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WHO: Alliance with industry raises concerns over medicine regulation
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Geneva, 19 May (K. M. Gopakumar) -- There are concerns that the World Health Organisation (WHO)'s alliance with an industry-led body facilitates regulatory capture of medicine regulation by pharmaceutical multinational corporations (MNCs).

A recent news report brought out the conflict of interest involved in the WHO's norms and standard-setting related to medicines due to the involvement of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).

(http://timesofindia.indiatimes.com/city/delhi/Conflict-of-interest-in-setting-norms-for-pharmaceuticals-in-WHO/articleshow/35261958.cms)

The article provides further details of the deep-rooted conflict of interest and regulatory capture through the WHO-ICH alliance. This "unholy alliance" with ICH is expected to come up during the World Health Assembly (WHA), which started its current annual session in Geneva on Monday.

A draft resolution titled "Regulatory System Strengthening for the Medical Products" urges Member States to implement the ICH guidelines.

The resolution refers to "implementing relevant guidance and science-based outputs of international regulatory harmonization and convergence efforts such as, where applicable, the Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use".

The text is currently in brackets, signifying lack of consensus among WHO member countries, and enjoys the full support of developed countries, especially the European Union.

However, Third World Network learnt that the United States is negotiating with the EU to remove the explicit reference to ICH.

The proposal is to remove reference to ICH but to retain words such as harmonisation and to push for regulatory harmonisation (read as ratcheting up of regulatory standards suited for pharmaceutical MNCs).

The WHO-ICH alliance also casts doubt on the effectiveness of WHO's framework for engagement with the private sector.

The current WHA session is expected to take a decision on whether to adopt the draft framework for Non-State Actors (NSAs), which includes a draft policy for engagement with the private sector.

The Draft NSA policy states that: "WHO's processes in setting norms and standards must be protected from any undue influence".

Further, the policy proposes the exclusion of NSAs from participating in the process of setting policies or norms. It also prevents the acceptance of resources for normative work.

Thus, the participation of WHO is contrary to the proposed draft policy on engagement with NSAs, which sets a boundary for such engagement.

However, in order to create room for participation of the private sector, especially initiatives like

ICH norm-setting activities, the policy divides the norm-setting activities into three phases viz. Phase 1: Information gathering; Phase 2: Preparation for, elaboration of and decision on the normative text; and Phase 3: Implementation.

It further states that reference to specific protection of the norms and standard-setting process refers to the second phase.

Thus, the draft policy creates room for the participation of the private sector in the early phase of norm-setting activities, in the form of information gathering.

The very participation of WHO in ICH activities de facto legitimises guidelines developed by the pharmaceutical multinational industrial association and developed country regulators together, with a primary objective of serving the interest of pharmaceutical MNCs.

Apart from this push for formal adoption of ICH guidelines, WHO has facilitated the backdoor entry of ICH guidelines into WHO's various guidelines adopted through the WHO's Expert Committee on Specifications for Pharmaceutical Substances (Expert Committee).

The Regulatory System Strengthening (RSS) resolution is an attempt to formally legitimise an alliance, which contradicts the neutrality of norm-setting and allows regulatory capture.

The WHO-ICH alliance is problematic in terms of the process as well as content. Apart from the concerns on the implication of ICH outcomes to affordability of medicines, it raises concerns on the neutrality and evidence-based decision-making, along with issues of participation and transparency in WHO's decision-making.

The implication on affordability of medicines is discussed below.

The ICH was established in 1990 as a public-private partnership (PPP) primarily to lower down the norms of registration (marketing approval) of new chemical entities. However, as shown below, increasingly the ICH started setting standards to build a set of technical barriers to prevent competition from the generic industry.

The founding members of ICH are the drug regulatory authorities of the EU (European Agency for the Evaluation of Medicinal Products, EMEA), Japan (Ministry of Health, Labour and Welfare, JMHLW), and the US (Food and Drug Administration, US FDA) and the research-based pharmaceutical industry associations of those countries (the European Federation of Pharmaceutical Industries' Associations, EFPIA; the Japan Pharmaceutical Manufacturers Association, JPMA; and the Pharmaceutical Research and Manufacturers of America, PhRMA).

