & deliverables

3.1 Tasks to perform

The general objective consisted in scoping the type and range of indicators that could be developed to monitor the extent to which the pharmaceutical sector is aligned with public health and other social objectives. Emphasis was made on indicators feasible now and in the future with improved data collection. The analysis also considered the range of non-statistical indicator forms such as process indicators or indicators related to regulatory conditions.

To meet this objective, the project was structured into two phases that happened in parallel:

- **Phase I:** Determining the scope of the exercise, through consultation with public health stakeholders;
- **Phase II:** Review of existing data and proposals for development.

Both phases were performed through 3 specific tasks as detailed in the sections hereafter.

3.1.1 Phase I: Determining the scope of the exercise, through consultation with public health stakeholders

The objectives were articulated mainly through quality, safety, relevance, affordability, accessibility and relative effectiveness of medicines. Three consecutive tasks were performed as follows:

- **Task 1:** Assessing the objectives and the interpretation of the use of indicators through consultation with public health stakeholders at European and national levels;
- **Task 2:** Development of a structure for the selection of indicators;
- **Task 3:** The scoping of the range of possible indicators. It included the evaluation of the measurability in terms of the quality and availability of data for 3 different kinds of indicators:
    a. High level indicators of pharmaceutical industry performance;
    b. Indicators for the wider pharmaceutical sector;
    c. In-depth indicators for specific disease areas.

3.1.2 Phase II: Review of existing data and proposals for development

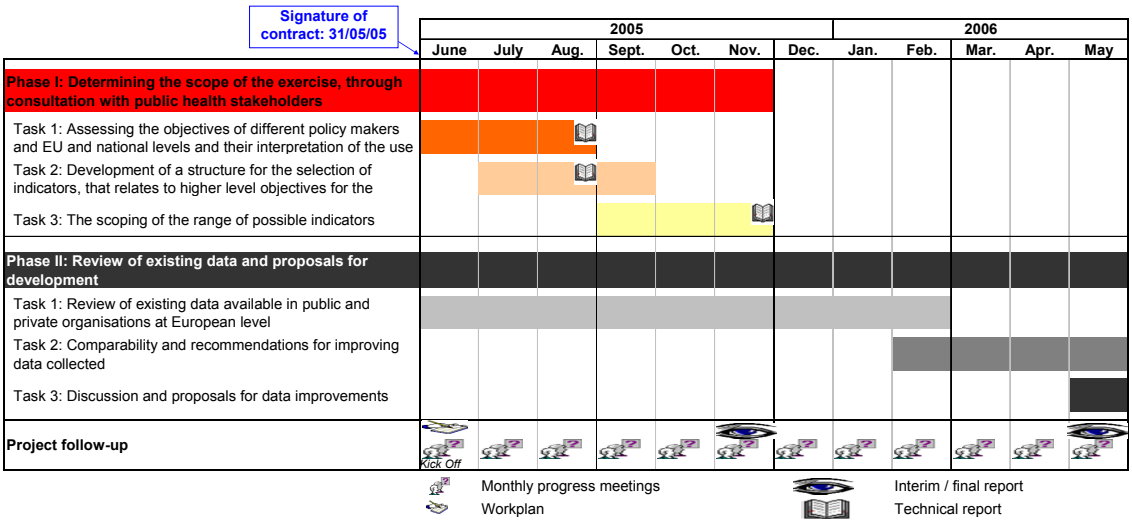
This second phase of the project consisted in reviewing and comparing data available in both public and private organisations. The work was carried out through three stages as follows:

- **Task 1:** Review of existing data available in both public and private organisations at European level;
- **Task 2:** Comparability and recommendations for improving data collected;
- **Task 3:** Discussion and proposals for data improvements.

3.2 Duration and work plan

The work plan was as follows:

Figure 2 : Work plan



The **duration** of the project was 12 months.

3.3 Deliverables

In the framework of this one year project, the following deliverables were provided:

Description	Deadline
Work plan	**30/06/2005**
Technical Report: Phase I – Tasks 1 and 2	**31/08/2005**
Interim Report	**31/10/2005**
Technical Report: Phase I – Task 3	**30/11/2005**
Final Report: Phases I and II	**30/05/2006**

3.4 Meetings

09/06/2005: Kick-off meeting at DG SANCO

This meeting gathered DG SANCO and SOGETI (see MM KickOff 090605.doc). The objectives and the planning of this project were presented. The general objective consists in scoping the type and range of indicators that could be developed to monitor the extent to which the pharmaceutical sector is aligned with public health and other social objectives.

The meeting document can be consulted in the following file: MD Kick off 090605.ppt

29/06/2005: Work meeting at DG SANCO

The purpose of this meeting concerned the Task 1 of the project. SOGETI suggested to DG SANCO a draft of the questionnaire that will be presented to several experts regarding the development of public health performance indicators for the pharmaceutical sector. DG SANCO validated this questionnaire (see Questionnaire.doc).

21/07/2005: Progress meeting at DG SANCO

The aim of this meeting was to deal with the evolution of the first two tasks of the project (see MM 210705.doc), i.e. assessing the objectives of different policy makers and EU and national levels and their interpretation of the use of indicators and secondly developing a structure for the selection of indicators.

The meeting document can be consulted in the following file: MD 210705.doc

02/08/2005: Work meeting at DG SANCO

The purpose of this meeting was to state the progress of the work carried out so far regarding the Tasks 1 and 2 of the first phase and to agree on the structure of the development of indicators related to higher level objectives for the pharmaceutical sector.

The meeting document can be consulted in the following file: MD 020805.doc

07/09/2005: Progress meeting at DG SANCO

This progress meeting addressed the main issues regarding all the project's tasks state of progress as (minutes available in MM 070905.doc):

- The Technical report on Phase I – Tasks 1 and 2 comments from DG SANCO submitted two weeks earlier;
- The summary outcomes of the Phase I-Task 1 to send to experts as a thanking and feedback of the consultation process;
- The approach and work plan proposed by SOGETI regarding:
  - The scoping of type and range of possible indicators (Phase I – Task 3);
  - The review of existing data available in organisations in EU (Phase II – Task 1).

The meeting document can be consulted in the following file: MD 070905.doc

17/10/2005: Progress meeting at DG SANCO

Final changes regarding the second version of the technical report on Phase I – Tasks 1 and 2 were agreed. Progress of Phase I – Task 3 was discussed (see the minutes MM 171005.doc).

The meeting document can be consulted in the following file: MD 171005.doc

21/11/2005: Progress meeting at DG SANCO

Progress of Phase I – Task 3 and Phase II – Task 1 was discussed (see the minutes MM 211105.doc).

The meeting document can be consulted in the following file: MD 211105.doc

05/12/2006: Progress meeting at DG SANCO

The purposes of this meeting (see meeting document MD 061205.doc) were to discuss about progress regarding the whole project and on the work plan proposed by SOGETI regarding the review of existing data available at European level (Phase II – Task 1).

24/01/2006: Progress meeting at DG SANCO

A list of indicators and the methodology for reviewing data availability were agreed. DG SANCO/C2 considered also as important the validation of the pharmaceutical indicators with experts in this domain.

The meeting document can be consulted in the following file: MD 240106.doc

02/03/2006: Progress meeting at DG SANCO

The aim of the meeting was to meet the new coordinator, Daniel Mann (see the minutes MM 020306.doc). The objectives and the planning of this project were introduced (MD 020306.ppt).

24/03/2006: Progress meeting at DG SANCO

The planning of the documents to provide for the final report was discussed (see the minutes MM 240306.doc).

The meeting document can be consulted in the following file: MD 240306.doc.

04/05/2006: Progress meeting at DG SANCO

The planning of the documents to provide and of the related deadlines for the final report was discussed (see the minutes MM 030506.doc).

The meeting document can be consulted in the following file: MD 030506.doc.

4 Phase I

Focus was made on scoping in detail the objectives identified in the first stages of the project (Phase I – Tasks 1 and 2) and drawing-up a first draft list of relevant indicators to address those issues (Task 3).

The technical reports regarding those three tasks were submitted and approved by DG SANCO (see the technical reports 050831SOL01_03.doc and 051130SOL02_01.doc). The reports are publicly available on DG SANCO website.

4.1 Tasks 1 and 2: Outcomes summary

The technical report regarding those two tasks was submitted and approved by DG SANCO (see the technical report 050831SOL01_03.doc). The report is publicly available on DG SANCO website.

Task 1 consisted in consulting the main public health stakeholders and experts. The purpose of the interviews was to gather expertise about the development of performance indicators of the pharmaceutical sector and to validate and identify the main issues to be addressed. As an outcome of this consultation, additional contacts and face-to-face interviews were conducted up to now. You will find hereafter a summary table of the experts contacted (see Table 1).

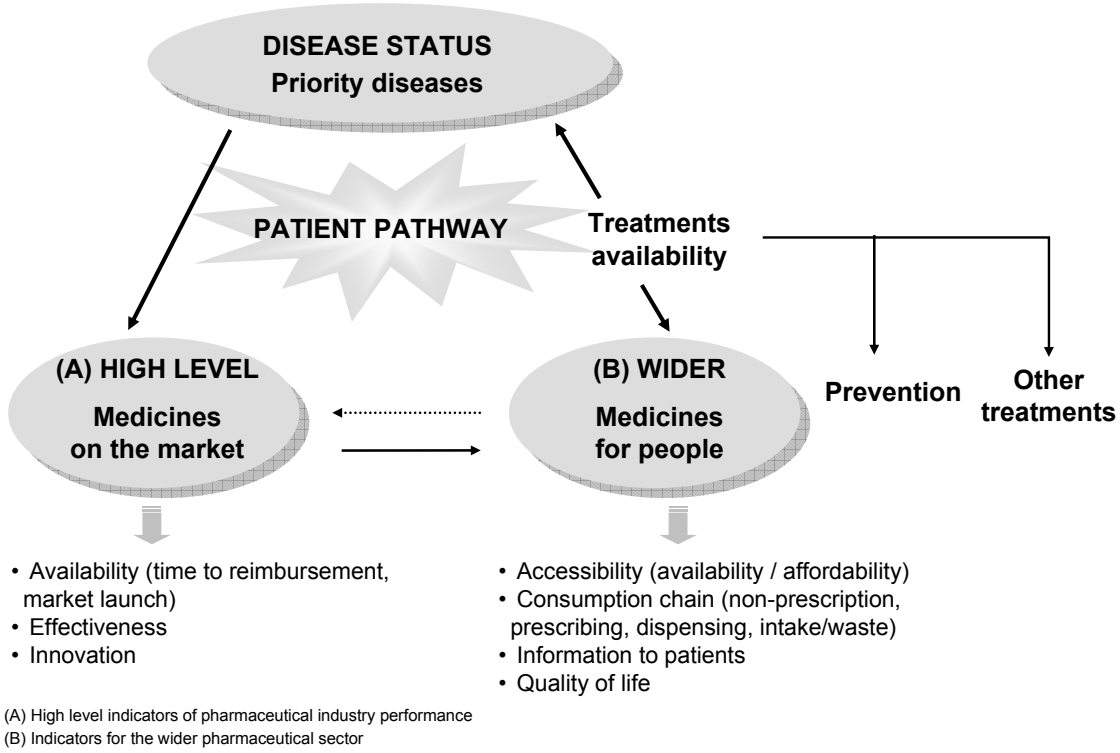
Contact with experts is necessary to ensure project outcomes relevance and will go on throughout the project course.

