

Medical Literature Monitoring Service Contractor Work Instruction (MLM WIN-03)

Processing and submitting ICSRs in EVWEB

Preamble

This WIN governs the activities of contractors working for the European Medicines Agency providing the Medical Literature Monitoring service. The WIN was created by the contractors and approved by the Agency.

1. Changes since last revision

New WIN.

2. Records

Not applicable.

3. Definitions

Term	Definition
DMTT	Literature Monitoring Tracking Tool – a subset of the Data Management Tracking Tool used by the contractor and the EMA to record & monitor work on EV data
EEA	European Economic Area
EMA	European Medicines Agency
EudraVigilance	The European data-processing network and management system, which has been developed according to internationally agreed standards and which allows the EMEA to manage the electronic data exchange of Individual Case Safety Reports (ICSRs) and to support the EU pharmacovigilance activities at Community level.
EV	EudraVigilance
FTA	Full text article

Term	Definition
Individual Case Safety Report (ICSR)	An ICSR is an electronic report which provides the most complete information related to an individual case at a certain point of time. An individual case is the information provided by a primary source to describe suspected adverse reaction(s) related to the administration of one or more medicinal products to an individual Patient at a particular point of time.
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Affairs
MLM	Medical Literature Monitoring
NCA	National Competent Authority

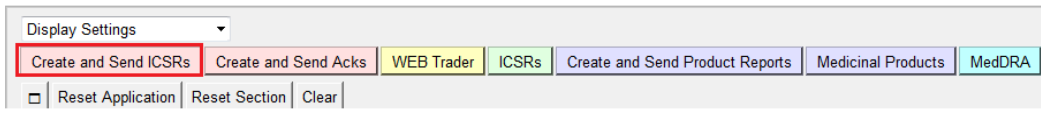
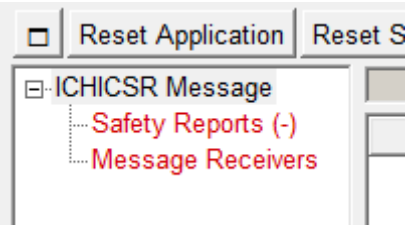
4. Instructions

General principles

All valid MLM ICSRs will be submitted in EudraVigilance using the EVWEB application.

ICSRs and any follow-up received will be submitted by day 7 for serious ICSRs, and by day 21 day for non-serious ICSRs.

4.1. Processing of ICSRs

Step	Action
1. Login	Log into EVWEB by going to URL: https://eudravigilance.ema.europa.eu/X/?6 <u>& enter username & password when prompted</u>
2. Main menu	To create and send an ICSR, select 'Create and Send ICSR' 
3. Tree menu	On the left hand side of the screen is a tree menu. Headers highlighted in Red require completion before an ICSR can be transmitted or validated 
4. General notes before commencing data	The main section of the screen is where data entry occurs. Click on the data field and then press 'enter' in order to type in the highlighted field.

entry

Description	Name/Value	
Message Number		Field is Mandatory
Message Type	ICHICSR (1)	
	Safety Reports (-)	Section is Mandatory
	Message Receivers	Section is Mandatory

Mandatory data elements are indicated on the right hand side until the field is completed.

A description of the field is shown at the bottom of the screen when the user selects a data element.

All entered values must have corresponding units if provided in the article or by the reporter.

Where a data field has been entered incorrectly, the text can be replaced by clicking on the field in question, pressing 'enter', and then deleting the incorrect data.

To remove 'rows' of data, mark it as (-), and then selecting 'Clear' from the menu options;

A screenshot of a software interface titled "Permanently remove the Rows marked for Deletion (-)". Below the title is a row of five colored buttons: "WEB Trader" (yellow), "ICSRs" (green), "Send Products" (purple), "Products" (blue), and "MedDRA" (cyan). Below these is a row of buttons: "Clear" (white with a red border), "Validate" (white with a dropdown arrow), "XML" (light blue), "RTF" (light blue), "Print" (light blue), "E" (light blue), "L" (light blue), and "R" (light blue). A red rectangle highlights the "Clear" button.

Rows of information can be duplicated in EVWEB where the information is largely the same and subsequently edited as appropriate

Where Duplication of cases is required, the duplicate function can be used to create multiple cases that are related (i.e. originate from the same article) with appropriate individual data subsequently entered.

