Identifiers to Enable Pharmaceutical Quality Knowledge Management (PQ KM) – a Progress Report

Background and Rationale

As pointed out in the 2022 Joint Reflection Paper (JRP), effectively managing changes to pharmaceutical manufacturing processes is challenging, especially to marketing authorization holders (MAH) submitting the same dossier to multiple regions. Different formats and contents in the dossier are expected due to country/region specific conventions and legal/regulatory expectations. Such inconsistencies also cause inefficiency amongst regulators and hamper mutual reliance efforts to share knowledge amongst regulators and facilities to be more nimble, agile in regulatory decision making. The envisioned PQ KM system aims at strengthening international collaboration to support global development, manufacture, and supply of pharmaceutical and biological/biotechnological products.

One key challenge to international collaboration stems from how to identify or confirm that it is the same product under assessment by different national regulatory agencies (NRA) in parallel or at different times. Solving this challenge would allow NRAs to effectively collaborate or share their assessment outcomes and decisions, and eventually make the same product available to the patients in multiple regions sooner. Although some authorities use national or regional identifiers, a common and interoperable limited set of identifiers for manufacturing facilities, pharmaceutical products, substances, marketing applications, and/or marketing application holders is not currently endorsed.

Purpose and Approach

Recognizing the above challenge, the JRP called for a cross-organization collaboration on defining identifiers. Subject matter experts from ICMRA, IPRP, ICH, and PIC/S member agencies were convened to form a working group. The group was tasked with considering the status of current standards, their implementation, potential need for new standards and approaches for the development, adoption, operation, governance, and maintenance of a limited set of internationally harmonized identifiers related to pharmaceutical products and the establishments that manufacture them.

In the development phase, the group focused on key quality information in the eCTD Module 3, and examined current practices by different NRAs (e.g., EMA, HPRA, PMDA and USFDA) and existing standards and initiatives, such as:

- Key organization information and quality attributes to identify the same product
- ISO IDMP standards (11615, 11616, and 11238) in identifying medicinal products, pharmaceutical products and substances
- Substance, Product, Organization and Referential (SPOR) Data Management Services from the EMA
- Global Substance Registration System (G-SRS), which provides common unique identifiers (UNII) for substances
- Pharmaceutical Inspection Co-operation Scheme (PIC/S) recommendation for unique facility identifiers

Additionally, the group verified the selected identifiers using information from global submissions received by two ICMRA Pilots (i.e., Collaborative Hybrid Inspection Pilot (CHIP) and Collaborative Assessment Pilot for Quality/CMC Post-Approval Change (PAC)) launched in 2022. The goal was to determine feasibility of the group's recommendations by assessing if these identifiers are commonly used in submissions, and to identify potential gaps or challenges in adopting these identifiers.

Version dated: September 15, 2025

The above effort resulted in a proposed identifiers framework, which should help NRAs to quickly confirm that the same drug product is under assessment to accelerate or better enable global collaboration and/or mutual reliance.

Outcome and Discussion

This framework, as proposed, contains two tiers of identifiers:

- Primary identifiers (in Appendix 1) are key information about drug substance and product, and associated organizations (e.g., MAH and manufacturers). Such information is currently mandatory and submitted in dossiers, typically using well formulated terms or codes in highly structured format. They can be easily located in submissions (e.g., the cover letter or application form) to serve as effective identifiers. It is estimated that using these primary identifiers collectively should give NRAs high confidence in determining product "sameness".
- Secondary identifiers (in Appendix 2) are additional, and contain more granular information about drug substances and products, and associated organizations. Using these additional identifiers should give a higher level of confidence in determining product "sameness"; however, it may take significantly more effort because they are typically text-based and deeply "buried" in submissions. Therefore, they are expected to be less effective as identifiers.

