FAQ – Licenses and Subscriptions 1st of January 2013

In this document you will find the answers to some of our most Frequently Asked Questions, FAQs.

Product abbreviations:

WHO Drug Dictionary – WHO DD
WHO Drug Dictionary Enhanced – WHO DDE

Limited Study License for Sponsors - LSLfS
Limited Study License for CROs – LSLfC

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The UMC definitions of sites and users per sites

Definition of Sites

The subscription is based on a price model where users are charged per geographical site and their number of users per geographical site.

If your company uses the WHO Drug Dictionaries (WHO DD, the WHO DDE or WHO DDE+WHO HD) in an intranet solution, this often means that the dictionary is only loaded in one geographical site, but the users within the organization are spread in a number of different geographical sites. This is regarded as different geographical sites and will be priced accordingly.

The minimum subscription is one site.

Definition of Users

Coders

Personnel that manually code data or use auto-encoders are considered users.

Data management and Technical personnel

Personnel that use the information to run analyses and create reports, that are based on the information (codes or texts) and the hierarchy of the dictionaries, are considered users.

Drug Safety & Statisticians

Personnel that make analytical interpretation based on the information (codes or texts) and the hierarchy of the Dictionaries, are considered users.

Temporary Staff

Personnel that use the data infrequently, or are temporary personnel, are according to UMC regarded users, subject to negotiation.

The minimum subscription is one user per site.

Sites and Users in the License agreement

In attachment 1 of the License agreement, it is stipulated the applicable limitations concerning sites and users. If the licensee would like make use of the WHO Dictionary information at any other site, outside the stipulated site/sites with corresponding users, or have more users allowed at the Geographical site/sites, the Licensee must contact UMC for an amendment to Attachment 1 and a change for the increased number of sites and/or number of users.
Under what conditions can a CRO and a Sponsor share data coded with the dictionaries?

When a CRO starts a subscription or upgrade to a more extended version of the Dictionary/ Dictionaries, they will always receive the less comprehensive versions, free of charge. This is to enable them to work with sponsors that have not yet upgraded their licenses.

Summary

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<tr>
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<th>CRO WHO DDE+ WHO HD</th>
<th>CRO WHO DDE</th>
<th>CRO WHO DD</th>
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<tbody>
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<td>Possible if the CRO upgrades to WHO DDE+WHO HD</td>
<td>Possible if the CRO upgrades to WHO DDE+WHO HD</td>
</tr>
<tr>
<td>Sponsor WHO DDE</td>
<td>OK *</td>
<td>OK</td>
<td>Possible if the CRO upgrades to at least WHO DDE</td>
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<tr>
<td>Sponsor WHO DD</td>
<td>OK *</td>
<td>OK **</td>
<td>OK</td>
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*CRO’s subscribing to the ‘WHO DDE+ WHO HD’ receives all dictionary types: WHO DD, WHO DDE and WHO DDE+WHO HD.

** CRO’s subscribing to the WHO DDE has access to both WHO DDE and WHO DD.

The CRO should always code the concomitant medication in accordance with the sponsor’s dictionary subscription.

Dictionary versions

In order to make sure that the coded data is compatible with the dictionary of the sponsor it is also important that the sponsor and the CRO agree as to which version (e.g. March 1, 2010) of the dictionary to use.

When using the Mandatory Validation Report Request procedure (described in the next section of this document) the UMC will provide a report of what common denomination the Sponsor and CRO have. Under the condition that both parties have ongoing subscriptions, the UMC has no objection to the Sponsor and the CRO using different versions of the dictionary but we strongly recommend that you use the same version while collaborating, to avoid running into problems.
Who has to have a License?

Section 3 d) of the UMC License agreement, addresses the regulations about collaborations between Sponsors, CROs, EDC providers and Vendors, using the WHO Dictionaries.

Each party in collaboration has to have a valid license of their own to the relevant WHO Drug Dictionary with a corresponding relevant subscription.