5. Safety report

Click on safety report in Tree menu

A screenshot of a tree menu in a software application. The menu is expanded to show the following hierarchy: "ICHICSR Message" (red text) is the root. Under it is "Safety Reports (1)" (red text), which is highlighted with a red rectangle. Under "Safety Reports (1)" is "Safety Report" (red text). Under "Safety Report" are four items: "Report Duplicates (1)" (blue text), "Linked Reports (1)" (blue text), "Primary Sources (1)" (blue text), and "Patient" (red text). Each item has a small icon to its left.

Select the 'New safety reports' in active area

Display Settings

Create and Send ICSRs

Create and Send Acks

WEB Trader

ICSRs

Create and Send Product Reports

Medicinal Products

MedDRA

Reset Application

Reset Section

Clear

Validate

Send

XML

RTF

Print

E

L

R

ICHICSR Message

Safety Reports (-)

Message Receivers

Num

Repor...

Safety Report ID

New Safety Report

5a.

Complete all mandatory A.1 Data elements as applicable

Description	Name/Value	
Report Version		
Safety Report ID		Field is Mandatory
Primary Source Country		Field is Mandatory
Occurrence Country		
Date		Field is Mandatory
Report Type		Field is Mandatory
Serious ?		
Results in death ?		
Life Threatening ?		
Caused/Prolonged Hospitalization ?		
Disabling / Incapacitating ?		
Congenital Anomaly ?		
Other medically important condition ?		
Receive Date		Field is Mandatory
Receipt Date		Field is Mandatory
Additional Documents ?		
Document List		
Fulfill Expedited Criteria ?		
Case Type		Field is Mandatory
Case Number		Field is Mandatory
Duplicate		
Report Nullification		
Nullification Reason		
Medically Confirmed ?		

Note:

Report version:

Enter '00' for initial cases.

A.1.0.1

Safety Report ID – Copy and pasted from the generated case ID in DMTT.

A.1.3b

Transmission date – This should be left blank in initial data entry as it is to be completed with the date the case is transmitted in EVWEB. A full precision date should be used (i.e., day, month, year).

A.1.4

Report Type – Select the appropriate option from the drop down:

Medical Literature Monitoring Service Contractor Work Instruction (MLM WIN-03) - PUBLIC
Effective date: 1 September 2015

Page 4/23

Select option

Press A - Z to find initial letter
 Press Enter to select, Escape to clear

Not available to sender (unknown) (4)

Other (3)

Report from studies (2)

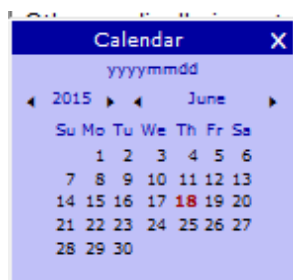
Spontaneous (1)

A.1.6b Receive date – The date of receipt of the initial report (i.e. day zero where four minimum criteria for a valid ICSR – reporter, patient, product, reaction). This date will remain the same in follow-up reports.

Receive Date

Field is Mandatory

Enter and select the date:



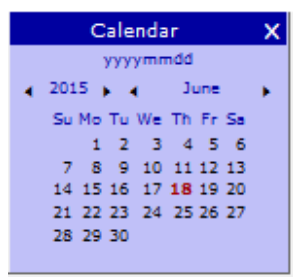
A calendar widget titled 'Calendar' with a close button (X). It shows the month of June for the year 2015. The days of the week are abbreviated as Su, Mo, Tu, We, Th, Fr, Sa. The date 18 is highlighted in red.

A.1.7b Receipt date – For initial reports it is the same date as 'Receive date' (**A.1.6b**). For follow-up reports it is the date of latest follow-up received date

Receipt Date

Field is Mandatory

Enter and select the date:



A calendar widget titled 'Calendar' with a close button (X). It shows the month of June for the year 2015. The days of the week are abbreviated as Su, Mo, Tu, We, Th, Fr, Sa. The date 18 is highlighted in red.

Case type: Enter and select the MAH.

Case Type

Field is Mandatory

Select Marketing Authorisation Holder / Sponsor form drop down:

Select option

Press A - Z to find initial letter
Press Enter to select, Escape to clear

Regulator Authority (1)

Marketing Authorisation Holder / Sponsor (2)

A.1.10.2 Case number – should be the same as entered in ‘A.1.0.1 Safety report Id’ and should be copied and pasted.

A.1.5.1 Serious – Select ‘Yes’ if case is serious and ‘No’ if case is non-serious from drop down.

Select option

Press A - Z to find initial letter
Press Enter to select, Escape to clear

No (2)

Yes (1)

A.1.5.2 Seriousness criteria – At least one of the data elements should be populated with the value ‘yes’ for each serious ICSR. Leave all reasons that are not populated blank.