Regarding the primary identifiers, the group has a high level of consensus on what the limited set of primary identifiers should be. Also, a majority of them have been well defined in ISO 11615/11616/11238, as noted in the appendices. In fact, these identifiers have been widely and effectively used by NRAs, following their own conventions and practices, and using different controlled terms and system generated codes. For instance, FEI and DUNS codes are used by the USFDA to identify manufacturing establishments; however, using such codes is not required by PMDA. EU/EEA NRAs and EMA use a system called "Organisation Management Service (OMS)" that supports EU regulatory activities and business processes; it stores master data comprising organisation name and location address for organisations such as MAHs, sponsors, regulatory authorities and manufacturers. For application types, different NRAs have different formats due to specific regional requirements. For dosage form, there is not a internationally agreed-upon list of controlled terms. Consequently, the same product can still be labelled differently using this proposed framework, compromising the interoperability of these identifiers across NRAs. Therefore, successful use of these identifiers for reliance is contingent upon the eventual adoption of internationally recognized and controlled terms or codes.

Through the verification effort referencing the two ICMRA pilots, the group found that 1) most primary identifiers are commonly used in global submissions, and 2) a few secondary identifiers may need to be elevated to primary due to their consistent usage. Below are some key observations.

- Most primary identifiers (i.e., drug substance name, marketing authorization holder name and address, application type, dosage form, route of administration, and indication) are included in global submissions. This demonstrated the feasibility of these primary identifiers.
- Product type (e.g., chemical/small molecule, biological molecule, other) can be another primary identifier or a substitute for Application Type.
- Unit of Presentation is an important primary indicator. Although not a required data field in the ICMRA pilot submission forms, it could be derived from information provided in other data fields (e.g., dosage form).
- Profile Class Code, a primary identifier, was not required in the pilot submission forms; no submissions mentioned this information either. This may suggest that

such an identifier is not necessary. However, it is important to acknowledge that certain identifiers may be meaningful or needed only in specific situations.

- Drug Product Name (text based), a secondary identifier, is a required data field in the pilot submission forms. Applicants consistently provided such information. This suggests that it may need to be elevated to primary identifier.
- Application Number, a secondary identifier, appears to be used commonly to identify a product, and may need to be elevated to primary identifier (at least for near future use). However, the data showed tremendous variation in the naming or coding conventions across NRAs.
- Regarding other secondary identifiers, the verification effort showed that they are rarely used.

The group sees the opportunities in ICH and global efforts, to augment the use of these identifiers. The ICH M4Q under revision could clearly specify these identifiers as mandatory for all future submissions and prescribe the desired locations. In addition, the upcoming ICH Structured Product Quality Submission (SPQS) effort can further harmonize submission content (i.e., data elements and format) and the associated conventions (e.g., business rules, controlled terms and coding strategies); for instance, SPQS can prescribe that all the identifiers are captured in a specific section of a well-structured submission form. Their implementation and adoption these ICH guidelines will greatly accelerate the usage of these identifiers. Additionally, the Global IDMP working group (GIDWG), formed in 2021, is leading to establish a framework for global implementation of the ISO IDMP standards and maintenance of global identifiers.

As resources permit, the group suggests a deeper dive into practices and conventions currently used by different NRAs to determine specific differences and potential approaches to harmonize the format/content of these identifiers, to enhance interoperability. The results from this exercise can also serve as a critical reference especially for the upcoming ICH SPQS effort.

Key references:

1. The 2022 PQ KMS Joint Reflection Paper
2. Considerations on use of unique identifiers to enable reliance through a global regulatory PQ KMS
3. EMA PMS ISO IDMP Implementation Guide Chapter 8 Practical example (July 2022)
4. ISO 11238: Data elements and structures for unique identification and exchange of regulated information on Substances
5. ISO 11239: Data elements and structures for unique identification and exchange of regulated information on pharmaceutical dose forms, units of presentation, routes of administration and packaging
6. ISO 11240: Data elements and structures for unique identification and exchange of units of measurement
7. ISO 11616: Data elements and structures for unique identification and exchange of regulated pharmaceutical Product information
8. ISO 11615: Data elements and structures for unique identification and exchange of regulated medicinal Product information

