Call for 'harmonisation of regulatory systems across the globe'

Rajashri Survase-Ojha, director and founder, Raaj Global Pharma Regulatory Affairs Consultants and Onkar Deshmukh, currently a student at The University of Greenwich, UK say harmonisation of the multiple regulatory systems in the pharmaceutical industry is very necessary for a hassle-free, safe and expeditious approval mechanism

Regard this whole world as our human body and think what would happen if there is no synchronisation or our body is inharmonious. The result is known to everyone and one cannot consider his/her body to be disharmonious. We assume that some of our body parts are quite important for us to live such as heart, lungs, liver etc. and we eventually lean towards their maintenance or become more concerned about them. Even though it is reasonably true to a certain level, we cannot turn our back on other parts of our body as they aptly do their part to maintain the harmony on the whole and as a result we are able to lead a whole life. This example can be co-related with the pharmaceutical regulatory system.

As we know the concept of regulated and semi-regulated markets and in connection with this presume that our brain, heart and liver are the regulated markets of body and rest of all parts as semi-regulated. Will that do? Of course not because every part of our body (here, every region) is significant and every cell (here, every pharma company) of that part makes their best. They should be regulated at the same level, like different parts of the human body. If this had not been so, I would have not been here to write this stuff. Same theory can be applied to a regulatory system in pharma domain on the global level. I am at a loss to understand why there is a difference as 'regulated and semi-regulated markets', why US, EU and Japan are considered as highly regulated markets when people are same throughout the world?. The final aim of every pharma company remains generating products that are of best quality, efficacy and are safe. Every company plans to do the same and so should be the rules to be implemented.

Every regulatory authority should be like a 'segment' of the same human brain and not like separate brains. If one brain can control the whole body then why don't regulatory bodies come together and form a unique brain to harmonise the whole system?

Now it is the time to start the ball rolling by setting up a totally harmonised system for the regulation of pharma industries. To start off, the harmonisation of pharma regulation on the global level can give the whole pharma world a new lease on life.

To broach the subject, we are acquainted with the ICH [International Conference on Harmonisation of.....] which is a inimitable venture that brings

together the regulatory authorities of Europe, Japan and the US along with the experts from the pharma industries within these three regions to discuss the scientific and technical aspects of product registration. So far as these three regions are considered, there seems a homogeneity in the regulation which is pretty advantageous and inspiring in safety, quality and efficacy standpoint. For instance, the concept of CTD, a common technical document that is well thought-out by the ICH. This document encompasses the five different modules covering all the essential data that is quite substantial for the effective regulation.

At this instant, I would like to expound upon few ideas that can be implemented or changed in order to have a better and greater harmonisation by taking on board the notion of CTD and e-CTD [electronic-CTD] ultimately to save precious time and cost to bring the best drug product into market. CTD is a common format for the preparation of a well-structured and organised application containing technical documents that will be submitted to regulatory agencies. As stated above, CTD has been accepted by three major regional agencies namely Japan, Europe and US. CTD being a common format for the technical documentation is projected to condense the time and its wherewithal needed to prepare and compile applications for product registration and which eases the application appraisal process and aids communication amidst the regulatory authority and the applicant. It also simplifies the exchange of regulatory data among regulatory agencies. CTD has been obligatory requirement in Europe and Japan. The US FDA has not made it compulsory while submitting the marketing applications (MA) but it has been highly recommended and from 2012 it will be mandatory to US also.

However, this concept should not be limited only to these three major regions rather every region in the world must tag along this common technical format as it has been proved to be of much assistance in all point of view so it should be enforced for each country to phase in the harmonisation at the end of the day. Nevertheless, it is significant to understand that, CTD endorses a format for submission of documents in a particular way and was not designed to indicate what studies are required for an actual product. The CTD comprises five modules namely,

Module 1: Administrative and prescribing information (not part of CTD)
Module 2: CTD summaries.
Module 3: Quality part (CMC).
Module 4: Non clinical part.
Module 5: Clinical part.

Harmonising the CTD

Out of these five modules, module 1 is not part of CTD and may differ in certain conditions from region to region but on the contrary, module 2-5 can be made compulsory and information or content of which should be identical for each country.

However, if there are certain requirements for the particular zone/region those can be included as a subsection in one of the five modules to help the regulatory authorities get all the necessary data (e.g. module 3.2 R, regional information).

There can be a local ICH committee in respective zones that will have a hold over the whole process of regulation and who can deliver seminars or can conduct training programmes in connection with the organisation and/or the subject matter of the CTD. As for the subtle or detailed factors of the CTD such as comprehensive table of contents [TOC], for all TOC and from module 1-5 there must be page numbers for which the regulatory authority can specify the guidelines in order to make it consistent. Moreover, glossary of terms ought to be there for use in CTD as it would help the uninitiated reader. Besides, font style usage must be the same for every country. The advised style of font is the 'Times New Roman 12 point'. Whatever is the font style, it has to be the same throughout the CTD modules. Some exceptions to be given for tables, figures, charts etc.

When it comes to a matter of communication, it all boils down to a language that has universally accepted. The content of CTD and e-CTD must be in the English language, being universally accepted, with the intention of minimising time and cost it takes for translation and linked activities. Only patient information leaflet (PIL) could be kept in local language (country-specific) from the customer or patient point of view. Braille language can be used for blind people across the globe.