Serious ?	Yes (1)
Results in death ?	No (2)
Life Threatening ?	Yes (1)
Caused/Prolonged Hospitaliza...	No (2)
Disabling / Incapacitating ?	No (2)
Congenital Anomaly ?	No (2)
Other medically important con...	No (2)

A.1.11 Duplicate

Enter ‘Yes’, in case of Duplicate report information is present.

Duplicate ☐

Select the ‘Report Duplicates’ (A.1.11) section in tree menu and Select ‘New Report Duplicate’ in active area

Safety Reports (1)	Num	Duplicate Source
<ul style="list-style-type: none"> Safety Report Report Duplicates (-) 	<input type="checkbox"/> New Report Duplicate	

Enter the related information in respective sections Duplicate source (A.1.11.1) and Duplicate number information (A.1.11.2)

Safety Reports (1)	Description	Name/Value
<ul style="list-style-type: none"> Safety Report Report Duplicates (1) Report Duplicate 	Duplicate Source	
	Duplicate Number	

A.1.12 Linked report

Where multiple ICSRs are identified from the same literature article, all ICSRs should be cross referenced in accordance with GVP Module VI, Table VI.3. If there are more than three ICSRs associated with one article, then only the first case should be cross-referenced to all other ICSRs, and all ICSRs should only be referenced to the first case.

Select the 'linked reports' (A.1.12) section in tree menu and select the 'new linked report' in active area.

Safety Reports (1)	Num	Link Report Number
<ul style="list-style-type: none"> Safety Report Report Duplicates (-) Linked Reports (-) 	<input type="checkbox"/> New Linked Report	

Enter the linked report number in ICH E2B format.

Safety Reports (1)	Description	Name/Value
<ul style="list-style-type: none"> Safety Report Report Duplicates (-) Linked Reports (1) Linked Report 	Link Report Number	

A.1.13 Report Nullification

Enter 'Yes' in Report nullification (A.1.13) section and 'reason for nullify' in Nullification reason (A.1.13.1) section in accordance with GVP Module VI Appendix V Table VI.12, in case nullification is required.

Report Nullification	
Nullification Reason	

NOTE: Nullification is final and cannot be reversed. If required, request confirmation from EMA MLM co-ordinators.

A.1.14 Medically Confirmed

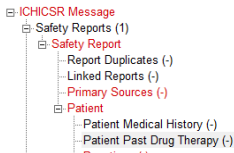
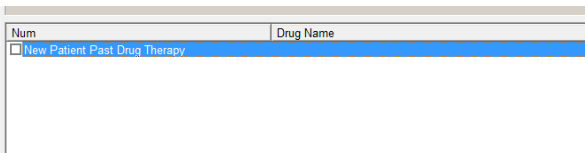
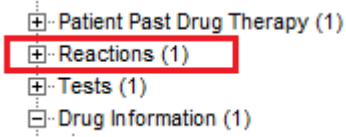
Should only be populated if the initial report was reported by a non-healthcare professional. The following conventions apply;

- Assume literature is from a healthcare provider based on journal title (normally assume physician unless e.g. Journal of Pharmacy).
- Leave 'blank', if the initial case reporter is Physician / OHCP / Pharmacist.
- Leave 'blank', if the initial case reporter is Physician / OHCP / Pharmacist and the follow up reported from Physician / OHCP / Pharmacist.
- Enter 'No', if the initial case reporter is Consumer / Lawyer / Non-HCP.
- Enter 'Yes', if Initial reporter is Consumer / Lawyer / Non-HCP and follow-up received from Physician / OHCP / Pharmacist and confirm that the event is

	<p>related to Suspect drug.</p> <div><div>Select option</div><div>Press A - Z to find initial letter Press Enter to select, Escape to clear</div><div>No (2)</div><div>Yes (1)</div></div>						
6. Primary source	<p>Select "Primary Source" (A.2.1) section from the tree area</p> <div><div><div><div><div></div></div><div>Safety Report</div></div><div><div><div></div></div><div>Report Duplicates (1)</div></div><div><div><div></div></div><div>Linked Reports (1)</div></div><div><div><div></div></div><div>Primary Sources (1)</div></div><div><div><div></div></div><div>Patient</div></div></div></div> <p>Select the 'New Primary Source' in active area.</p> <div><div><div>Safety Reports (1)<div><div>Safety Report</div><div>Report Duplicates (-)</div><div>Linked Reports (1)<div><div>Linked Report</div><div>Primary Sources (-)</div></div></div></div></div><div><table><tr><th>Num</th><th>Title</th><th>Given Name</th></tr><tr><td><input type="checkbox"/></td><td>New Primary Source</td><td></td></tr></table></div></div></div>	Num	Title	Given Name	<input type="checkbox"/>	New Primary Source	
Num	Title	Given Name					
<input type="checkbox"/>	New Primary Source						