Appendix 1: Primary Identifiers

Identifier Name	IDMP Term	Rationale	Regulatory Note
Drug Substance Related Identifiers			
Drug Substance Name	Active Substance (Moiety) Name	A key identifier to determine the same product	Currently available naming convention include International Non-proprietary Names (INN) and IUPAC names, and CAS Registry Number (CAS RN). Also available is the GSRS Unique Identifiers (UNII, combo of numbers and characters). EMA assigns SMS ID, using as a combination of numbers. Although there is no harmonization of the identifier at the global level, GIDWG has demonstrated at ISO TC215 WG6 and other venues business rules conforming to the ISO IDMP 11238 standard to achieve global harmonization between NRAs.
Active Substance Master File (ASMF) / Drug Master File (DMF) Holder Name & Address	Master File Holder (Organization)	This is critical because different holders or manufactures may use different synthetic routes, which may bear different risk profiles (thus different level of quality assessment effort).	EMA's PMS includes Org and Loc IDs.
Manufacturing Site Identifier, Name and Address	Organization -Manufacturer ID, Name, Address	This identifies the specific drug substance manufacturer. Based on the identifier code, the name and address can be further identified (see Secondary Identifiers)	Currently used identifiers include FEI, DUNS, Geocoordinates mainly by the EMA and USFDA. From an EMA perspective, identification in the OMS system uses Org and Loc IDs.
Drug Product Related Identifiers			
Marketing Authorization Holder (MAH) Name & Address	Marketing Authorization Holder Name, Address	Identify the application owner.	EMA's PMS assigns Org/Loc IDs, using a combination of numbers.
Application Type	Application Type	Identify the type of products/application (e.g., biologics, innovator or generic drugs).	This is regulator specific currently. USFDA uses NDA/ANDA/BLA + 6-digit number. EMA's RMS capture application type IDs, as combination of numbers. Potentially to establish an international standard/practice to capture key basics (e.g., Legal basis + Large/Small molecule + Numbers).

Identifier Name	IDMP Term	Rationale	Regulatory Note
Dosage Form	Dose Form (Administrable Dose Form; Pharmaceutical Dose Form; Administered Dose Form)	The same MAH may have different dosage forms for the same drug substance.	In general, controlled terms are used by different NRAs but not harmonized. USFDA has controlled terms and concept codes for commonly seen dosage forms via NCI EVS. EMA's RMS has dose form IDs (codes) for different dose forms (EDQM as the owner). Although there is no harmonization at the global level, GIDWG has demonstrated at ISO TC215 WG6 and other venues business rules conforming to the ISO IDMP 11239 standard to achieve global harmonization between NRAs across different terminologies.
Route of Administration (ROA)	Rout of Administration	Different route of administration may warrant different level of scrutiny during the quality assessment.	USFDA has controlled terms and concept codes for commonly seen ROAs via NCI EVS. EMA's RMS has Routes and Methods of Administration terms and IDs (EDQM ownership) in the RMS.
Indication	Therapeutic Indication	Different indications (including target population) may lead to different risk-benefit profiles, which may warrant different level of scrutiny during the quality assessment.	EMA's RMS has Medical Dictionary For Regulatory Activities list (MedDRA)(MSSO ownership). USFDA uses SNOMED for indication.
Manufacturing Site Identifier, Name, and Address	Manufacturer/ Establishment (organization)	This identifies the specific drug substance manufacturer. Based on the identifier code, the name and address can be further identified (see Secondary Identifiers).	Currently used identifiers include FEI, DUNS, and Geocoordinates mainly by the EMA and U.S. FDA. Advocate for Geocoordinates to be internationally used in submissions. From an EMA perspective, identification in the OMS system uses Org and Loc IDs also captures the name and address.
Profile Class Codes	None	Reflects Product classes produced by the site and is updated during the inspections.	EMA: During MRA process, PCC used by USFDA and EU nomenclature used on GMP certs and listed in Eudralex was mapped.
Unit of Presentation	Unit of Presentation	Identify the final delivery format of the drug product. Certain final delivery format may warrant additional level of scrutiny during the quality assessment.	It is a discrete field in IDMP. USFDA: this is typically imbedded in or implied by the finished product name.