Table 2 : Experts contacted

DATE	ORGANISATION	EXPERTS
13/07/2005	DG ENTR	*Mr Copping and Mr Van der Spiegel*
14/07/2005	DG SANCO	*Ms Takki*
18/07/2005	Organisation for Economic Co-operation and Development (OECD)	*Mr Kelley, Mr Lafortune and Mrs Docteur*
29/07/2005	European Agency for the Evaluation of Medicinal Products (EMEA)	*Ms Moulon, Mr Vamvakas and Mr Purves*
04/08/2005	OBIG – Pharmaceutical Pricing and Reimbursement Information (PPRI) project	*Ms Rosian and Ms Vogler*
25/08/2005	Department of Innovation for the Italian Ministry of Health and G10	*Mr Silano*
26/08/2005	EuroMedstat – IRPPS- National Research Council	*Mr Folino*
28/09/2005	World Health Organisation (WHO) Regional office	*Mr Laing*
11/10/2005	WHO Regional office OBIG – PPRI project	*Mr de Joncheere, Ms Lyager Thomsen* *Ms Habl*
12/10/2005	Pharmaceutical Group of the European Union (PGEU)	*Ms Giorgio-Gerlach*
12/10/2005	European Federation of Pharmaceutical Industries and Associations (EFPIA)	*Mr Bouvy, Mr Barnes*

From the interviewees' perspective, the purpose of the indicators is to **balance how** do the **patients' needs with regard to disease are met by treatments (including diagnosis and prevention)** and more specifically **medicines available on the market.** Diagnosis, prevention and other forms of treatment (e.g. surgery) should not be excluded of the scope of the indicators while not being a major objective.[2]

Figure 3: Objectives overview



Task 2 involved the development of a structure for the selection of indicators for monitoring the performance of the pharmaceutical sector with regard to public health. A literature review was performed regarding indicators development methodologies and to identify priority diseases and specific populations to be considered.
A methodology review on evaluation of **indicators** with regard to quality and **validity** of indicators was conducted. The scope of the indicators to be developed includes both indicators feasible now and also in the future. Moreover, the selected indicators will have to be a useful and relevant tool for the users regarding their matters of concern as for the policy makers. Hence, evaluation of the indicators for this project should first focus on facing and constructing valid indicators as defined by the Agency for Healthcare Research and Quality[1] (AHRQ). Selection criteria would come as a next step.

From our perspective at this stage, the monitoring should consider specific population groups as country, elderly, children[5] and women. Suffering often from different diseases and reacting differently with medicines, these populations should be treated separately.

With regard to the **choice of up to 3 case-studies diseases** to pilot in the first stage of our project, it should include priority diseases that are likely to throw up different issues for the pharmaceutical response. Therefore, these diseases should include both chronic and acute conditions, may concern wide and small population groups and may allow balancing medicines against other treatments.

In a **second stage**, as proposed in Task 1, the list of diseases would be completed according to the Healthy Life Years[3] (HLYs) and the work already carried out by the "Priority Medicines for Europe and the World"[4] (PRIMs). The list of 14 priority diseases in EU-25 provided in the PRIMs report covers more than 50% of the burden of disease in Europe and could be adapted and be a good starting point for the monitoring.

References

1. "Agency for Healthcare Research and Quality" (AHRQ) website.
2. Communication from the Commission to the Council, the European Parliament, the economic and social committee and the committee of the regions. 2003. A stronger European-based Pharmaceutical Industry for the Benefit of the Patient - A call for action.
3. European Commission website regarding Healthy Life Years.
4. Kaplan W. and Laing. R., 2004. *Priority Medicines for Europe and the World. World Health Organisation* - Department of Essential Drugs and Medicines Policy.
5. "Medicines and Healthcare products Regulatory Agency" (MHRA) website. Medicines for children.

4.2 Task 3: Scope of indicators

From the objectives to be monitored by the indicators presented in Task 1 and the methodologies developed in Task 2, the aim of the Task 3 was to scope the type and range of relevant indicators. The review of indicators was determined regarding priority diseases and specific populations from literature.
These indicators should allow the monitoring and evaluation of which treatments (including diagnosis issues), prevention measures and medicines are available according to the health status targets in terms of:

- Disease status (diagnosis, prevention, health status with regard to disease: DALYs, HLYs);
- Medicines available for people (accessibility, consumption chain, information and quality of life);
- Medicines available on the market (availability, effectiveness and innovation).

4.2.1 Priority diseases

From the consultation of public health stakeholders and the work carried out by WHO ("Priority Medicines for Europe and the World -PRIMs") the list of priority diseases to start with for this monitoring is as follows:

- Infections due to antibacterial resistance;
- Pandemic influenza;
- Diabetes (both types 1 and 2);
- Osteoarthritis;
- Cardiovascular disease (secondary prevention);
- Cancer;
- Acute stroke;
- HIV/AIDS;
- Rare and neglected diseases (e.g. from PRIMs: leishmaniasis);
- Mental health: schizophrenia, depression in the elderly and adolescents;
- Alzheimer disease;
- Chronic obstructive pulmonary disease, asthma;
- Alcohol use disorders.

It is important to clarify the concepts of rare diseases, neglected diseases and orphan medicines (source: European Conference on rare diseases report Luxembourg 21-22 June 2005):

- Rare diseases are firstly characterised by their low prevalence (less than 1/2000) and their heterogeneity. They affect both children and adults, anywhere in the world. Because rare disease patients are minorities, lacking public awareness and not representing public health priorities, little research is performed. Because the market is so narrow for each disease, the pharmaceutical industry is reticent to invest in research and to develop treatments for rare diseases. There is therefore a need for economic regulation in this field.
- Neglected diseases are common, communicable diseases that mainly affect patients living in the poor developing countries. Because they do not represent public health priorities in the industrialised countries, little research is performed on these diseases. They are neglected by the pharmaceutical industry

because the market is usually seen as unprofitable. There is a need for economic regulation and alternative approaches in this field in order to create incentives aimed at stimulating research and developing treatments to fight neglected diseases, which are prevalent in developing countries. Neglected diseases are therefore not rare diseases.

4.2.2 Background of proposed indicators

We propose two different sets of indicators:

- **Core indicators** to be always collected;
- **Recommendations for supplementary indicators** for in-depth analyses.

Only a small number of core indicators are recommended. They should be kept to a minimum to maintain the focus on proposal areas. The proposed indicators[44] measure all important aspects and provide a simple tool for quickly and reliably assessing a few critical aspects of our objectives. This list would contain robust, easily understandable indicators. As all simple tools, the indicators would not cover all the different aspects of the main objective but will focus on the main ones identified throughout the projects according to experts and literature review.

In addition to the core indicators, a set of supplementary indicators was identified. These indicators are to be less important.

It is important to note that some indicators may not be relevant for all the diseases included in the monitoring and that few additional ones may be needed for specific diseases.

These sets of indicators should be estimated **at the national level and European level** when relevant.

The review of data availability and feasibility assessment of indicators is detailed later in this report in Phase II. According to these results the list of indicators first proposed in the technical report 051130SOL02_01.doc was specified and reviewed.

In the next sections, the indicators related to each purpose (disease status, medicine for people and medicines to the market) or each main objective identified are listed with their operational definition.

4.3 Task 3: Disease status indicators

The purpose of this set of indicators is to give an overview of the disease status of the population by priority disease at European and national level when relevant. The information can be used to help identify major problems in health status.

Table 3: List of indicators regarding disease status

LABEL	CALCULATION
DISEASE STATUS	
Crude death rate (CDR)	$\frac{\text{Total number of deaths recorded in one year}}{\text{Total mid - year population (all ages, same year)}} \times 100\,000$
Standardised death rates (SDR)	$\text{Sum of}\left(\begin{array}{l}\text{age - specific death rate weighted by the proportion}\\ \text{of the standard population in age groups}\end{array}\right) \times 100\,000$
Prevalence of disease	$\frac{\text{Number of sick persons}}{\text{Total number of persons}}$
5-year survival rate	5 - year observed survival rate = $\frac{\text{Number of patients diagnosed surviving five years after diagnosis}}{\text{Number of patients diagnosed}}$ 5-year relative survival rate = $\frac{\text{Observed rate of patients diagnosed surviving five years after diagnosis}}{\text{Expected survival rate of a comparable group from the general population}}$
Health-adjusted life expectancy (HALE)	The years of ill-health are weighted according to severity and subtracted from the expected overall life expectancy to give the equivalent years of healthy life
Disability Adjusted Life Years (DALY)	Years of life lost due to premature mortality (YLL) in the population + years lost due to disability (YLD) for incident cases of the health condition

LABEL	CALCULATION
Healthy Life Years (HLY)	Calculated following the Sullivan method. It is based on prevalence measures of the age specific proportion of population with and without disabilities and on mortality data. Detailed methodology: methodological description on DFLE
Co-morbidity	3 levels indicators based on prevalence estimates: $\text{Prevalence} = \frac{\text{Number of sick persons}}{\text{Total number of persons}}$
Wrong or misdiagnosis issues	3 levels indicators based on national surveys estimates of the share of patients either wrong or misdiagnosed for a specific disease
Prevention	Indicator disease specific: - Mammography screening rate for breast cancer - Cervical cancer screening rate - Influenza vaccination for adults over 65
Exposure to main risk factors	- Body mass index (BMI) - Smokers by number of cigarettes - Smokers - Consumption of alcohol

Therapies availability overview	Qualitative indicator identifying the therapies available for a specific disease by main group, e.g:
	- Medicines
	  o Curative
	  o Substitutive
	  o Symptom-alleviating
	  o Preventive
	- Surgery
	- Radiation therapy
	- Hormone therapy
	- Nutrition
	- Psychotherapy

LABEL	CALCULATION
Inadequate care or treatment	3 levels indicators based on national surveys estimates of the share of patients receiving inadequate care or treatment for a specific disease
Main active ingredients sales and status	Sales in volume per Defined Daily Dose of marketed active ingredients
Share of visits with general practitioner compared to specialists	$\frac{\text{Number of patients contacts with GP}}{\text{Number of patients contacts with specialist within a calendar year}}$

4.4 Task 3: Medicines for people indicators

Indicators for monitoring the medicines available for people should address the following issues: accessibility (which concerns both availability and affordability), consumption chain, information and quality of life.

