Reneging on Doha

An MSF analysis of recent attempts to restrict developing countries' use of compulsory licensing to a set list of diseases. May 2003.

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Summary

Almost as soon as the Doha Declaration on TRIPS and Public Health was agreed, negotiators started backtracking on the commitments made. Countless attempts have been made to limit the scope of the "paragraph 6 solution" to a set list of diseases or to cases of national emergency. Developing countries should not accept any restrictions to their rights, as recognized under the Doha Declaration on TRIPS and Public Health.

If the aim of the paragraph 6 solution is to help developing countries increase access to badly needed treatments for public health problems, then the main causes of mortality in Africa should be covered by the agreement. Yet only a small random selection of the top 20 causes of mortality in Africa are included in the list of "approved" diseases proposed by the US and endorsed by the EU.

Which of the major causes of mortality in Africa have been included in the list?
Virtually all diseases for which no treatment exists, or for which treatment are so old as to be off-patent.

Which of the top 20 causes of mortality in Africa have been left off the list?
The 14 diseases or conditions that are common in the west or have multiple patented treatments. In fact, excluding HIV/AIDS, almost all causes of high mortality and morbidity for which patented Western drugs can be used have been excluded from the list.

Restricting the agreement to a set list of diseases makes no public health sense. This clear attempt to protect Western drug company interests will contribute to keeping essential medicines out of reach of people in developing countries.

The following analysis shows that proposals to restrict the scope of the "paragraph 6 solution" of the Doha Declaration to a set list of diseases are deeply flawed. The disease lists which have so far been put forward do not correlate with the major causes of morbidity and mortality in Africa: many public health threats have been omitted from the list. In particular, virtually all major African diseases for which there are patented medicines have been excluded from the list. Almost all the list's "approved" diseases are those for which there is no drug treatment, or where existing treatments are already off patent. In other words, diseases for which there is neither "risk" nor opportunity to issue a compulsory license.

This approach looks like an attempt to protect Western drug company interests, rather than a genuine effort to improve access to the medicines needed to save millions of lives in developing countries.

"Paragraph 6": a brief history

The past three years have seen heated debates on access to medicines in developing countries, in particular with regard to the impact of the WTO TRIPS Agreement, which sets out the conditions and the options countries have to over-ride patents on pharmaceuticals (the TRIPS flexibilities). What these flexibilities are, and when and how they could be used, was clarified by the Doha Declaration, agreed by WTO Members at the WTO Ministerial Meeting in November 2001. This Declaration stated that "*The TRIPS Agreement does not and should not prevent Members from taking measures to protect public health. Accordingly, while reiterating our commitment to the TRIPS Agreement, we affirm that the Agreement can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all.*" However, one issue was not resolved by the Doha Declaration: the so-called Paragraph 6 issue, as outlined in the box below.

Excerpt from the Declaration on the TRIPS Agreement and Public Health, also known as the "Doha Declaration". (Adopted 14 November 2001)

Paragraph 6. *We recognize that WTO Members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement. We instruct the Council for TRIPS to find an expeditious solution to this problem and to report to the General Council before the end of 2002.*

The last 18 months have seen a debate aimed at resolving this "Paragraph 6" inequity so that the Doha Declaration will in the future be useful for all countries, not just those which have a pharmaceutical industry. Unfortunately, a number of Western countries, while maintaining their own unfettered rights, have sought to dramatically restrict the scope of the Doha Declaration for developing countries.

Some negotiators have sought to limit a "Paragraph 6" solution to a handful of countries, or a set list of diseases, or both. Originally, the US argued that compulsory licensing should be restricted to a handful of infectious diseases – AIDS, TB, malaria and "other epidemics of comparable gravity and scale" - later extending this to a shortlist of AIDS, TB, malaria, plus an additional 19 infectious diseases. Eventually, on December 16th 2002, the Paragraph 6 negotiations broke down completely: although all other WTO Members had agreed to the 16th December "Motta text", the US rejected it because it made no reference to a limited scope of diseases.