Appendix 2: Secondary Identifiers

Identifier Name	IDMP Term	Rationale	Regulatory Note
Drug Substance Related Identifiers			
Active Substance Master File (ASMF) / Drug Master File (DMF) Number & Version Number	Master File Version	To further help triangulate the drug substance manufacturer.	Assigned by the regulators; but different formats used are in different countries. The version number is typically generated by the ASMF/DMF holder and critical to determine the same version of a given ASMF/DMF is being assessed by regulators for mutual reliance.
Synthetic Route Description	Manufacturing Type, Production Method Type, Production System Type, and Critical Process Version Number	(Optional) In principle, different synthetic routes may result in different impurity profiles and hence safety concerns.	This is not an efficient identifier to quickly triangulate the drug substance/product. A global IT effort to render the same CMC/CMC PAC package to multiple regulators is more effective than using this as an ID.
Stability Specifications	Specifications	(Optional) In principle, the same drug substance from different manufacturers or DMF holders may have different specification.	Same as above.
Drug Product Related Identifiers			
Application Number	Marketing Authorization Number	In conjunction with the Application Type (primary ID) to identify the drug product.	Currently regulator specific regarding its format (e.g., 6-digit number for USFDA)
Drug Product Name (established)	Common name	Identify the product using commonly known non-proprietary (established) name.	Naming convention is different for different regulators.
Strength	Strength	This identifier can be critical for PAC as some PACs are only intended for certain strength under the same market authorization (application)	IDMP can help address this need. Although there is no harmonization at the global level, GIDWG has demonstrated at ISO TC215 WG6 and other venues business rules conforming to the ISO IDMP 11240 standard to achieve global harmonization between NRAs.
Packaging Configuration	Packaging	Different packaging configurations may result in different unit operations and stability considerations (e.g., blister pack vs. bottle vs. pharmacy bulk	May not be a stable identifier as it may change (due to PACs) throughout the product lifecycle. IDMP can help address this need.

Identifier Name	IDMP Term	Rationale	Regulatory Note
		pack). From the quality assessment perspective, this aspect is critical.	
Sterile or non-sterile	Sterility Indicator	Help to identify if sterile processing is involved or not. If sterile, additional scrutiny during the quality assessment is warranted.	Currently not captured in a structured way in most countries. It may not be an efficient identifier.
Component & Composition	Pharmaceutical Product (=Qualitative and Quantitative Composition)	Ensure sameness of formulation (or allows discussion of insignificance of differences like flavours, colours, etc);	In general, this should not be an identifier. However, this is the level or granularity of "sameness" should be defined. In other words, what kind of differences are insignificant (and still consider the finished product being the "same") from the quality assessment perspective.
Product Design (especially for solids-based drug products)	None.	This can be critical for certain product types. For instance, the same drug substance can be formulated into extended release tablets using different release control mechanisms (e.g., matrix-based or osmotic-pump controlled). Such difference will result in different manufacturing process and process controls, which are critical to quality assessment.	Same as above.
Specifications	Specifications	(Optional) In principle, the same drug substance from different manufacturers or DMF holders may have different specification.	This is not an efficient ID to quickly triangulate the drug substance/product. A global IT effort to render the same CMC/CMC PAC package to multiple regulators is more effective than using this as an ID.
Manufacturing process (e.g., flow diagram, and critical process parameters)	Manufacturing Type, Production Method Type, Production System Type, and Critical Process Version Number	Such details are important to quality assessment.	Too granular to be an effective identifier.