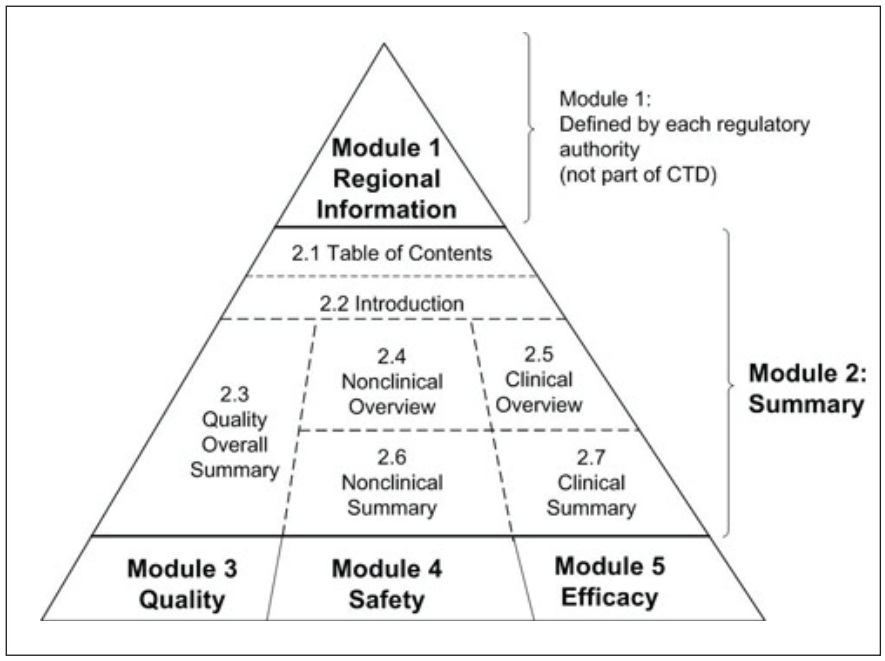
Also the content of Quality Module3-CMC i.e. each section and sub-sections for 'Drug Substance' and 'Drug product' should be harmonised for different range of products (for example, tablets, capsules, liquid orals, ointment-creams, parenterals etc).

Furthermore, there may be some documents that are generated externally in laboratories. For example, analytical reports, CoA, chromatographs, IR, NMR, DSC spectra, figures etc. It expects to have some definite guidelines for headers, footers, naming convention, scale etc for such documents. Additionally, as for the herbal products, veterinary products it can also be presented in the CTD and/or e-CTD format.

Until now, the discussion was based on the harmonisation of the common technical format and its content for product registration for every region in the world but apart from this there are few things that also need overall global harmonisation. Such as fees structure, approval timings, regulatory systems (US, EU, Japan, Asian countries (ACTD), Rest of the World (Row), different terminologies used for same types of applications (e.g. IND/IMPD, or ANDA/ANDS).

For getting a single drug product MA across the globe, an applicant has to go through various cumbersome filing and submission process along with country-specific requirements, form fee, agents fees, different formats, legal documentation etc which is really time consuming, costly and tedious. As we know the fact that US follows different regulatory systems for approval of IND/NDA/ANDA/BLA etc. whereas Europe follows national procedure, DCP, CP, MRP etc

Similarly South Africa follows MRF-1/2 process whereas Asian countries follows ACTD format along with their country-specific system and fees. UAE, follows their own MoH system, Japan (MHLW) whereas 'RoW = Rest of the World' follows different procedures.



Fees

In the ICH region also the fees structure is different for different countries but as for other areas there can be some difference. If we think of the regulation on the global level then the matter of the fees should also be taken into consideration. Whatever is the currency, fees can be determined according to types and timings of submissions. For instance, one particular fees structure for dossier submission, one definite fee constitution for further changes in the submission or late submissions fees etc. There can be a facility where an applicant can pay the full fees at their local point.

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Specific time period for the approval

Above and beyond, the approval timings may vary from agency to agency but there must be some specific time period for the approval or its stages like starting from dossier review, Technical evaluation, validation, inspection until overall approval. That is the time between the dates imprinted on receipt and the date on the certificate or letter that permits the legal marketing authorisation.

Uniformity between RX and non-Rx drugs

One more thing that needs an emphasis is the uniformity of the prescription and non-prescription drugs. There are various types of drugs that have been banned in some countries and on the other hand, in some regions their use is still at full tilt. For example, certain pain killers. Hazardous side effects do not rely on specific atmosphere or people so the regulatory authority must keep an eye on such matters.

With all the above discussions; we would also like to suggest the term to be used as 'GTD = Global Technical Dossier' once we accept the harmonisation of regulatory system global.

Towards a GTD

In the nut shell, the ultimate goal of any health authority is to 'protect public health' and to check whether the drugs or drug products manufactured and distributed in any country are safe, of good quality and effective in whatever dose prescribed.

Nonetheless, for all this an applicant needs to submit an application along with dossier to different regulatory bodies with the necessary information as per respective country-specific format. Adopting the CTD and e-CTD formats along with uniformity in content, fees structure, filing and approval process, language would really help each country and region get the hassle free system which will eventually be safe, qualitative and effective for human beings.

Also it will help to save the time to reach the drug product to market and to patient.

Hence, experts from all regions should take a call on 'harmonisation of regulatory system across the GLOBE'. Also the term 'GTD = global technical dossier' could be used in future in ICH regions and by all other health authorities worldwide.

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