Comparison Concerning Pharmaceutical and Clinical Regulatory Situations in China, Japan and Korea

No	Category	Item	Japan(2016)	Korea(2016)	China
1	Global studies	General pharmaceutical regulations concerning multinational clinical study	Three regulations concerning MRCT have been issued by MHLW; “Basic Principles on Global Clinical Trials,” Notification No. 0928010 by the Evaluation and Licensing Division of the MHLW, dated September 28, 2007, “Basic Principles on Global Clinical Trials(Reference Cases)” Administrative Notice by the Evaluation and Licensing Division of the MHLW, dated September 5, 2012, and “Basic Principles for Conducting Phase I Trials in the Japanese Population Prior to Global Clinical Trials” by the Evaluation and Licensing Division of the MHLW, Administrative Notice dated October 27, 2014. All the documents are available both in	There is no special regulation concerning multi-national clinical studies. However, "Guidelines for an evaluation of bridging data" and other related publications are published on the website.	"Drug Registration Regulation(article 44)" issued by SFDA, dated July 10, 2007, give basic principles for global clinical trial.

			Japanese and in English.		
		Definitions of a multi-national clinical study	A clinical study conducted in two or more countries	A clinical study conducted in two or more countries	no clear regulation, But normally agreed, a clinical study should be conducted in three or more countries or areas, HK and Taiwan are not counted in.
		Usability of an unapproved drug as a comparator	In principle, only approved comparators may be used. If it can be explained objectively that a drug is an international reference product, using the descriptions in guidelines of other countries etc., such a drug may be used even if it is not approved in Japan.	In principle, approved comparators may be used. Although unapproved in Korea, they can be used as comparators in global clinical trial if it can be confirmed as being safe and effective.	The comparators and its indication used for the trial should be already marketed/approved in China.

		Number of local patients in a multi-national clinical study (number required for NDA approval)	In a multi-national clinical trial, sample size can be calculated assuming results from the entire study population across regions. In this case, a sufficient statistical power to detect statistically significant difference should not necessarily be secured	There are no clear provisions concerning specific numbers of Korean patients for NDA approval. The number of Koreans should be decided considering the number of total subjects. And it is necessary to secure enough number of Korean subjects to compare ethnic difference and trend of results between total population and Koreans.	No requirement for the local patients number in multi-national clinical trial. But if intend to use these local patient data for NDA approval, it should meet the clinical requirements for registration and submit the complete the data of the whole multi-national clinical study("Drug Registration Regulation (article 44)" issued by SFDA, dated July 10, 2007
2	IND applicatio n	Flow of clinical trial notification, IND application and IRB permission	In Japan, a clinical trial is conducted based on notification, not on application. The IRB application is required after 30 days from the clinical trial notification (14 days from the second trial onwards).	In Korea, a sponsor who intends to conduct a clinical trial shall submit an IND Application to MFDS and IRB.(can proceed in parallel) Permission from MFDS and IRB is mandatory in Korea.	Application for clinical trial permission(CTP) from SFDA is mandatory in China. IRB applications are followed by SFDA issuing CTP.

		Time required for clinical trial notification, IND application and IRB permission obtainment	The rule of “after 30 days from the first clinical trial notification” The clinical trial can be started after 14 days from clinical trial notification for the second trial onwards (for the same product).	Time for clinical trial permission from MFDS in regulation is 30 WD. Time for clinical trial permission from IRB is depend on itself.	Time for clinical trial permission in regulation is 105~115 WD depend on whether the special examination and approval process is applied or not. Time for IRB permission obtainment usually in 2-3 months
3	IND application materials	Application form	Yes: Clinical trial notification form (in Japanese)	Yes (in Korean)	Yes(in Chinese)
		A statement regarding the reason why the sponsoring of the proposed clinical trial is scientifically justified	Yes	No	Detailed technical dossier package which cover CMC, Pre-clinical and clinical, is necessary for IND application. The reason why the sponsoring of the proposed clinical trial is
		Protocol	Yes (in Japanese, in principle)	Yes (in Korean) However, in the case of phase 1 clinical study on healthy adults (excluding cell/gene therapy product, prophylaxis vaccine), the protocol in English is acceptable.	Yes (in English and Chinese translation)

		IB	Yes (in Japanese, in principle, English is acceptable in part)	Yes (English is acceptable./ But any other foreign languages should be translated in Korean.)	Yes (in English and Chinese translation)
		CRF (sample)	Yes (in Japanese, in principle, English is acceptable in part)	Submission is not required.	No
		Informed consent	Yes (in Japanese)	Yes (in Korean)	No
		Investigator's CV	No	No	No
		Non-clinical summary	No	Yes	Yes (in English and Chinese translation)
		Non-clinical report	No	No	Yes (in English and Chinese translation)
		Clinical summary	No	Yes	Yes (in English and Chinese translation)
		Clinical report	No	No	Yes (in English and Chinese translation)
		CMC summary	No	Yes	Yes (in English and Chinese translation)
		CMC report	No	No	Yes (in English and Chinese translation)
		Sample of the investigational drug (for IND review)	No	No	Yes

4	Clinical trials	EC/IRB procedure	IRB reviews at each site → Multicenter IRB	There are centralized IRB and individual IRB in institution. But many sites conducts IRB's review itself.	There are centralized IRBs, but many sites conducts IRBs review itself.
		Procedure for protocol changes, CMC changes, premature termination etc. during the clinical trial	Submission of the notification of clinical trial plan change, notification of premature termination, notification of termination and notification of development suspension etc. are required.	There is a criteria for what changes is needed a approval from MFDS or not. If Protocol changes or CMC changes are substantial and are likely to have an significant impact on the safety of the subjects or reliability of the study, the sponsor should submit amendments to MFDS and IRB. Also the sponsor should notify some kinds of non-substantial amendments to MFDS. In the case of	No clear regulation for this, but from current practice, once clinical trial is approved, there is no official channel to submit the CMC changes, protocol changes during the clinical trial. Significant change needs another CTP application, and the minor change could submit for EC approval.