These founding members along with the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), a federation of national associations of research-based pharmaceutical industry associations, WHO, Health Canada (Canadian regulatory agency), and the European Free Trade Area constitute the highest decision-making body of ICH, the steering committee.

However, only the steering committee members enjoy voting rights and the other four members including WHO have no voting rights. The ICH secretariat operates out of the Geneva office of IFPMA.

According to the ICH website, since its establishment in 1990, each of its six co-sponsors (EMEA, EFPIA, JMHLW, JPMA, US FDA, and PhRMA) has had two seats on the steering committee. Other parties have a significant interest in ICH and have been invited to nominate observers to the committee.

According to researcher Stephanie Dagron: "The steering Committee oversees all activities. First, it determines the harmonization activities to be pursued (i. e. initiative for guidelines and other instruments). Second, it adopts the guidelines and instruments that have been finalized and accepted by the parties through consensus. Third, it supervises the implementation and monitoring of ICH commitments. The IFPMA exercises an important role since it provides the

secretariat and participates..."

(http://www.irpa.eu/wp-content/uploads/2012/01/IRPA.WP.2012.2.Dagron.pdf)

There is an effort to reach out and co-opt ICH-established Global Cooperation Groups (GCG).

GCG includes Regional Harmonisation Initiatives (RHIs) namely, APEC, ASEAN, EAC, GCC, PANDRH and SADC, in addition to eight Drug Regulatory Authorities/Departments of Health (DRAs/DoH) in Australia, Brazil, China, Chinese Taipei, India, Republic of Korea, Russia and Singapore that are invited to the ICH bi-annual meetings.

RHI/DRA/DoH representatives participate in the Global Cooperation session of the ICH Steering Committee to discuss capacity-building and share experience/challenges on the implementation of ICH Guidelines.

Dragon notes: "In 1999 the ICH-SC created the Global Cooperation group as a subcommittee, to allow the 'participation' of representatives from non-ICH regions. In 2008, the ICH (steering committee) also created a structure called the Regulators Forum. But these two structures do not offer any participation opportunities to their members within the elaboration process of the ICH guidelines. They only constitute platforms for discussion, information, and training. Their role is to allow the dissemination of ICH standards worldwide".

According to the ICH website, representatives also listen to ICH technical topics discussed by the steering committee during meetings and are invited to nominate technical experts in Expert Working Groups/Implementation Working Groups to contribute to the development of ICH Guidelines. However, participation in the GCG is without any substantial say, without voting rights.

Industry representatives act as one of the coordinators as well as in the working group. The role of WHO is not limited merely to an observer to ICH. It actively participates in the ICH Expert Working Group.

(http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q4B/Presentation/Q4B_Presentations.pdf)

The ICH, during the last 24 years, has worked as a partnership between the regulatory agencies of industrialised countries and pharmaceutical industry without any effective participation from developing countries and generic industries.

However, the important question is how regulatory agencies and WHO set norms in a body where the industry has a veto power through voting?

Thanks to the alliance with WHO, many ICH guidelines found a place in the Report of WHO's Expert Committee on Specifications for Pharmaceutical Substances.

In other words, the norms and standards set by ICH without the participation of a substantial majority of Member States got imported to the WHO Expert Committee process and adopted as norms and standards for the regulation of medicines.

For instance, the Pharmaceutical Development of Multisource (generic) Pharmaceutical Products contained in the 46th Report of the Expert Committee states that "... document provides a structured approach for industry following the International Conference on Harmonisation (ICH) common technical document (CTD) format".

The 44th Report of the WHO Expert Committee also contains WHO Good Manufacturing Practices for Active Pharmaceutical Ingredients (API), which are based on the ICH guidelines.