A Licensee to any of the dictionaries is NOT allowed to provide a non-license holder or a license holder with a non-matching subscription with access to the dictionary information. This also applies to the WHO-DD Browser.

The CRO and Sponsor shall always use their own dictionary; they are not allowed to share their dictionaries/dictionaries with anybody outside their licensed organisation.
Validation Report Request

Before a CRO can start collaboration with a Sponsor, the CRO and the Sponsor need to check with the UMC, the license status for the Sponsor – this is the Validation Report Request procedure.

In the agreement, clauses 3 A and 3 D stipulate that both the CRO and the Sponsor have to have a valid license/subscription of the same dictionary type, if they want to use the dictionaries to code concomitant medication and to share coded data.

In order to ensure compliance with the agreement the CRO needs to request a validation report for all companies that they conduct clinical trials for, requiring the use of WHO DD, WHO DDE or WHO DDE+WHO HD. Both parties need to verify the existence of each other’s valid license via our on-line validation request procedure - www.umc-products.com/validation under the customer area - before the clinical trial is started.

The UMC will verify each party’s License / valid subscription in a Validation Report, normally within 3 business days.

The Validation Report is needed before information is shared, to protect both CRO and Sponsor from being in breach of the license agreement.

The Difference between a Subscription and a Valid License

A subscription means that the company has an ongoing subscription to a dictionary.

The validation Report will state: the dictionary type/types, what release/releases and the current subscription time period.

Without subscription, a licensee may hold a valid license to an old version of a dictionary.

The Validation Report will state the conditions under which the two parties can collaborate. If one of the companies does not hold an ongoing subscription, the lowest common denominator will determine which type and version they can use in their collaboration.

If there is no lowest common denominator the validation will be denied.

UMC staff will help you find the best possible solution.
Using an EDC-Tool

An increasing number of electronic data capture (EDC) tools and Drug Safety tools are available as hosted services. This means that they host the coded data and load the WHO Drug Dictionaries. If you are a user or a provider of such a system, please contact Sales@umc-products.com for information about the validation procedure for EDC-tool providers.

Suggested wording for CRO to use in their standard terms.

A number of CROs in both US and Europe have added this procedure into their standard term contract. Please feel free use our suggested wording.

“As a CRO, we are under obligation to ascertain that you as a future sponsor will have a relevant license to the WHO DD, WHO DDE or WHO DDE+WHO HD. You may not request any compensation from us for such license.

For the sake of good order, we also remind you of the license terms of the UMC license, especially section 3. There is no right for any licensee of the UMC to sub-license. There is an obligation on CRO and Sponsors before any clinical trials to validate via the UMC that the counter party has the proper license.

The validation request application is to be found at the following URL:

http://www.umc-products.com/validation

We hereby agree with you that our validation obligations (and yours) towards the UMC will in effect be an exception from any confidentiality undertaking to reveal existing co-operation.”
Limited Study License for Sponsors

The Limited Study License for Sponsors, LSLfS, was made available as of the 1st of June 2006, to make the WHO DDE, WHO DD, WHO HD or combinations of the products available for small pharmaceutical and Biotech companies at a favorable price.

With a LSLfS, the Sponsor will be granted a license for a limited number of clinical trials to be performed by a CRO. The CRO will continue to use their own licensed version of WHO DDE / WHO DD / WHO HD or the combination of the products for these clinical trials.

The LSLfS is available under the following conditions:

- **The Sponsor company and/or company group has a annual revenue less than 10 Million US$**

- **Clinical trials are conducted only in Phase 1 and/or Phase 2.**

The price is 1100 US$ / Year and CRO.

If a Sponsor would like to work with multiple CROs, one LSLfS will have to be obtained for each CRO.

**The Sponsor will not receive any data files of the Dictionary when they have a LSLfS.**

The Sponsor will be entitled to receive the final study report from the CRO as well as elements from the Dictionary such as drug and ATC codes that is needed in order to illustrate the study result.