In January this year, EU Commissioner for Trade Pascal Lamy proposed an initiative to break the negotiation deadlock. Lamy's list was the same as the one originally put forward by the US, but his proposal introduced an advisory role for the WHO: *"This covers at least HIV/AIDS, malaria, tuberculosis, yellow fever, plague, cholera, meningococcal disease, African trypanosomiasis, dengue, influenza, leishmaniasis, hepatitis, leptospirosis, pertussis, poliomyelitis, schistosomiasis, typhoid fever, typhus measles, shigellosis, hemorrhagic fevers, and arboviruses. When requested by a Member, the World Heath Organization shall give its advice as to the occurrence in an importing Member, or the likelihood thereof, of any other public health problem."*[1]

Both the EU and US proposals create a two-tier system, whereby countries without pharmaceutical production capacity must not only meet more onerous conditions than producing countries, but also lose the right to determine what constitutes a public health need in their own territories. Developing countries should reject all attempts to restrict the agreement to certain diseases. Here is why.

THE APPROVED LIST OF DISEASES FAILS TO INCLUDE MANY MAJOR PUBLIC HEALTH PROBLEMS IN DEVELOPING COUNTRIES.

Table 1 below shows what diseases Africans die of, and whether these are included in the "approved disease" list. This table shows that:

- Apart from HIV/AIDS, the list bears little relationship to common causes of mortality in Africa;
- Two of the four top causes of mortality for children under five in Africa are either omitted (pneumonias) or restricted (several common causes of diarrhoeal disease are excluded).
- The list excludes all non-infectious diseases, even though WHO statistics show that nearly half of the top 20 killer diseases in Africa are the same diseases or conditions that kill people in the West. All of these diseases (highlighted in grey in table 2) have a range of patented drugs available for their management in the West, and all have been omitted from the approved disease list. Let's take just one example: pneumonias are the second major cause of death in Africa, killing over one million people a year: the first pneumococcal vaccine for use in children was registered in the US in 2000. Yet pneumonias are not included in the approved disease list. This means developing countries would be unable to issue a compulsory license to access affordable sources of a patented pneumococcus vaccine, for instance.

In short, the list is clearly not based on any public health rationale.

THE PROPOSED APPROVED DISEASE LIST, WHICH PURPORTS TO LIST DISEASES FOR WHICH DEVELOPING COUNTRIES CAN OVERRIDE PATENTS BY SEEKING A COMPULSORY LICENCE, INCLUDES MOSTLY DISEASES FOR WHICH PATENTS ARE NOT A BARRIER (BECAUSE THERE IS NO TREATMENT, OR NO PATENTED TREATMENT).

Table 2 below shows the proposed list of diseases, whether drug therapies exist for these diseases, and whether these therapies are patented. The table shows that, apart from HIV/AIDS, the proposed list includes:

- diseases for which there is no treatment;
- diseases where virtually all the recommended treatments are so old as to be off-patent;
- diseases for which little R&D is being conducted, i.e. for which few new treatments exist or are likely to be developed in the near future.

In other terms, this "compulsory licensing" list includes mostly commercially irrelevant diseases, and excludes many commercially important diseases for which treatments could require a compulsory license. Any agreement based on such a list would clearly create false assurances, as it consists primarily of diseases for which patent barriers are not an issue.

NB: The non-existence of treatments for many developing country diseases highlights the shameful neglect of research and development (R&D) into poor country diseases by the pharmaceutical industry and governments.

[1] Excerpt of letter from Pascal Lamy to trade ministers dated 7 January 2003

ANNEX

TABLE 1: MAJOR CAUSES OF MORTALITY IN AFRICA BASED ON NATIONAL VITAL REGISTRATION FIGURES (WHO WORLD HEALTH REPORT 2002)

We have chosen Africa as a case because this region would presumably derive the greatest benefit from a Paragraph 6 solution restricted to infectious diseases: the burden of infectious disease is relatively higher there than in other developing regions (e.g. South East Asia or Latin America).