With regard to indicators on affordability of medicines, related work is ongoing in the framework of the PPRI project (PPRI web page, web link on the Public Health website). The proposed indicators in the framework of this project should be reviewed upon the outcomes of the PPRI project. The PPRI project started in April 2005 and is designed to run for two years, until the summer of 2007 (see in Annex for details).

Specific aims of this project will be very useful for our project:

- The systematic collection, reporting and analysis of relevant information and data on pharmaceutical pricing and reimbursement in the Members States. This will result in 25 "Pharma profiles" which are country reports describing the national pharmaceutical pricing and reimbursement systems.
- The development of indicators for the comparative analysis of pricing and reimbursement.
- The benchmarking of pharmaceutical pricing and reimbursement in the enlarged Europe.

Table 4: List of indicators regarding medicines for people

LABEL	CALCULATION
ACCESSIBILITY TO MEDICINES	
AVAILABILITY OF MEDICINES	
Accessibility to pharmacies	$\frac{\text{Number of community pharmacies (or pharmacists)}}{\text{Population}}$
Share of non-marketed medicines in newly authorised medicines	$\frac{\text{Number of non - marketed medicines}}{\text{Number of newly authorised medicines}}$ during the last 3 years
AFFORDABILITY OF MEDICINES	
National reimbursement systems	Qualitative and descriptive indicator of - Availability of list of medicines reimbursed (positive/negative lists) - The reimbursements rates
National Co-payment systems	Qualitative and descriptive indicator of the main cost-sharing types: - Co-payment (fixed amount per service) - Deductible (fixed amount to be born before the third-party gets involved) - Co-insurance (share of the price)
Share of public expenditure on pharmaceuticals	$\frac{\text{Public pharmaceutical expenses}}{\text{Total pharmaceutical expenses}}$
Number of reimbursed medicines	Number
Share of reimbursed medicines on outpatient market	$\frac{\text{Number of active ingredients eligible for reimbursement for ATC code}}{\text{Number of active ingredients for ATC code on the market of the country}}$
Number of reimbursed medicines by reimbursement type	Number

LABEL	CALCULATION
Price per Defined Daily Dose (DDD)	$\frac{\text{Price of the pack (euros)}}{\text{Number of DDDs in the pack}}$
Price of medicines in number of days wages	$\frac{\text{Median treatment unit price}}{\text{Daily wage}}$ Unit price = $\frac{\text{price of pack}}{\text{pack size}}$
CONSUMPTION CHAIN	
SELF-MEDICATION	
Share of non-prescription market in outpatient market	$\frac{\text{Sales of non-prescription medicines}}{\text{Total sales of medicines}}$
Rx to OTC switching	$\frac{\text{Number of non-prescription medicines}_{year}}{\text{Number of non-prescription medicines}_{year-1}}$
PRESCRIBING	
Average number of reimbursed medicines prescribed per patient encounter	$\frac{\text{Number of medicines prescribed}}{\text{Number of patients encounters}}$
Average number of reimbursed medicines prescribed per inhabitant	$\frac{\text{Number of medicines prescribed}}{\text{Total population}}$
Prescribed Daily Doses (PDDs)	1. For each drug and at each strength of tablet (e.g. simvastatin 10mg tablets), the number of prescriptions are recorded noting the quantity (in numbers of tablets) and the number of times per day (usually once for statins). From this, an average daily number of tablets for that dose form is derived 2. The total number of doses per day for each strength of tablet is estimated by multiplying total prescriptions number by the average daily dosing for each form

LABEL	CALCULATION
	3. This is converted into total milligrams per day by multiplying number of tablets for each form by the relevant strength 4. These are summated for all dosage forms and divided by the total numbers of prescriptions to give an average prescribed daily dose for that drug
DISPENSING	
Market share of generics on outpatient market	$\frac{\text{Generic medicines sales (volume)}}{\text{Whole pharmaceutical market (volume)}}$
Utilisation in Defined Daily Doses per 1000 inhabitants per day	$\frac{\text{Packages number sold x DDD of the package}}{\text{Days number in the period of data collection x inhabitants number}} \times 1000$
Share of medicines actually dispensed	$\frac{\text{Number of medicines actually dispensed}}{\text{Number of medicines prescribed}}$
ADHERENCE	
Adherence to treatment	$\frac{\text{Prescribed doses (D) taken at the prescribed time interval (T)}}{\text{Period of time}}$
MEDICATION ERRORS AND ADVERSE EVENTS	
Medication errors	Number of patient deaths, paralysis, coma, or other major permanent loss of function associated with a medication error
Death and complications from medication error	Number of patient deaths or serious complications (CNS damage with squeal, myocardial infarction, pulmonary embolism, blood disorders) likely to be caused by medication errors
Adverse events	- Number of hospitalisations due to adverse events - Number of compensations granted (DE, AT, DK) for adverse event - Another alternative is to look at Adverse Drug Reaction (ADR) reports

LABEL	CALCULATION
INFORMATION TO PATIENTS	
Guidelines from main institutes	Qualitative indicator identifying if there exists standard national, European or international guidelines and plans or programmes to support guidance implementation available for priority diseases exist
Public health campaigns addressed to citizens	Number of public health campaigns addressed to citizens, distinguishing campaigns by government or others organisations (professionals or patients associations)
Websites providing information	Number or number of hits or visits of websites providing medicines and treatment information to patients
Patients' knowledge of correct use and diagnosis	Share of patients who can adequately report the dosage schedule for all medicines divided by the total of patients interviewed
QUALITY OF LIFE	
Time devoted to treatment per day	$\frac{\text{Sum of number of minutes for treatment in the day}}{\text{Treatment duration in days}}$
Medicines taken per day	Number of distinct medicines taken in a treatment day
Ease of use	3 levels indicator: - 3= High assistance (e.g. hospitalisation) - 2= Some assistance needed (e.g. assistance of a nurse) - 1= Self treatment
Share of recovery	3 levels indicator: - 3= Complete recovery - 2= Partial recovery - 1= No recovery
Autonomy	Qualitative indicator regarding main types of standard treatment side-effects on patient autonomy: feeding, personal hygiene, dressing, limitations in seeing, hearing, speaking, biting, agility

LABEL	CALCULATION
Enhancing quality of life by treatment	Qualitative measure of quality of life improvement from medicinal treatment, e.g. autonomy gain.

4.5 Task 3: Medicines on the market indicators

Medicines on the market indicators aim at monitoring issues such as medicines accessibility to market, medicines effectiveness and pharmaceutical industry innovation.

Table 4: List of indicators regarding medicines on the market

LABEL	CALCULATION
MEDICINES ACCESSIBILITY TO MARKET	
Time from license to market	Number of average days or years - from marketing authorisation to price - from price to reimbursement Median, min and max market delays
Average time for orphan medicines procedures	Average number of days
MEDICINES EFFECTIVENESS	
Therapeutic benefits	Statistical tests significance
Incremental cost-effectiveness ratio (ICER)	$\frac{(\text{Cost of treatment - cost of alternative})}{(\text{Effect of treatment - effect of alternative})}$
ASMR	Number of ASMR evaluations by level since 1995, 7 levels: - I: Major therapeutic improvement - II: Important therapeutic improvement in terms of therapeutic efficacy and/or reduction of side effects

LABEL	CALCULATION
	- III: Moderate therapeutic improvement in terms of therapeutic efficacy and/or reduction of side effects - IV: Minor therapeutic improvement in terms of therapeutic efficacy and/or usefulness for clinical trial (tolerance, ease of use, observance), medicines class gap or potential advantage according to its pharmaceutical properties or lower risk of interactions with other medicines - V: No therapeutic improvement but approving notice for inscription - VI: Disapproving notice for inscription to collectivity or Social Security - 00: Unable to assess improvement
Market withdrawals	Number of medicines withdrawals covering the priority diseases during the last 5 years
INNOVATION	
Innovative medicines initiatives	Existence of specific actions or initiatives plans for innovative medicines as: - a separate list for innovative medicines as in France and Germany - national disease plan - small and medium-sized enterprises (SMEs) fee reductions and deferrals for a number of EMEA services, such as scientific advice (Commission Regulation 2049/2005 laying down special financial and administrative provisions for SMEs, adopted on 15.12.2005 and published on 16.12 in the EU Official Journal L 329) - other initiatives in favour of better access of patients to innovative medicines (e.g. specific budget for new cancer drugs in Denmark) - national plans in place for few diseases (e.g. cancer, rare diseases)
Taxation discounts depending on investments on R&D	Qualitative indicator describing the main types of national initiatives to encourage the pharmaceutical companies to invest on R&D
Uptake of new medicines	$\frac{\text{Sales of NMEs launched within the last 5 years from 2001}}{\text{Sales of the whole pharmaceutical market}}$
Share of New Chemical Entities covering priority diseases within the last 5 years	$\frac{\text{Number of NCEs covering the priority diseases}}{\text{Total number of NCEs}}$ within the last 5 years

LABEL	CALCULATION
Share of New Active Substances launched covering priority diseases in the last 5 years	$\frac{\text{Active substance number covering the priority diseases}}{\text{Total number of active substance}}$ within the last 5 years
Medicines under clinical development	Number of active substances or NCEs
Number of people working on a specific disease	Number of employees
Share of R&D personnel in total persons employed	$\frac{\text{Number of R\&D employees}}{\text{Total number of persons employed}}$
Pharmaceutical patents granted	Number or share of patents granted covering the priority diseases or selected therapeutic areas
Share of R&D expenditure in value-added	$\frac{\text{R\&D expenditure}}{\text{Value added}}$
Share of R&D expenditure by therapeutic area	$\frac{\text{R\&D expenditure in therapeutic area}}{\text{Total R\&D expenditure}}$
Share of marketing investment in turnover	$\frac{\text{Investment}}{\text{Turnover}}$
Generics penetration rate in prescriptions	$\frac{\text{Number of generic medicines prescribed}}{\text{Total number of medicines prescribed}}$

5 Phase 2

In order to be close to reality, the selection of indicators needed to be associated to existing information. Consequently, the second phase of the project consisted in reviewing and comparing data available in both public and private organisations. The work was carried out in three stages.
The first one reviewed existing data available in both public and private organisations at European level. The selection of indicators is based on Public Health studies, either accomplished or still in progress. The main characteristics of these indicators were detailed, e.g. data type, feasibility and frequency of data collection.
From the data availability review, the second stage established the comparability of these data and recommendations. Data comparability depended on several criteria regarding data quality.
Finally, the last stage provided discussion and proposals for indicators. Priorities were set according to indicator importance and readiness for implementation.
The detailed report is available in Annex "Phase 2 report".