**As stated in the License Agreement, the CRO is never allowed to provide the Sponsor with the complete Dictionary Data files.**
How to obtain the Limited Study License for Sponsors

The Limited Study License for Sponsor application form is found at: www.umc-products.com/limitedstudy, under the Customer area. The application has to be done by the Sponsor.

The application form will create a License Agreement that will be sent to the applicants email address.

The signed agreement should be sent to the UMC by Email to sales@umc-products.com

The UMC will, normally within 3 business days, process the application and issue an invoice according to the number of required protocols.

The Sponsor will, when the license has been approved, receive a confirmation email and a countersigned copy of the License agreement.

The License is renewed annually, read more about this on page 11.

When does the License no longer apply?

If the total revenue of the Sponsor would exceed 10 Million US$ and/or when the Sponsor initiates studies other than phase 1 and phase 2 with a CRO, the LSLfS agreement needs to be upgraded into a full license. LSLfS fees paid during the 12 months period prior to the upgrade will be deducted from the first year subscription fee.
Limited Study License for CROs

The UMC created a model for a Limited Study license for CROs, LSLfC, at a favourable price. To make the dictionary, WHO DDE+WHO HD available for small CROs, A CRO with a limited License will get access to the full version of the WHO DDE+WHO HD, WHO DDE and WHO DD, four times per year, through our web based, WHO DD Browser.

The criteria that need to be met in order to be approved for a LSLfC:

- The CRO or the company that the CRO is owned by, have an annual turnover/revenue less then 33 000 000 SEK. (3 500 000 Euro)

The License can be used for a total of 5 studies. When the CRO exceeds the annual turnover / revenue of 33 000 000 SEK or start their 6th study/protocol, the CRO is no longer able to work under the Limited Study License for CROs, and will be upgraded to a full license following our current price list.

The CRO will continue to subscribe to the WHO DDE+WHO HD for the full price. First year as full price customer, a discount, equal to the amount paid for the Limited Study License protocols 12 months prior to the upgrade, will be deducted from the subscription fee.

For example; if the CRO use the Dictionary at one site and one user when they upgrade to a full license, and have had 5 studies ongoing on the Limited Study License the last 12 months, 100 000 SEK will be deducted from first year subscription fee.

To apply for the Limited Study License for CROs, please contact sales@umc-products.com
Developer License for Software vendors and EDC providers.

UMC have Developer License arrangements with the major software and EDC providers. This includes among other things that UMC provides those vendors/EDC providers with quarterly updates of WHO Drug Dictionary Enhanced extended with WHO Herbal Dictionary, WHO Drug Dictionary Enhanced and WHO Drug Dictionary.

Before a Developer license holder are allowed to give a customer access to WHO DDE+WHO HD/ WHO DDE and/or WHO DD through their commercial software and/or Services to their Customer, they will first have to go through the mandatory EDC-validation procedure. The UMC will provide a Validation Report for the customer, stating the current subscription status for the customer.

The end users [sponsor or CRO] should NOT send their dictionary to the Vendor / EDC provider. The Vendor/EDC should use their own master files to load the dictionary for their client, in accordance to the sponsors subscription stated in the Validation Report.
Renewal & Invoicing

Renewal

The UMC will automatically extend the subscription unless actively asked to discontinue the subscription according to the License agreement clause 9. The subscription is renewed on a yearly basis, and the licensee will be informed, with a Renewal Acknowledgement 60 days in advance that the subscription will expire and will be renewed automatically. When the licensee receives the renewal notice, he/she must do the following:

- To determine how many sites and users per site have access to the dictionary, please find our definitions in the attached file. "FAQ 1st of May 2010.pdf".
- Validate the correct contact person for delivery and invoicing.
- Submit your PO number, if needed.
- Please inform UMC if any corrections are needed.