Shaded rows represent causes of high morbidity or significant mortality in the US (asterisked diseases are those in the Top 10 causes of US mortality).

	Disease	Mortality in Africa 2001 (000)	Common US disease &/or multiple patented treatments**	Included in the "approved disease" list
1	**HIV/AIDS**	2,197	Yes	Yes
2	**Lower respiratory infections (pneumonias)***	1,026	Yes	No
3	**Cardiovascular diseases***	985	Yes	No
4	**Malaria**	963	No	Yes
5	**Diarrhoeal diseases** Only shigella dysentery is included. Salmonella and non-shigella dysenteries, such as campylobacter, are excluded.	703	Yes Reported shigella is rare in the US (22,922 cases in 2002) but estimated unreported shigella is as high as 448,000 cases/yr.	Yes
			Yes Campylobacter is common (est. 2 million cases/yr). Reported salmonella is rare (39,574 in 2002) but estimated unreported cases as high as 1.4 million cases in US/yr)	No
6	**Perinatal conditions**	576	Too general to analyse & frequently surgical rather than medical treatment	No
7	**Malignant neoplasms (cancer)***	544	Yes	No
8	**Measles**	426	No	Yes
9	**TB**	335	No	Yes
10	**Maternal conditions**	240	Too general to analyse.	No
11	**Respiratory diseases non-infectious (asthma, COAD including smoking-related)***	234	Yes	No
12	**STDs (syphilis, chlamydia, gonorrhoea)**	103	Yes 1,092,663 cases reported in US in 2002. (Off-patent drugs play a major role in treatment but growing resistance means newer patented antibiotics are coming into play eg. cefixime)	No
13	**Digestive diseases non-infectious (cirrhosis of the liver)**	200 (70)	Yes 41.5 million US outpatient or physician visits for digestive disorders 2000.	No

14	**Genito-urinary diseases non-infectious (nephritis)***	121 (80)	Yes	No
15	**Whooping cough, diphtheria, polio**	159	No	Yes
16	**Nutritional deficiencies**	151	No	No
17	**Tetanus**	110	No	No
18	**Neuropsychiatric disorders (excluding epilepsy)***	56	Yes	No
19	**Diabetes mellitus***	54	Yes	No
20	**Trypanosomiasis**	49	No	Yes
21	**Endocrine/nutritional disorders**	36	Yes An estimated 13 million Americans have thyroid disease	No
22	**Epilepsy**	24	Yes 1.4 million diagnosed epileptics in US 1996	No
23	**Meningitis** The commonest causes of meningitis are meningococcus, H.flu – particularly in children – and pneumococcus. Of these, only meningococcal meningitis is included in the list.	22	No Meningococcal meningitis is rare - CDC estimates 2,256 cases in the US each year	Yes
			Yes Pneumococcal infections far more common: 200,000 cases/year of pneumococcal meningitis, bacteraemia and pneumonia	No
			No H.flu increasingly uncommon due to vaccination (1,398 invasive cases in US in 2000)	No
24	**Upper respiratory and ear infections (otitis media)**	12	Yes 7 million cases of otitis media/yr in US 2000	No
25	**Leishmaniasis**	9	No	Yes
26	**Schistosomiasis**	5	No	Yes
27	**Other tropical and DC diseases (filariasis, onchocerciasis, leprosy, dengue, Chagas, intestinal nematode infections etc)**	3	No	Yes

****Important provisos on reading Table 1**: The statements above are general, for example, cardiovascular disease (CVD) includes many pathological entities (ischaemic, rheumatic, congenital etc) and many treatments. Although not *all* CVD drugs may be patented, it is nevertheless true to say that most CVD patients in the West have access to a large range of patented modern treatments – thus CVD would be included in the "Yes" list of US diseases with common patented treatments.