5.1 Data availability and recommendations

From all the information gathered and documents provided by experts, this section reviews existing data available at European level. From the objectives introduced in Tasks 1 and 2, a first stage of this Task concerned the review of the most significant organisations.

Emphasis was put on international organisations, including European ones, and on national organisations or databases either with a European perspective or being a good example of what could be done. The main organisations and databases relevant for the purpose of the study and to be focused on in a first stage are described in Annex "International and European organisations review".

5.1.1 Methodology

This section presents a summary of the conceptual framework and the indicator's profiles including indicator's description, data sources availability, limitations, evaluation and, finally, recommendations. The selection of core indicators was realised according to different criteria: from a disease point of view, from the point for view of the main objectives one or from quantitative and qualitative criteria (see Annex "Phase 2 report").

Categorisation scheme

The indicators are split into **three main categories**:

STRUCTURAL INDICATORS
This first set of indicators is intended to provide data on the pharmaceutical context related to public health issues in a given country. These indicators provide qualitative and quantitative information to assess the pharmaceutical system's capacity to achieve

its public health and social objectives. They are intended to check whether the key structures/systems/mechanisms necessary with regard to public health exist in the country.
The report provides 28 structural indicators.

PROCESS INDICATORS
These indicators provide quantitative information on the processes by which treatment is provided to patients. They assess the degree to which activities necessary to attain the objectives are carried out and their progress over time.
These process indicators are based on information available at the central level and/or obtained through surveys. The results of the process indicators should be analysed together with the results of the structural indicators.
The report provides 18 process indicators.

OUTCOME INDICATORS
These indicators measure the results achieved and the changes that can be attributed to the pharmaceutical industry. They have been selected to assess the effects of medicines: therapeutic benefit, adverse reaction, withdrawals, impact on patients' quality of life. These outcome indicators are based on information available at the central level and/or obtained through surveys.
The report provides 25 outcome indicators.

Table 3: Indicators taxonomy

	Level / dimension	Specificity	Breakdowns[4]
DISEASE STATUS			
Crude death rate (CDR)	Outcome	General	Disease
Standardised death rates (SDR)	Outcome	General	Disease
Prevalence of disease	Outcome	General	Disease
5-year survival rate	Outcome	General	Disease
Health-adjusted life expectancy (HALE)	Outcome	General	-
Disability Adjusted Life Years (DALY)	Outcome	General	Disease
Healthy Life Years (HLY)	Outcome	General	-
Co-morbidity	Outcome	General	Disease
Wrong or misdiagnosis issues	Structure	Disease specific	Disease
Prevention	Structure/Process	Disease specific	Disease
Exposure to main risk factors	Structure	General	-
Therapies availability overview	Outcome	General	Disease
Inadequate care or treatment	Outcome	General	Disease
Main active ingredients sales and status	Structure	General	Disease, medicine
Share of visits with general practitioner compared to specialists	Process	General	-
ACCESSIBILITY TO MEDICINES			
Accessibility to pharmacies	Structure	General	-
Share of non-marketed medicines in newly authorised outpatient medicines	Structure	General	-
National reimbursement systems	Structure	General	-
National co-payment systems	Structure	General	-
Share of public expenses on Pharmaceuticals	Structure	General	-
Number of reimbursed medicines	Structure	General	Disease, medicine
Share of reimbursed medicines on outpatient market	Structure	General	Disease, medicine
Number of reimbursed medicines by reimbursement type	Structure	General	Disease, medicine
Price per Defined Daily Dose (DDD)	Structure	General	Disease, medicine
Price of medicines in number of days wages	Structure	General	Disease, medicine

[4] If feasible and disease relevant

	Level / dimension	Specificity	Breakdowns[4]
CONSUMPTION CHAIN			
Share of non-prescription market in outpatient market	Process	General	Disease
Rx to OTC switching	Process	General	Disease
Average number of reimbursed medicines prescribed per patient encounter	Process	General	-
Average number of reimbursed medicines prescribed per inhabitant	Process	General	-
Prescribed Daily Doses (PDDs)	Process	General	Disease
Market share of generics on outpatient market	Process	General	Disease
Utilisation in DDD/1000 inhabitant/day	Process	General	Disease, medicine
Share of medicines actually dispensed	Process	General	-
Adherence to treatment	Process	General	-
Medication errors	Process	General	-
Death and complications from medication error	Process/Outcome	General	-
Adverse events	Process/Outcome	General	-
INFORMATION TO PATIENTS			
Guidelines from main institutes	Process	General	Disease
Public Health campaigns addressed to citizens	Process	General	Disease
Websites providing information	Process	General	Disease
Patients' knowledge of correct use and diagnosis	Process	General	-
QUALITY OF LIFE			
Time devoted to treatment per day	Outcome	General	Disease
Medicines taken per day	Outcome	General	Disease
Ease of use	Outcome	General	Disease
Share of recovery	Outcome	General	Disease
Autonomy	Outcome	General	Disease
Enhancing quality of life by treatment	Outcome	General	Disease
MEDICINES ACCESSIBILITY TO MARKET			
Time from license to market	Structure	General	-
Average time for orphan medicines procedures	Structure	General	-
MEDICINES EFFECTIVENESS			
Therapeutic benefits	Outcome	General	Disease, medicine
Incremental cost-effectiveness ratio (ICER)	Outcome	General	Disease, medicine
ASMR	Outcome	General	Disease, medicine
Market withdrawals	Outcome	General	Medicine
INNOVATION			
Innovative medicines initiatives	Structure	General	-
Taxation discounts depending on investments on R&D	Structure	General	-
Uptake of new medicines	Structure/Outcome	General	-
Share of New Chemical Entities covering priority diseases within the last 5 years	Structure/Outcome	General	Disease
Share of New Molecular Entities launched covering priority diseases in the last 5 years	Structure/Outcome	General	Disease
Medicines under clinical development	Structure	General	Disease
Number of people working on a specific disease	Structure	General	Disease
Share of R&D personnel in total persons employed	Structure	General	-
Pharmaceutical patents granted	Structure	General	Disease
Share of R&D expenditure in value-added	Structure	General	-
Share of R&D expenditure by therapeutic area	Structure	General	Disease
Share of marketing investment in turnover	Structure	General	-
Generics penetration rate in prescriptions	Structure	General	-

Scope of indicators

Only **medicines** as defined hereafter should be considered in the framework of this monitoring:

- According to Article 1 of Directive 2001/83 EC: a medicinal product is any substance or combination of substances presented for treating or preventing disease in human beings. Any substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in human beings is likewise considered a medicinal product;
- for human use excluding homeopathy and veterinary products;
- classified according to the WHO Anatomical, Therapeuthical, Chemical (ATC) classification system;
- identified by its non-proprietary name of its active ingredient;
- for ambulatory care for most indicators, except for specific priority diseases for which ambulatory care is not representative and hospital medicinal treatment are significant, e.g. cancers;
- prescription medicine or not;
- reimbursed or not;
- over-the-counter (OTC) medicines: only include preparations used therapeutically (exclude simple food supplement, nutrients) and exclude herbal and homeopathic preparations. Analysis should be based on listing such as the British National Formulary[5] or similar source.

All references to medicines will be given according to its active ingredient (or substance) as defined within the European Union, Article 1 of Directive 2001/83 EC as follows: a substance is any matter irrespective of origin which may be:

- human, e.g. human blood and human blood products;
- animal, e.g. micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products;
- vegetable, e.g. micro-organisms, plants, parts of plants, vegetable secretions, extracts;
- chemical, e.g. elements, naturally occurring chemical materials and chemical products obtained by chemical change or synthesis.

Since available data on medicines are not linked to diagnosis, the proposed approach is the following:

1. First identify the therapies available in the Member States
2. Then select the main medicines covering the priority diseases. The medicines should be selected according to the following criteria:
   - Market share: significant sales data on the market. The threshold should ensure a good coverage of the market and may differ from disease to disease (e.g in case of highly concentrated markets). Differences from country to country should also be taken into account.
   - Representativeness of the market: e.g share of generics;
   - Effectiveness;

[5] http://www.bnf.org/bnf/

- Include innovative products;
- Cover the available types of medicines for the disease concerned (curative, substitutive, symptom-alleviating, preventive).

A less time-consuming alternative approach would be to:

1. First identify the main medicines on the Member States markets;
2. Then evaluate if those medicines cover the priority diseases.

Some medicines may cover more than one priority disease.

Indicators profile

The core reference section of the Phase II report available in Annex "Phase 2 report" is the detailed description, data availability assessment, evaluation and recommendation presented for each indicator as a profile that includes:

INDICATOR NAME: SHORT TITLE TO IDENTIFY THE INDICATOR

Description

Purpose

What is the purpose of the indicator?
Why is this indicator important?

Prerequisites

What are the prerequisites for the indicator?

Definition

What is the content of the indicator?
What will this indicator measure?
What are the definitions of key terms?
What is the scope of the indicator?
How can the results be interpreted?

Taxonomy

Structure/Process/Outcome indicator
Disease specific

Breakdown

Country/Disease/Medicine

Calculation

How should the indicator be calculated?

Unit

What is the unit of the indicator?

Data sources and availability

What are the main sources and methods of data collection?
Are the data available?
- Publicly
- Regularly

What is the coverage?
- Geographic
- Time

Breakdowns available:
- For which breakdowns or groups does the indicator apply for?
- For which breakdowns or groups will the indicator be calculated?

Limitations What are the main limitations of the indicator?	
EVALUATION	
Importance	Core / Supplementary indicator
Validity: - Face validity - Construct validity - Content validity	Yes, good measure of what it is intended to / No
Reliability	Yes, consistent when repeated / No, too much variability
Evidence	Yes, scientific evidence available in literature or already in use, collected in other institutions or reviewed by an expert panel / No
Feasibility:	Very high / High/ To be confirmed/ Low / Not feasible yet / Further research required
- Data availability	Regularly (international / national) / Occasional / Not available
- Geographical coverage	EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU aggregate
- Reporting burden	Yes, complex estimation process / No, straightforward estimate
- Accessibility, cost	Public / Restrictive access / Free / On payment
- Comparability	Yes / No, definitions or classifications not comparable
Regularity, timeless	Regular updates available / non available Future availability reliable / non reliable Delivery time frame good or too long
Easy to understand	Yes / No, composite measure
Further work required	Additional research and development work required to complete the indicator's specification to a level appropriate for large scale monitoring
RECOMMENDATION	Core indicator to be implemented - generally on a routine basis - by periodic survey - data source recommended Supplementary indicator / excluded To be further developed either because - the indicator specification is incomplete - data should be available later on (ongoing projects) - new data collection set up needed

The selection of core indicators was realised according to different criteria: from disease point of view, from main objectives one or from a quantitative and qualitative one (see Annex "Phase 2 report" for details).