				premature(early) termination, the sponsor must notify the end of the trial and the reason expeditely.	
		Adverse drug reaction reporting during clinical trial	ADR reporting is required for Suspected Unexpected Serious Adverse Reactions (SUSAR). (Separate notification based on the same principle as the ICH)	The sponsor must notify all ADRs that are both serious and unexpected to MFDS, investigators and IRB expeditely. The sponsor should notify MFDS of findings that could affect adversely the safety of subjects, impact the conduct of the trial, or alter the IRB's approval/favorable opinion to continue the trial.	ADR reporting is required during clinical trial.

		Investigational drug labeling (requirements and language)	A sponsor shall indicate the following information in the Japanese language on the container or package of the investigational products: (1) Statement of “For clinical trial use only” (2) Name and address of the sponsor (if the sponsor resides outside Japan, name of the sponsor and name of the country where the sponsor is located, and name and address of the clinical trial in-country representative) (3) Chemical name or identification code 17 (4) Manufacturing number or manufacturing code (5) Information on storage method, expiration date, etc., if necessary (Indication in English is acceptable)	The sponsor is responsible for labeling of the investigational Drugs. The labels must be written in Korean. The labels should include : code(general name), lot number, the period of use(expiry date or re-test date), storage conditions, name & address of the sponsor and “for clinical trials use only”.	In Chinese. The sponsor is responsible for properly packing and labeling the investigational product and marking that the drug is specially to be used in a clinical trial. (GCP issued by SFDA, article 57)

5	NDA Application	New drug approval review (Dealing with a drug containing a new API)	Both locally manufactured pharmaceuticals with NCEs and imported pharmaceuticals with NCEs can be registered as new products: drugs that are already approved for manufacturing and marketing and listed in the Japanese Pharmacopoeia.	NCEs can be registered as new pharmaceuticals (both imported products and locally manufactured products).	New drug classification is for local developed drug, not for import drug.
		New drug approval review (inspections (GCP, GLP and GMP) and reliability investigation)	In order to assure the reliability of application materials, investigation of related document data (document-based conformity audit, GCP, and GLP) is conducted*. * This investigation can be replaced with the Certificate of Conformity to GLP.	GCP and GMP inspections are conducted as a part of the NDA review process. During registration of drug substance DMF as a part of the NDA review process, GMP inspections (including the inspection of overseas plants) are conducted.	SFDA may organize the on-site inspection about the research status and manufacturing status, and take sample.

		New drug approval review (Certificates(CPP, GMP certificates etc.) required for application)	CPP from other countries are not required for NDA approval.	CPP is required for NCE approval.	CPP is required for NDA approval.
		Import permission holders	Domestic importer (marketing authorization holder)	Importer (marketing authorization holder)	Importer (marketing authorization holder)
		Marketing of imported drugs	Domestic importer (marketing authorization holder)	Importer (marketing authorization holder)	Marketing Company (marketing authorization holder)
		DMF requirements	The submission of MF is optional.	In the NCEs approval process, submission of DMF is required.	No specific requriement
		Acceptability of CTD format	The CTD system has been introduced (ICH). Reception through eCTD is also possible. Indication in English is accepted except for M1 and M2.	The CTD system was introduced in 2009 (in compliance with the ICH). English is accepted except for M1 and M2.	SFDA accept CTD format. Both English and Chinese version should be submitted.

6	Others	Consultation (For IND submission and NDA submission)	There is a paid consultation with PMDA. (IND Scientific consultation / NDA pre-review consultation)	Yes There are non-official and official consultation. Non-official consultation is used more often in practice.	Yes. There are non-official and official consultation. Non-official consultation is used more often in practice and no minutes to the consultation. Official consultation is for the submissions which comply with the Special Review.
		Accelerated review system (for life-threatening issues such as treatment, preventive drugs, vaccines etc. for SARS, avian flu, swine flu, and so on)	Yes	Fast track process is operated for selected cases.	Yes. Accelerated Review is applicable to 1) New drug material and its preparation, active ingredients and its preparation extracted from plant, animal and minerals, which have not been marketed in China and; 2) chemical drug raw material and its preparations, and/or biological product that have not been marketed domestically or outside China; 3) new drugs for AIDS, cancer and orphan disease that are superior to the marketed drugs. 4) new drugs which treat

					disease for which there is no effective therapy. ("Drug Registration Regulation (article 44))"
		Re-examination period (monitoring period)	NCE: 8 years New indication, new route of administration, etc.: 4 years Orphan drug: 10 years	NCE : 6 years New indications, etc: 4 years	No monitoring period for import drug. For other drugs, the longest monitoring period would be 5 years.

		Disclosure of review reports	Review reports and application materials are disclosed on the website of the PMDA (with masking). Around 40 review reports are translated into English and published every year.	Application material items are disclosed on the website of the MFDS. However, the detailed reports and confidential parts are not disclosed.	Review reports and application material will not be disclosed.
		Renewal of the approval certificate	There is no specific process for renewal of the approval certificate, but GMP conformity audit must be conducted every five years following approval. In addition, the company's marketing authorization license becomes invalid unless renewed every five years.	Yes, renew the approval certificate every 5 years.	Yes, renew the approval certificate (Imported drug licence) every 5 years.