TABLE 2: LIST OF PROPOSED SCOPE OF DISEASES ("APPROVED" DISEASE LIST)

Disease	Recommended specific drug therapy	Patent status	Additional drugs currently accessible under this Para 6 approach
HIV/AIDS	All WTO members agree that these three diseases should be covered by the paragraph 6 solution.		
Malaria			
Tuberculosis			
Yellow fever	None exists	Not applicable (n/a)	None
Dengue	None exists	n/a	None
Influenza	None exists	n/a	None
Pertussis	None exists	n/a	None
Polio	None exists	n/a	None
Measles	None exists	n/a	None
Haemorrhagic fevers	None exists	n/a	None
Arboviruses	None exists	n/a	None
Cholera	None exists (*Some clinicians use doxycycline/ciprofloxacin*)	n/a *(Doxy/cipro off patent)*	None
African trypanosomiasis	Suramin, pentamidine, melarsoprol, eflornithine, (nifurtimox)	Off patent	None
Plague	Streptomycin, sulfonamides, chloramphenicol, cyclines	Off patent	None
Leptospirosis	Penicillin, tetracycline, erythromycin	Off patent	None
Typhoid fever	Chloramphenicol, amoxycillin, cotrimoxazole, ciprofloxacin, dexamethasone	Off patent	None
Typhus	Doxycycline	Off patent	None
Shigellosis	Ciprofloxacin, pivmecillinam, nalidixic acid, ampicillin, cotrimoxazole (*Growing resistance means drugs such as cefotaxime and ceftazidime may increasingly be options in the future*)*	Off patent	None
Schistosomiasis	Praziquantel, oxamniquine, metrifonate	Off patent	None
Meningococcal disease	Oily chloramphenicol, chloramphenicol, ampicillin, ceftriaxone, gentamicin, cefotaxime, vancomycin	Off patent **	None
Leishmaniasis	Sodium stibogluconate, aminosidine, amphotericin B, pentamidine, miltefosine (registered in India)	Off patent except some forms of amphotericin in some countries. • Basic amphotericin off-patent; • Improved composition amphotericin off-patent in all DCs. • Improved composition amphotericin patented in most developed countries till 2004-2008.	Improved composition amphotericin till 2004/2008.

Hepatitis A, B, C	Interferon (effective in only 10-20% of cases) Interferon + ribavirin (effective in 30-50% of cases)	Yes	Ribavirin. Some forms of Interferon (although it is doubtful these would be widely used, given their relatively low efficacy).

* Cefotaxime is off-patent except in Canada, where a patent extension is due to expire in 2010.
Patents on ceftazidime basic molecule have expired. Patents protecting ceftazidime pentahydrate are due to expire in September 2003 in most developed countries; patents on anhydrous ceftazidime are due to expire in April 2004 in most developed countries. Patents on cristalline formic acid of ceftazidime hydrochloride are due to expire in Feb 2009 in most developed countries.

**Cefotaxime is off-patent except in Canada, where a patent extension is due to expire in 2010. Ceftriaxone is off-patent everywhere, however some specific formulations (e.g. aqueous solution) still have patents alive in South Africa.

(NB: Recommended treatments are based on literature searches, WHO and US Centers for Disease Control recommendations, and MSF's own protocols.)

References for Table 1:

* Diseases that rank in the Top 10 causes of death in the US, as per the US National Vital Statistics Report, Vol. 49. No. 11, Oct 12, 2001, Causes of Death ranking.

- *STD figures*: Health United States report, Table 53, accessed at www.cdc.gov/nchs/data/hus/hus02.pdf
- *Digestive diseases*: Statistics from the US National Centre for Health Statistics, accessed at www.cdc.gov/nchs/fastats/digestiv.htm
- *Epilepsy*: Figures from US National Centre for Health Statistics, accessed at www.cdc.gov/nchs/fastats/epilepsy.htm
- *Otitis media*: Accessed at www.cdc.gov/od/oc/media/pressrel/r2k0622d.htm
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