5.1.2 Outcomes summary

The table below presents the list of indicators reviewed in the framework of this project for all objectives identified (disease status, accessibility to medicines, consumption chain, information to patients, quality of life, medicines' accessibility to market, medicines effectiveness and innovation). It gives an overview of the outcomes of the data availability assessment and presents the main recommendations.

A wide range of indicators were identified and reviewed from the consultations and literature review. Then a selection was realised identifying core and supplementary indicators. Finally, proposals and recommendations were made.

For each indicator, it reviews:

- its importance (core, supplementary or excluded indicator)
- its type (quantitative or qualitative indicator)
- the breakdowns to be used (by country, disease, medicine)
- its feasibility, detailing the availability (see below for details), accessibility (publicly available, restrictive access, on payment), the geographical coverage (EU-25 for more than 22 Member States covered, Partial: between 11 and 22 Member States covered, limited if less than 10 Member States are covered and EU agg. When EU aggregate only is available)
- the further work required so the indicator can be implemented. It ranges from further data source research to improve indicator specification in terms of definition and characteristics. For few indicators, an in depth feasibility study may need to be conducted
- the recommendations in terms of periodicity of data collection (e.g. on a yearly basis, 5-year), the data source recommended if any.

Data availability assessments were given a qualitative indication of the degree to which data/indicators are regularly available, or more of a developmental nature:

- data **regularly** available from
    - **A**: **international** sources
    - **B**: **national** sources
- **C**: rely on **incidental** national or regional sources
- **D**: data needed but generally **not available**.

Importance: C=Core / S=Supplementary / E=Excluded Type: Quant= Quantitative / Qual= Qualitative Breakdown: C= Country / M= Medicine/ D=Disease
Access: P=Public / OP=On payment / R=Restrictive Coverage: EU-25 (≥23)/Partial (11 to 22 countries)/Limited (≤10)/ EU agg. = EU aggregate only
Availability: A=International sources / B= National sources / C=Rely on incidental national or regional sources / D=Generally not available / F=Future
Feasibility: "++"= Very high / "+"= High / "+/-"= To be confirmed / "-"= Low / "--"= Not feasible yet

A sharp distinction is not always possible, those evaluations, recommendations and classifications may need more improvements. Still, these classes represent a gradient from data/indicators which can be considered as reasonably standard, to those for which much developmental work has to be carried out on data collection, indicator definition and enhancement of data comparability.

Table 4: Indicators recommendations summary

Domain	Impor-tance	Type	Break-down	Feasibility				Further work	Recommendations	
					Avail.	Access	Coverage		Periodicity	Data source
DISEASE STATUS										
Prevalence of disease	**C**	**Quant**	**C/D**	**+**	**A/B**	**P/R**	**EU-25**	**Data source disease specific**	**Yearly**	**Diabetes: IDF Cancer: IARC Acute: incidence instead of prevalence**
Disability Adjusted Life Years (DALY)	**C**	**Quant**	**C/D**	**++**	**A**	**P**	**EU-25**		**2-year**	**WHO**
Exposure to main risk factors	**C**	**Quant**	**C**	**++**	**A**	**P**	**EU-25**		**Yearly**	**EUROSTAT**
Therapies availability overview	**C**	**Qual**	**D**	**+**	**C**	**P/OP**	**EU-25**	**Data source Indicator specification**	**Yearly**	**Literature review and experts**
Main active ingredients sales and status	**C**	**Quant**	**C/D/M**	**+**	**A/F**	**P**	**EU-25**	**Data source availability to confirm**	**Yearly**	**EuroPharm database (EMEA)**
Standardised death rates (SDR)	S	Quant	C/D	++	A	P	EU-25		Yearly	WHO
5-year survival rate	S for cancer	Quant	C/D	+	C/D	OP	EU-25		Yearly	OECD HCQI project: planned for breast, cervical, colorectal cancers
Co-morbidity	S: few diseases	Qual / Quant	C/D	+/-	C	P	Limited	Data source Indicator specification	2 to 5 year	
Wrong or misdiagnosis issues	S	Qual	D	+/-	C	R/OP	EU-25	Data source Indicator specification	5-year	
Prevention	S	Quant	C/D	+	A/D/F	OP	Partial	Indicator specification	Yearly	OECD for immunisation EUROSTAT for breast and cervical cancer screening rates OECD HCQI project: planned vaccination indicators
Inadequate care or treatment	S	Qual	C/D	+/-	C	P/OP	EU-25	Data source Indicator specification	Yearly	Literature review and experts

Importance: C=Core / S=Supplementary / E=Excluded Type: Quant= Quantitative / Qual= Qualitative Breakdown: C= Country / M= Medicine/ D=Disease
Access: P=Public / OP=On payment / R=Restrictive Coverage: EU-25 (≥23)/Partial (11 to 22 countries)/Limited (≤10)/ EU agg. = EU aggregate only
Availability: A=International sources / B= National sources / C=Rely on incidental national or regional sources / D=Generally not available / F=Future
Feasibility: "++"= Very high / "+"= High / "+/-"= To be confirmed / "-"= Low / "--"= Not feasible yet

Domain	Impor-tance	Type	Break-down	Feasibility				Further work	Recommendations	
					Avail.	Access	Coverage		Periodicity	Data source
Crude death rate (CDR)	*E*	*Quant*	*C/D*	++	*A*	*P*	*EU-25*		*Yearly*	*WHO*
Health-adjusted life expectancy (HALE)	*E*	*Quant*	*C*	+/-		*P*	*EU-25*		*Yearly*	*WHO*
Healthy Life Years (HLY)	*E*	*Quant*	*C*	+	*A*	P	*EU-25*		*Yearly*	*EUROSTAT*
Share of visits with general practitioner compared to specialists	*E*	*Quant*	*C*	+/-		*P*	*EU-25*	*Future availability to be assessed*	*Yearly*	*EUROSTAT*
ACCESSIBILITY TO MEDICINES										
Share of non-marketed medicines in newly authorised outpatient medicines	**C**	**Quant**	**C**	**+/-**	**A**	**P/OP**	**EU-25**	**Data source Feasibility study**	**Yearly**	**IMS Health**
National reimbursement systems	**C**	**Qual**	**C**	**++**	**A/F**	**R**	**EU-25**		**Yearly**	**PPRI project**
National co-payment systems				**++**	**A/F**	**R**	**EU-25**		**Yearly**	**PPRI project**
Share of public expenditure on pharmaceuticals		**Quant**		**++**	**A**	**OP/R**	**Partial**		**Yearly 5-year for EU-25 non OECD**	**OECD PPRI project: future for EU-25 non OECD**
Share of reimbursed medicines on outpatient market	**C**	**Quant**	**C/D/M**	**+**	**A/B**	**P**	**Partial**	**Data source: contact ESIP**	**Yearly**	**ESIP**
Price of medicines in number of days wages	**C**	**Quant**	**C/D/M**	**+/-**	**B**	**P/OP**	**Partial**	**Data source Price definition Feasibility study**	**Yearly**	
Accessibility to pharmacies	S	Quant	C	++	A	P	EU-25		Yearly	PGEU
Number of reimbursed medicines	*E*	*Quant*	*C/D/M*	*+/-*	*A/B*	*P*	*EU-25*	*Data source*	*Yearly*	
Number of reimbursed medicines by reimbursement type	*E*	*Quant*	*C/D/M*	-	*B*		*EU-25*		*Yearly*	
Price per Defined Daily Dose (DDD)	*E*	*Quant*	*C/D/M*	*+/-*	*B/F*	*P*	*EU-25*	*Data source Price definition*	*Yearly*	
CONSUMPTION CHAIN										
Average number of medicines prescribed per inhabitant	**C**	**Quant**	**C**	**+**	**A/F**	**R**	**EU-25**		**Yearly**	**PPRI project**
Utilisation in DDD/1000 inhabitants/day	**C**	**Quant**	**C/D/M**	**+**	**A/F**	**P**	**Partial**		**Yearly**	**EURO-MED-STAT[6]**
Share of medicines actually dispensed	**C**	**Quant**	**C**	**+/-**	**C**	**P/R**	**Limited**	**Data sources**	**5-year**	
Adherence to treatment	**C**	**Quant**	**C**	**--**	**D**		**Limited**	**Data source Indicator**	**5-year**	

[6] Partial geographical coverage and future availability to be confirmed

Importance: C=Core / S=Supplementary / E=Excluded Type: Quant= Quantitative / Qual= Qualitative Breakdown: C= Country / M= Medicine/ D=Disease
Access: P=Public / OP=On payment / R=Restrictive Coverage: EU-25 (≥23)/Partial (11 to 22 countries)/Limited (≤10)/ EU agg. = EU aggregate only
Availability: A=International sources / B= National sources / C=Rely on incidental national or regional sources / D=Generally not available / F=Future
Feasibility: "++"= Very high / "+"= High / "+/-"= To be confirmed / "-"= Low / "--"= Not feasible yet

Domain	Impor-tance	Type	Break-down	Feasibility				Further work	Recommendations	
					Avail.	Access	Coverage		Periodicity	Data source
								specification		
Share of non-prescription market in outpatient market	S	Quant	C/D	+	A	P/OP	EU-25		Yearly	DG ENTR Benchmark: whole market only IMS Health
Rx to OTC switching	S	Quant	C/D	++	A	P	EU-25		Yearly	AESGP
Prescribed Daily Doses (PDDs)	S	Quant	C/D	+	A	OP	Partial	Data source	Yearly	
Market share of generics on outpatient market	S	Quant	C/D	+	A	P/OP	EU-25		Yearly	EGA: whole market only IMS Health
Medication errors	S	Quant	C	+/-	C	OP	Partial	Data source	Yearly	OECD HCQI project: no planned data collection
Adverse events	S	Quant	C	--	D		Limited	Data source Indicator specification	Yearly	
Average number of medicines prescribed per patient encounter	*E*	*Quant*	*C*	-	*A*	*P*	*Limited*		*Yearly*	*AESGP*
Death and complications from medication errors	*E*	*Quant*	*C*	--	*D*					
INFORMATION TO PATIENTS										
Guidelines from main institutes	S	Qual	C/D	--	C	P/R	Partial	Data source	Yearly	
Public Health campaigns addressed to citizens	S	Quant	C/D	--	C	P	Partial	Indicator specification	Yearly	
Websites providing information	S	Quant	C/D	--	C	P	Partial		Yearly	
Patients' knowledge of correct use and diagnosis	S	Quant	C	--	D		Limited	Outcomes of the Working Group of the Pharmaceutical Forum	5-year	
QUALITY OF LIFE										
Ease of use	**C**	**Qual**	**C/D**	**+/-**	**D**			**Data source: new data collection** **Indicator specification**	**5-year**	
Medicines taken per day	S	Quant	C/D	+/-	C			Data source Indicator specification	Yearly	EUROSTAT
Time devoted to treatment per day	*E*	*Quant*	*C/D*	--	*D*			*Data source* *Indicator specification*	*Yearly*	
Share of recovery	*E*	*Qual*	*C/D*	--	*D*			*Data source*	*Yearly*	