For the second year, an invoice will be sent 30 days before release date of the first delivery for the subscription period. This gives you as a subscriber an opportunity to get access to the product on release day. The invoice needs to be settled before access to the dictionary data is granted. Release dates are; March 1st, June 1st, September 1st and December 1st.

Invoicing

A new subscription period will run for one year from the date the UMC has processed the signed license agreement. The licensee will receive the first invoice directly after the UMC has received the signed license agreement. The invoice is to be paid within 30 days. The invoice must be settled before access to the dictionary data is granted.

During the subscription period, the licensee will receive one or more releases of the dictionary product, according to your current subscription.

When a subscription is started, it will be renewed automatically each year.
Concomitant medication in Clinical Trials

A White Paper from Uppsala Monitoring Centre

This paper describes important issues encountered by organizations that collect and interpret information about concomitant medication in clinical trials – issues that have been the guiding principles in the development of the WHO Drug Dictionary Enhanced.

Patients and clinical trial subjects often take other drugs apart from the trial substance. This may confound the outcome of the study – and many organizations choose to exclude subject that take certain drugs in their studies or exclude them from certain types of analysis.

The information about the concomitant medication can be of high value – since this information can be an important clue to how the trial substance will work once it is on the market and both positive and negative interactions can be discovered.

Important concerns

Global

The world is getting more and more integrated – people travel more than ever and medicinal products are being sold over the internet without any geographical restrictions. This is important to keep in mind when collecting information about concomitant medication – drugs taken by the subjects may come from any country, not just the country where the trial is conducted.

When a drug name is mentioned in a verbatim it is important to have a global source – which makes it possible to distinguish which products are available in different markets.

Up-to-date

Many new drugs are launched every year and many drugs change their composition or other important properties. Even if a drug name has been identified in a verbatim and it has been found to contain a certain active ingredient this may not be true in the future. The product may have other active ingredients – or the same trade name may have been used for a completely different product in another country.

Organization without a comprehensive drug dictionary that make ad-hoc investigations when drug names appear in concomitant medication verbatims may miss the fact that a product has changed or that alternative products are available. When analyzing concomitant medication it is important that the selected product is correct – that it reflects the active ingredients taken by the trial subject.
Harmonized

Clinical data is often shared between regions and organization. In order for all parties to interpret the data in the same way the same dictionary should be used and the same principles for classification should be used throughout the dictionary.

If an organization conducts a trial and later collaborates with – or even sells the product to – another organization, the value of the clinical data will increase if internationally accepted standards have been used.

Structured

The most important issue in the coding and interpretation of concomitant medication data is that trade names are mapped to their active ingredients. It is also important that these products and substances are placed in a hierarchical classification. This makes it possible to select whole groups of products that should be avoided in a specific trial – so called protocol violation lists. The hierarchies also make it possible to aggregate statistics in order to analyze the data and find patterns.

The WHO Drug Dictionary Enhanced

The need for an international, structured dictionary for medicinal product information was identified by the WHO in the 1960’s. The dictionary was first used in drug safety monitoring, but it was soon accepted by the life sciences as an important tool in other areas – especially clinical development. The WHO Drug Dictionary Enhanced is an information service that is used for coding, communication and analysis of drug information.

The dictionary is maintained by Uppsala Monitoring Centre (UMC), which is the field name for the WHO Programme for International Drug Monitoring. The organization is in the center of a network of regulatory agencies in over 100 countries. These regulatory agencies provide the UMC with reliable sources with information about products available in their countries. The UMC also collaborate with IMS Health that collect product information from 63 countries - and other reliable sources are frequently used to find or to verify information about medicinal products.

In order to optimise the dictionaries and to ensure that they meet the requirements from new legislation or changing user needs. The development of the dictionary is driven by the user community and new tools for analysis and classification are added. The UMC is also active in relevant standardization organizations.

An on-line browser is available to make sure that subscribers can access all features of the dictionary.