It states: "A major change to the analytical procedure, or in the composition of the product tested, or in the synthesis of the API, will require re-validation of the analytical procedure. Note: Further guidance on validation of analytical procedures is available in the following: Guideline

elaborated by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)".

The ICH and IFPMA participate at the meetings of the WHO Expert Committee on Specifications on Pharmaceutical Substances.

Researchers also question the ICH claims that its guidelines are purely science-based. They point out that commercial and political interests play an important role in the finalisation of ICH guidelines.

A set of research papers shows that ICH served the pharmaceutical MNCs' interest in two ways.

First, it set norms to lower the threshold level of technical requirements for the registration of medicines containing new chemical entities and new products obtained by biotechnology through harmonising the drug registration process.

Second, ICH started setting norms and standards for generic products and pharmaceutical substances (starting materials) and created a new entry barrier for small brand name and generic companies, especially those in developing countries.

Health researchers even warn against the drive on harmonisation.

In an article, Karin Timmermans writes: "... increasing the standards beyond the technological capacity of pharmaceutical companies in developing countries would effectively exclude their competitive, generic products from the international market".

Another researcher warns that: "The production of generics but also of pharmaceutical starting material in developing countries is endangered. In fact, ICH guidelines have introduced a tightening of specifications for pharmaceutical starting materials, which is not always justified by additional safety benefits. Another source of prohibitive costs for smaller companies is the Good Manufacturing Practice Guide for active pharmaceutical ingredients adopted by ICH in 2000".

The same sentiment is expressed by an expert consultation organised by WHO in 2001.

The experts state: "ICH has relied increasingly on advanced pharmaceutical technology in its standard setting, on the assumption that this technology will lead to greater safety of new drugs, while the ICH guidelines relating to drug quality have introduced a general tightening of specifications for pharmaceutical starting materials. For example, ICH guideline Q3A ("Impurities in new drug substances") includes the requirement that each organic impurity (whether identified or unidentified) present in a substance in the amount of 0.1% or more (in some cases 0.05% or more) should be considered as a qualified impurity (i. e. its safety should be established). This raises the question of the basis for the selection of the borderline figure, as the additional safety benefits from these rigorous standards have not been demonstrated but the costs incurred by manufacturers in meeting the requirements are significant."

Further, the experts warn against making ICH norms as global standards.

The report states: "Setting such norms may have considerable repercussions on current manufacturing practices, as only pharmaceutical companies with substantial resources can achieve the necessary standards. This is a concern if the guidelines are intended for global application. Smaller pharmaceutical companies, generic companies and many larger companies responsible for essential drug production in developing countries may be effectively squeezed out of drug manufacturing if ICH guidelines start to be interpreted as the only global standard."

However, the experts recommended to continue WHO's engagement with ICH.

The report states: "WHO attends meetings of the ICH Steering Committee and the Global Cooperation Group as an observer. These roles are important and should be maintained. However, appropriate strategies for consultation and communication with Member States need

to be developed to ensure that WHO is not seen as de facto automatically endorsing ICH products, but as providing advice on the potential impact of those products on non-ICH Member States."

The WHO has continued with the ICH process for more than 24 years without the close scrutiny of Member States because the issues of norms and standards are considered as technical subjects; therefore, the World Health Assembly never deliberates the merits of the Expert Committee Reports, which contain norms and standards for the regulation of medicine.

The Report of the Expert Working Group is placed before the WHA Executive Board to take note of the Report along with many other expert reports. Normally, the Executive Board takes note of expert reports without any discussion.

The ICH adopts guidelines with political and economic considerations and successfully projects these guidelines as science-based and exported to WHO Expert Committees. The WHO's alliance with ICH facilitates this repackaging.

In the past, Member States had forced WHO to discontinue its engagement with the International Medical Product Anti-Counterfeit Task Force (IMPACT) due to its close association with the pharmaceutical industry.

The challenge at this point is for Member States to scrutinise WHO's alliance with ICH and prevent any further conflict-of-interest situations. +