Importance: C=Core / S=Supplementary / E=Excluded Type: Quant= Quantitative / Qual= Qualitative Breakdown: C= Country / M= Medicine/ D=Disease
Access: P=Public / OP=On payment / R=Restrictive Coverage: EU-25 (≥23)/Partial (11 to 22 countries)/Limited (≤10)/ EU agg. = EU aggregate only
Availability: A=International sources / B= National sources / C=Rely on incidental national or regional sources / D=Generally not available / F=Future
Feasibility: "++"= Very high / "+"= High / "+/-"= To be confirmed / "-"= Low / "--"= Not feasible yet

Domain	Impor-tance	Type	Break-down	Feasibility				Further work	Recommendations	
					Avail.	Access	Coverage		Periodicity	Data source
								Indicator specification		
Autonomy	*E*	*Qual*	*C/D*	--	*D*			*Data source* *Indicator specification*	*Yearly*	
Enhancing quality of life by treatment	*E*	*Qual*	*C/D*	--	*D*			*Data source* *Indicator specification*	*Yearly*	
MEDICINES' ACCESSIBILITY TO MARKET										
Time from license to market	**C**	**Quant**	**C**	**++**	**A**	**R**	**Partial**		**Yearly**	**EFPIA**
Average time for orphan medicines procedures	S	Quant	C	++	A	P	EU-25	Breakdown by country feasibility and relevance	Yearly	EMEA
MEDICINES EFFECTIVENESS										
Incremental cost-effectiveness ratio (ICER)	**C**	**Quant**	**D/M**	**+/-**	**C**	**P/OP**	**Limited**	**Indicator specification**	**Yearly**	**NICE** **EUNetHTA** **Literature review**
ASMR	**C**	**Qual**	**D/M**	**+/-**	**C**	**P**	**FR**	**Methodology review**	**Yearly**	**HAS**
Market withdrawals	S	Quant	C/M	+	A/B	P	EU-25	Significance of results	Yearly	EMEA EURO-MED-STAT[7]
Therapeutic benefits	*E*	*Quant*	*C/D/M*	-	*C*	*R/OP*	*Partial*	*Data source* *Indicator specification*	*Yearly*	*Literature review*
INNOVATION										
Uptake of new medicines	**C**	**Quant**	**C**	**++**	**A**	**P/OP**	**Limited**		**Yearly**	**DG ENTR Benchmark: whole market only**
Share of New Chemical Entities covering priority diseases within the last 5 years	**C**	**Quant**	**D**	**++**	**A**	**OP**	**EU agg.**		**Yearly**	**CMR** **IMS Health**
Innovative medicines initiatives	S	Qual	C	+	B		EU-25	Data source Indicator specification	Yearly	
Share of New Molecular Entities launched covering priority diseases in the last 5 years	S	Quant	D	++	A	OP	EU agg.		Yearly	CMR IMS Health
Medicines under clinical development	S	Quant	D	++	A	OP	EU agg.		Yearly	CMR

[7] Partial geographical coverage and future availability to be confirmed

Importance: C=Core / S=Supplementary / E=Excluded Type: Quant= Quantitative / Qual= Qualitative Breakdown: C= Country / M= Medicine/ D=Disease
Access: P=Public / OP=On payment / R=Restrictive Coverage: EU-25 (≥23)/Partial (11 to 22 countries)/Limited (≤10)/ EU agg. = EU aggregate only
Availability: A=International sources / B= National sources / C=Rely on incidental national or regional sources / D=Generally not available / F=Future
Feasibility: "++"= Very high / "+"= High / "+/-"= To be confirmed / "-"= Low / "--"= Not feasible yet

Domain	Impor-tance	Type	Break-down	Feasibility				Further work	Recommendations	
					Avail.	Access	Coverage		Periodicity	Data source
Share of R&D expenditure by therapeutic area	S	Quant	D	+	A	OP	EU agg.		Yearly	CMR
Taxation discounts depending on investments on R&D	*E*	*Qual*	*C*	*+/-*	*C*		*Limited*	*Data source Indicator specification*	*Yearly*	
Number of people working on a specific disease	*E*	*Quant*	*C/D*	-	*D*		*Partial*		*Yearly*	
Share of R&D personnel in total persons employed	*E*	*Quant*	*C*	*+/-*				*Data source*	*Yearly*	
Number of pharmaceutical patents granted	*E*	*Quant*	*C/D*	*+/-*	*A*	*P/OP*	*EU-25*		*Yearly*	*EPO EUROSTAT*
Share of R&D expenditure in value-added	*E*	*Quant*	*C*	+	*A*		*EU-25*		*Yearly*	*EUROSTAT*
Share of marketing investment in turnover	*E*	*Quant*	*C*	--	*D*	*R*		*Data source*	*Yearly*	
Generics penetration rate in prescriptions	*E*	*Quant*	*C*	+	*A*	*OP*	*Partial*		*Yearly*	*IMS Health*

Importance: C=Core / S=Supplementary / E=Excluded Type: Quant= Quantitative / Qual= Qualitative Breakdown: C= Country / M= Medicine/ D=Disease
Access: P=Public / OP=On payment / R=Restrictive Coverage: EU-25 (≥23)/Partial (11 to 22 countries)/Limited (≤10)/ EU agg. = EU aggregate only
Availability: A=International sources / B= National sources / C=Rely on incidental national or regional sources / D=Generally not available / F=Future
Feasibility: "++"= Very high / "+"= High / "+/-"= To be confirmed / "-"= Low / "--"= Not feasible yet

5.1.3 Discussion and proposals

A wide range of indicators were identified and reviewed from the consultations and literature review. Two sets of indicators were identified:

- A **core** list to be regularly collected for all priority diseases
- A **supplementary** list to be collected on a less regular basis to focus on specific issues or diseases.

The remaining indicators were excluded.

One of the main difficulties was to link the areas identified and find a way to evaluate the impact of the use of medicines on health. Availability of routine data was also a major concern. The main criteria for selecting the indicators once defined according to the needs were to have fairly simple and routinely collectable indicators. The lack of aggregate data which are comparable and valid at national and EU level was a major difficulty.

Finally, proposals and recommendations were made. The sets of indicators identified include both indicators ready to be implemented and ones requiring further research or development work to complete the specification of the indicator to a level appropriate for large-scale monitoring (see Table 5: Number of indicators ready to be implemented or requiring further work below). From the analysis presented in Table 4: Indicators recommendations summary, the access of data regarding a few indicators can be simultaneously described as public and restrictive, or public and on-payment. For information, on-payment data was always defined as restrictive one. An explanation is that data regarding these indicators come from several sources for which the access level is different. To establish the following table, we considered only one access level by indicator. Consequently, the selection was based on recommended data sources selected on both best geographical coverage and time coverage to decide whether data accessibility can be evaluated as only public or restrictive.

Table 5: Number of indicators ready to be implemented or requiring further work

		CORE	SUPPLEMENTARY
Ready to be implemented	Public	3	6
	Restrictive	7	4
	TOTAL	10	10
Further work required	Public	5	5
	Restrictive	4	5
	No data source	2	4
	TOTAL	11	14
TOTAL	Public	8	11
	Restrictive	11	9
	No data source	2	4
	TOTAL	21	24

Assessment of data availability could not be made in detail for all indicators reviewed, some requiring a great deal of effort at national level, and being in-depth projects in themselves to be explored further, for instance through feasibility studies. Such areas include innovation from the patient perspective, effectiveness of medicines, quality of life and information to patients. Indeed, some issues are very controversial with neither standardised nor agreed methodology to monitor them. Outcomes of several ongoing projects at EU and national level concerning these issues have been identified and mentioned for consideration.

For instance, access to innovative medicines, the relative effectiveness of medicine and enhanced information to patients were other recommendations of the G10 Medicine Group (recommendations 2, 7 and 10 respectively). Actions are in progress on those issues and the state of progress of the work was not developed enough yet to enable us to propose relevant indicators.

Our recommendation and proposal is to select a number of indicators by priority area identified. Depending on the importance of priority area in terms of public health concerning the pharmaceutical industry performance and on the number of distinct issues covered by this area, monitoring of a number of indicators is recommended (see Table 6: Number of indicators proposal by priority area). This is then balanced with the number of core indicators identified in the framework of this project and the competitiveness indicators (work carried out by the Commission in response to G10 recommendations: development of 9 competitiveness indicators[8]) covering the area. Indeed, some of our priority areas overlap with the issues tackled by the competitiveness indicators[8] such as innovation (uptake of new medicines indicator), generics market, OTC market and the time to market of medicines. Still, the set of competitiveness indicators do not address priority diseases as our public health approach.

[8] http://pharmacos.eudra.org/F2/register/index.htm

Table 6: Number of indicators proposal by priority area

PRIORITY AREAS	INDICATORS NUMBER		COMMENTS
	Recommended	**Identified** *(among which CI*)*	
Disease status	4	5	Select fewer indicators from the identified set
Accessibility to medicines	3	4	Select fewer indicators from the identified set. Wait for outcomes of the PPRI project
Consumption chain	3	6 *(2)*	Select fewer indicators from the identified set *CI*: Indicator 4. Market Share of Generics* *CI*: Indicator 5. OTC market*
Information to patients	1	0	Wait for outcomes from the Working Group "Information to Patients" of the Pharmaceutical Forum
Quality of life	1	1	Further expert validation required
Medicines accessibility to market	1	1 *(1)*	*CI*: Indicator 6. Time elapsed between application for market authorisation in first world market to launch in specific market*
Medicines effectiveness	1	2	The indicators identified are complementary. No single and relevant indicator was identified. Further expert validation required to select fewer indicators from the identified set or identify a more relevant indicator if any
Innovation	1	2 *(1)*	Choose only one indicator from the ones proposed that covers some priority therapeutic area *CI*: Indicator 3. Uptake of new medicines*
TOTAL	**15**	**21**	

* CI = Competitiveness Indicator from the Commission response to G10 recommendations: development of 9 indicators, http://pharmacos.eudra.org/F2/register/index.htm

From a pragmatic perspective and in line with to the work carried out by the Commission to develop 9 competitiveness indicators[9], the final proposal and outcome of this project is a **set of key indicators** selected from the core set of indicators previously identified. Since 8 priority areas were identified, it would be rather difficult to include fewer than 8 indicators if all priority areas are chosen to be covered. In fact, each of these priority areas includes quite important issues to be monitored to how the public health needs of the European population are being met by the pharmaceutical sector. Thus, the **final key set** of proposed indicators includes **8** indicators, considering that two of them are already collected in the framework of the competitiveness indicators[9] but cover the whole market only (see table below).

Table 7: Final key set of indicators proposal

PRIORITY AREAS	INDICATOR	COMMENTS
Disease status	DALY	Available every 2 years in average
Accessibility to medicines	Share of non-marketed medicines in newly authorised outpatient medicines	Access to data on payment
	Share of reimbursed medicines on outpatient market	*Further work required: data source or "Price of medicines in number of days wages" indicator, if feasibility study conclusive*
Consumption chain	*Utilisation in DDD/1000 inhabitant/day*	*Further work required: partial geographical coverage and future availability to be confirmed*
	Adherence to treatment	*Further work required*
Information to patients	_	*Further work required*
Quality of life	*Ease of use*	*Further work required, 5-year periodicity enough*
Medicines accessibility to market	Time from license to market*	
Medicines effectiveness	_	*Further work required*
Innovation	Uptake of new medicines*	*Further work required: adapt it so it covers some priority therapeutic areas*

[9] from the Commission response to G10 recommendations: development of 9 indicators, http://pharmacos.eudra.org/F2/register/index.htm

* Already considered in the framework of the Commission response to G10 recommendations: development of 9 indicators, http://pharmacos.eudra.org/F2/register/index.htm

A complementary approach could be to complete the core indicators monitoring, developed for a set of (10-15) priority diseases, with a **profile analysis** for two to three specific diseases including a selection of supplementary indicators. These profiles could either concern diseases from the priority set selected for the monitoring or other ones such as emerging health threats not yet considered. For instance, these profiles and selected diseases could be established and updated on a yearly basis so that all the priority diseases are covered at least once after a five to six years monitoring period.

The next steps to follow-up the work completed in the framework of this project would be to:

- Set up a secretariat and a roundtable of experts to:
  - Review the work carried out on this project
  - Further define and evaluate the sets of indicators proposed
- Conduct further case-studies and improve the indicator definitions based on secretariat recommendations, including assessment of indicators coverage
- Select a first set of indicators to start the monitoring.

5.1.4 Conclusions

A list of monitoring indicators to be the most sufficiently acute and relevant for the purpose of this monitoring was reviewed with regard to data availability.

Two different sets of indicators were proposed:

- **21 core indicators** to be always collected;
- Recommendations for **24 supplementary indicators** for in-depth analyses. These indicators are less important and were not all considered as much in detail. Such indicators should be considered if the proposed diseases profile approach is chosen. Disease profiles for two or three priority diseases could be established and updated on a yearly basis so that all the priority diseases are covered at least once after a five to six years monitoring period.

The 21 remaining ones reviewed were excluded. The indicators proposed can not cover all the different aspects of the main objectives and issues to be tackled, but focus was made on the main ones identified throughout the project according to experts and literature review.

From the core set of indicators, a stringent selection of **8 key indicators** was also proposed.

Such a project of developing indicators for the purpose of monitoring is a multi-cycle process. The proposed indicator, methodology and set of diseases selected should be reviewed and improved a couple of times through the follow-up of a network or advisory committee.

5.2 Case studies

The analysis of case-studies (details available in Annex "Case-studies report") complements the description and evaluation work of performance indicators carried out in the framework of this project. It allows applying the theoretical and global approach to specific important priority diseases in Europe.

In this report, only recommended sources are included. All research work and data extractions are available in Annex "Case-studies annex - Common indicators", in Annex "Case-studies annex - Diabetes mellitus" and in Annex "Case-studies annex - Acute stroke".

5.2.1 Case-studies choice

The intention behind being to confirm or evaluate the feasibility of the indicators, the selection criteria used for the choice of the priority diseases for the case-studies were the following:

- Diseases from the priority diseases list according to burden of disease in the European Union;
- Including at least one chronic and one acute condition;
- Including the main patient pathway steps issues such as prevention, diagnosis, …;
- May concern a specific population group, e.g elderly, women;
- With some data available on each priority objective identified;
- With international guidelines available.

The two conditions chosen are most leading conditions in Europe which raise a major public health problem. These conditions account for over 7% of the EU-25 total burden of disease as described in the WHO report[10] with a DALY of 2.0% regarding diabetes mellitus and 5.3% for acute stroke.

[10] "Priority Medicines for Europe and the World." Kaplan W. and Laing R., 2004. World Health Organization.

5.2.2 Outcomes and recommendations

The pilot study is organised in three parts according to indicators specificity and disease breakdown as follows:

1. Common indicators broken down by country and not by disease;
2. Indicators for a chronic condition: diabetes mellitus;
3. Indicators for an acute condition: acute stroke.

At the end of each case-study section, a synthetic table in chapter "Conclusions and recommendations" is presented according to several criteria:

Domain
Each indicator is ranked according to its importance within main objectives.

Importance
The categorisation Core/Supplementary is conformed to those described in Phase 2.

Collected
Data of few indicators are not collected for two main reasons:

- Too specific indicators
- Information coming from data sources with restrictive access

Access
The indicators data are classified as publicly available, with restricted access and/or on payment. It depends on data sources.

Data source
Main data sources are mentioned in this table.

Coverage
The classification EU-25 / Partial / Limited / EU-25 agg. is still used.

Comments and further work
For each indicator, few comments are added and then known improvement of this information already available.

Importance: C=Core / S=Supplementary Access: P=Public / OP=On payment / R=Restrictive
Coverage: EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU agg. = EU aggregate only

Common indicators

The Table 8 describes all common indicators ranked by main objectives and importance.

Table 8: Common indicators summary

Domain	Impor-tance	Collected	Access	Data source	Coverage	Comments	Further work
DISEASE STATUS							
Exposure to main risk factors	**C**	**Yes**	**P**	**EUROSTAT**	**EU-25**		
5-year survival rate	S for cancer	Yes	OP / F	OECD	Limited	For few cancers only Not at disease level	
ACCESSIBILITY TO MEDICINES							
Share of non marketed medicines in newly authorised medicines	**C**	**No**					**Data source** **Feasibility study for priority diseases**
National reimbursement systems	**C**	**Yes**	**P**	**OBIG**	**EU-25**		
National co-payment systems	**C**	**Yes**	**P**	**OBIG, OECD**	**EU-25**		
Share of public expenses on Pharmaceuticals	**C**	**Yes**	**R / OP**	**OBIG**	**EU-25**	**PPRI project: future for EU-25 non OECD**	
Price of medicines in number of days wages	**C**	**No**					**Data source** **Price definition** **Feasibility study**
Accessibility to pharmacies	S	Yes		PGEU	EU agg.		
CONSUMPTION CHAIN							
Average number of medicines prescribed per inhabitant	**C**	**No**					
Share of medicines actually dispensed	**C**	**No**					
Adherence to treatment	**C**	**No**	**R**	**WHO**	**EU agg.**	**No standard for measuring patients' adherence**	
Share of non-prescription market in outpatient market	S	No					
Rx to OTC switching	S	Yes	P	AESGP	Partial	No access to previous data	
Prescribed Daily Doses (PDDs)	S	No					

Importance: C=Core / S=Supplementary Access: P=Public / OP=On payment / R=Restrictive
Coverage: EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU agg. = EU aggregate only

Domain	Impor-tance	Collected	Access	Data source	Coverage	Comments	Further work
Market share of generics on outpatient market	S	Yes	P	EGA	EU-25	Definition of generics not consistent	
INFORMATION TO PATIENTS							
Public Health campaigns addressed to citizens	S	No					Data source Indicator specification
Patients' knowledge of correct use and diagnosis	S	No					Data source Indicator specification
QUALITY OF LIFE							
Medicines taken per day	S	No					Data source Indicator specification
MEDICINES' ACCESSIBILITY TO MARKET							
Time from license to market	**C**	**Yes**	**P**	**EFPIA**	**Partial**	**EMEA and not EMEA data**	**Expand to all EU-25**
Average time for orphan medicines procedures	S	Yes	P	EMEA	EU agg.		Break it down by country if relevant
INNOVATION							
Uptake of new medicines	**C**	**Yes**	**P**	**DG ENTR**	**Limited**		**Expand to all EU-25**
Share of New Chemical Entities covering priority diseases within the last 5 years	**C**	**No**					
Innovative medicines initiatives	S	No					Data source Indicator specification
Share of New Medicines Entities launched covering priority diseases in the last 5 years	S	No					
Medicines under clinical development	S	No					
Share of R&D expenditure by therapeutic area	S	No					

Importance: C=Core / S=Supplementary Access: P=Public / OP=On payment / R=Restrictive
Coverage: EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU agg. = EU aggregate only

Diabetes mellitus

The Table 9 describes all indicators available and developed for diabetes mellitus. This list is ranked by main objectives and importance.

Table 9: Indicators: diabetes mellitus summary

Domain	Impor-tance	Collected	Access	Data source	Coverage	Comments	Further work
DISEASE STATUS							
Prevalence of disease	**C**	**Yes**	**P**	**WHO**	**EU-25**	**Number, percentage**	**Earlier time series availability**
		No	**R**	**ECHI**	**EU-25**	**ICD-10 classification**	
		Yes	**P**	**IDF**	**EU-25**	**2000, 2001 and 2003**	
Disability Adjusted Life Years (DALY)	**C**	**Yes**	**P**	**WHO**	**EU-25**		**Earlier time series availability**
Therapies availability overview	**C**	**No**	**R**	**WHO NICE**			**Data source Indicator specification**
Main active ingredients sales and status	**C**	**No**	**R / OP**	**IMS Health**	**Partial**		**Data source**
		No	**P**	**EURO-MED-STAT**	**EU-25**	**Availability on April or May 2006**	
Standardised death rates (SDR)	S	Yes	P	EUROSTAT	EU-25	ICD-10 classification	
		Yes	P	WHO	EU-25		Earlier time series availability
		Yes	R / OP	OECD	Partial	ICD-10 classification	
Co-morbidity	S	No	R	EUDIP		Include indicators for each complication	Data source Indicator specification
		No	R	Literature review			
		No	R	EuroDiab	Partial	Diabetes Type 1 only	
Wrong or misdiagnosis issues	S	No	R	Literature review		Problem of comparability	Data source Indicator specification
ACCESSIBILITY TO MEDICINES							
Share of reimbursed medicines on outpatient market	**C**	**No**	**R**	**National organisations**	**Partial**	**Systems very different according to MS**	**Expand to all EU-25**
CONSUMPTION CHAIN							
Utilisation in DDD/1000 inhabitant/day	**C**	**No**	**P**	**EURO-MED-STAT**	**EU-25**	**Availability on April or May 2006**	
		Yes	**R**	**National organisations**	**FI**		**Expand to all EU-25**
Medication errors	S	No	R	Literature review			Data source
Adverse events	S	Yes	P	EMEA	EU-25	Only centralised procedures	Data source Indicator specification

Importance: C=Core / S=Supplementary Access: P=Public / OP=On payment / R=Restrictive
Coverage: EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU agg. = EU aggregate only

Domain	Impor-tance	Collected	Access	Data source	Coverage	Comments	Further work
INFORMATION TO PATIENTS							
Guidelines from main institutes	S	Yes	P	International and national organisations	Limited	Mostly national organisations	Data source Indicator specification
Websites providing information	S	Yes	P	International and national organisations	Limited	Mostly national organisations	Data source Indicator specification
QUALITY OF LIFE							
Ease of use	**C**	**No**	**R**	**Literature review**	**Limited**		**New data collection Indicator specification**
MEDICINES EFFECTIVENESS							
Incremental cost-effectiveness ratio (ICER)	**C**	**No**	**R**	**Literature review**	**Limited**		**Indicator specification**
ASMR	**C**	**Yes**	**P**	**French organisation (HAS)**	**FR**		**Expand to all EU-25 Indicator specification Methodology to review**
Market withdrawals	S	Yes	P	EMEA	EU-25	Only central applications	Significance of results

Accessibility

Data accessibility of indicators is classified as public, restricted and/or on payment. Data collection of a few indicators was not completed for all the Member States when data were too specific, concerned restricted and incidental sources such as for Co-morbidity" and "Wrong or misdiagnosis issues".

Data sources selection

For several indicators such as disease status indicators, a number of data sources were available. For instance regarding standardised death rate, EUROSTAT was recommended data instead of WHO or OECD for geographical and time coverage reasons (see table hereafter).

Importance: C=Core / S=Supplementary Access: P=Public / OP=On payment / R=Restrictive
Coverage: EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU agg. = EU aggregate only

Table: SDR data sources characteristics

	EUROSTAT	WHO	OECD
Geographical coverage	All EU Member States	All WHO Member States	19 EU Member States
Time coverage	For EU-15 and EFTA (without LI) from 1994 onwards (BE, DE: 1992, IE: 1993).	2002	1960-2003 (for a few countries only)
Periodicity	Annual	Annual	Annual
Number of causes	65 whose DM	129 whose DM	38 whose DM

DM: Diabetes Mellitus

Another example concerns the prevalence of disease indicator for which International Diabetes Federation (IDF) data source was chosen instead of WHO for a wider geographical coverage and availability of data broken down by diabetes mellitus Types 1 and 2.

Table: Prevalence data sources characteristics

	IDF	WHO
Geographical coverage	All EU Member States	Some EU Member States data not available
Time coverage	2000, 2001 and 2003	2000, 2001 and 2002
Number of causes	1 (DM only)	200

DM: Diabetes Mellitus

Limitations

Data was not always available for both diabetes mellitus Type 1 and 2. Moreover, diabetes mellitus type may be undefined for a few data sources. Thus data comparability is not always good. In our framework, aggregated data were preferred and data by diabetes mellitus type were collected as often as available to ensure comparability.

Acute stroke

The Table 10 describes all indicators available and developed for acute stroke. This list is ranked by main objectives and importance.

Table 10: Indicators: acute stroke summary

Domain	Impor-tance	Collected	Access	Data source	Coverage	Comments	Further work
DISEASE STATUS							
Prevalence of disease	**C**	**Yes**	**P**	**WHO**	**Partial**	**Data for Cerebrovascular disease Data not available each year for each country Incidence instead of prevalence**	
		No	**R**	**ECHI**	**EU-25**	**ICD-10 classification**	
Disability Adjusted Life Years (DALY)	**C**	**Yes**	**P**	**WHO**	**EU-25**	**Data for Cerebrovascular and stroke**	**Earlier time series availability**
Main active ingredients sales and status	**C**	**No**	**R / OP**	**IMS Health**	**Partial**		**Data source**
		No	**P**	**EURO-MED-STAT**	**EU-25**	**Availability on April or May 2006**	
Standardised death rates (SDR)	S	Yes	P	EUROSTAT	EU-25	Data for Cerebrovascular disease (ICD-10)	
		Yes	P	WHO	EU-25	Data for Cerebrovascular disease	Earlier time series availability
		Yes	R / OP	OECD	Partial	Data for Cerebrovascular disease (ICD-10)	
Co-morbidity	S	No	R	Literature review	Limited		Data source Indicator specification
Prevention	S	No	R / F	Literature review	Limited	Important indicator for stroke	Indicator specification
ACCESSIBILITY TO MEDICINES							
Share of reimbursed medicines on outpatient market	**C**	**No**	**R**	**National organisations**	**Partial**	**Systems very different according to MS**	**Expand to all EU-25**
CONSUMPTION CHAIN							
Utilisation in DDD/1000 inhabitant/day	**C**	**No**	**P**	**EURO-MED-STAT**	**EU-25**	**Availability on April or May 2006**	
		Yes	**R**	**National organisations**	**FI**		**Expand to all EU-25**
Adherence to treatment	**C**	**No**	**R**	**Literature review**			**Data source Indicator specification**

Importance: C=Core / S=Supplementary Access: P=Public / OP=On payment / R=Restrictive
Coverage: EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU agg. = EU aggregate only

Domain	Impor-tance	Collected	Access	Data source	Coverage	Comments	Further work
Adverse events	S	Yes	P	EMEA	EU-25	Only centralised procedures	Data source Indicator specification
INFORMATION TO PATIENTS							
Guidelines from main institutes	S	Yes	P	International and national organisations	Limited	Mostly national organisations	Data source Indicator specification
Websites providing information	S	Yes	P	International and national organisations	Limited	Mostly national organisations	Data source Indicator specification
MEDICINES EFFECTIVENESS							
Incremental cost-effectiveness ratio (ICER)	**C**	**No**	**R**	**Literature review**	**Limited**		**Indicator specification**
ASMR	**C**	**Yes**	**P**	**French organisation (HAS)**	**FR**		**Expand to all EU-25** **Indicator specification** **Methodology to review**
Market withdrawals	S	Yes	P	EMEA	EU-25	Only central applications	Significance of results

Selection of data source

For a number of indicators, several data sources are available as for standardised death rate. Indeed, EUROSTAT data was recommended instead of WHO or OECD for geographical and time coverage reasons (see Table hereafter).

Table: SDR data sources characteristics

	EUROSTAT	WHO	OECD
Geographical coverage	All EU Member States	All WHO Member States	19 EU Member States
Time coverage	For EU-15 and EFTA (without LI) from 1994 onwards (BE, DE: 1992, IE: 1993).	2002	1960-2003 (for a few countries only)
Periodicity	Annual	Annual	Annual
Number of causes	65 whose CVA	129 whose CV	38 whose CV

CV: Cerebrovascular, CVA: Cerebrovascular accident

Importance: C=Core / S=Supplementary Access: P=Public / OP=On payment / R=Restrictive
Coverage: EU-25 (≥23) / Partial (11 to 22 countries) / Limited (≤10) / EU agg. = EU aggregate only

Limitations

The definition of acute stroke is different according to data sources. For some, acute stroke is defined as a cerebrovascular disease as a whole or is defined as an acute stroke so data are not quite comparable.

5.2.3 Conclusions

Acute stroke is the third leading cause of disability and death (as DALYs) in EU-25 (DALY = 5.3%) after depression (DALY = 7.8%) and ischemic heart disease (DALY = 7.4%)[11]. Despite improvements in stroke care, treatment of the long-term effects remains one of the major problems.

Diabetes mellitus and its complications have become a major public health problem in all EU-25 countries (DALY = 2.0%)[11]. It causes significant physical and psychological morbidity, disability and premature mortality among those affected and imposes a heavy financial burden on health services.

As these two conditions are most leading conditions in the world and in Europe, it implies that accurate information is available regarding general indicators with regard to disease status. Moreover, this information may come from several data sources. Concerning other priority areas, information increasingly becomes patchy. Only literature reviews or specific surveys are available to provide information on health in Europe, but only regarding a specific population or a specific European region.

However, differences also occur between these two chosen conditions particularly regarding data availability. The main reason is that there is an association collecting data on diabetes mellitus, the International Diabetes Federation which centralises all data on this topic. Even if for all main indicators few organisations contain data, data regarding specific indicators of supplementary objectives are only available on this specific website. Another explanation comes from the disease type, acute or chronic. Approaches to treat these diseases differ. By definition, the perspective to treat a chronic condition implies temporality notions contrary to acute ones. Besides, few indicators are more related to chronic condition than acute ones. For instance, to measure the importance of a disease, prevalence is recommended for chronic conditions, while for acute diseases incidence is more relevant and preferred.

One of the main difficulties was to link the areas identified and find a way to evaluate the impact of medicines use on health. A medical expert validation would be required for a few indicators as for completing the list of active substances used to treat diseases. This expertise will improve the analysis by checking the adequacy between treatments and diseases.

Availability of routine data was also a major concern. The main criteria for selecting the indicators once defined according to the needs were to have fairly simple and routinely collectable indicators. The lack of aggregate data which are comparable and valid at national and EU level was a major difficulty.

Assessment of data availability could not be made in detail for all indicators, some requiring a great deal of effort at national level and being projects in themselves. Among 43 non excluded indicators, 13 common ones were studied in details in these case-studies, including 17 for diabetes mellitus and 15 for acute stroke (see table hereafter). In each of these three categories, several indicators are ready to be implemented whereas others need further work. This work necessitates identification of data sources, definition of indicators, expansion to all EU-25 Member States, earlier time series or actual data availability. To obtain missing data on specific indicators, a

[11] "Priority Medicines for Europe and the World." Kaplan W. and Laing R., 2004. WHO

solution would be to set up new data collection either through existing international surveys in adding supplementary questions. For instance, the European Commission gathers several general or specific surveys e.g. EHSS, ECHI or EURODIAB regarding diabetes. In cases where a topic is too different, a second step would be to create new surveys on a regional area.

Table: Number of indicators detailed

		Common indicators	Diabetes mellitus	Acute stroke
Core indicators	Ready to be implemented	5	2	4
	Further work required	3	7	4
	Total	8	9	8
Supplementary indicators	Ready to be implemented	4	3	2
	Further work required	1	5	5
	Total	5	8	7
Total		**13**	**17**	**15**

6 Annexes