	<p>Complete all mandatory A.2 Data elements as applicable</p> <table border="1"> <thead> <tr> <th>Description</th><th>Name/Value</th></tr> </thead> <tbody> <tr><td>Title</td><td></td></tr> <tr><td>Given Name</td><td></td></tr> <tr><td>Middle Name</td><td></td></tr> <tr><td>Family Name</td><td>Field is Mandatory Optional</td></tr> <tr><td>Organization</td><td>Field is Mandatory Optional</td></tr> <tr><td>Department</td><td></td></tr> <tr><td>Street</td><td></td></tr> <tr><td>City</td><td></td></tr> <tr><td>State</td><td></td></tr> <tr><td>Postcode</td><td>Field is Mandatory Optional</td></tr> <tr><td>Country</td><td>Field is Mandatory Optional</td></tr> <tr><td>Qualification</td><td></td></tr> <tr><td>Literature Ref.</td><td>Field is Mandatory Optional</td></tr> <tr><td>EudraCT Number</td><td>Field is Mandatory Optional</td></tr> <tr><td>Study Name</td><td>Field is Mandatory Optional</td></tr> <tr><td>Study Number</td><td></td></tr> <tr><td>Study Type</td><td></td></tr> </tbody> </table> <p>Reporter Title (A.2.1.1a)</p> <p>A.2.1.4 Qualification - to be included for all primary sources entered (at least 1 of the data fields required)</p> <p>Note: Cases originating from Spain require reporter state and postcode (seeAnnex 1).</p> <p>A.2.2 Literature Ref. – copy and paste in Vancouver style from DMTT.</p> <p>Enter only the lead author.</p>	Description	Name/Value	Title		Given Name		Middle Name		Family Name	Field is Mandatory Optional	Organization	Field is Mandatory Optional	Department		Street		City		State		Postcode	Field is Mandatory Optional	Country	Field is Mandatory Optional	Qualification		Literature Ref.	Field is Mandatory Optional	EudraCT Number	Field is Mandatory Optional	Study Name	Field is Mandatory Optional	Study Number		Study Type	
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Study Type																																					
7. Sender	Leave this blank.																																				
8. Patient	<p>Select "Patient" from the tree-view menu</p> <ul style="list-style-type: none"> [-] Primary Sources (1) <ul style="list-style-type: none"> [-] Patient <ul style="list-style-type: none"> [-] Patient Medical History (1) [-] Patient Past Drug Therapy (1) [-] Reactions (1) [-] Tests (1) 																																				
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	<p>At least a the definite existence of a patient would be required to enter in this section.</p> <p>B.1.1 Patient Initials – if unknown or not provided leave BLANK, except for when the need is to differentiate ICSRs where multiple ICSRs are retrieved from the same article (i.e. PT1, PT2, PT3 etc.)</p> <p>When performing follow-up, if the initials are provided enter ‘PRIVACY’,</p> <p>B.1.2.3 Patient Age Group – Where patient age is known, this field does not require completion.</p>																																																																														
9. Medical history	<p>Select ‘Patient Medical History’ from the tree-view menu</p> <div><div><div>ICHCSR Message<ul style="list-style-type: none">Safety Reports (1)<ul style="list-style-type: none">Safety Report<ul style="list-style-type: none">Report Duplicates (-)Linked Reports (-)Primary Sources (-)Patient<ul style="list-style-type: none">Patient Medical History (-)</div><div><table><tr><th>Num</th><th>Structured M...</th><th>Start Date</th><th>Conti...</th><th>End Date</th></tr><tr><td colspan="5"><input type="checkbox"/> New Patient Medical History</td></tr></table></div></div></div>	Num	Structured M...	Start Date	Conti...	End Date	<input type="checkbox"/> New Patient Medical History																																																																								
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Continuing ?															
End Date	.														
Comments															
10. Past drug therapy	<p>Select 'Past drug therapy' (B.1.8) from the tree-view menu.</p> <div>   </div> <p>Enter the all the information in related fields, if reported in article.</p> <p>Use lookup for MedDRA LLT to code the terms under Indication and reaction fields.</p> <p>Use free text field for information that does not code in MedDRA or for example can be attribute to a class of drugs instead of individual active substances</p> <table border="1"> <thead> <tr> <th>Description</th><th>Name/Value</th></tr> </thead> <tbody> <tr> <td>Drug Name</td><td></td></tr> <tr> <td>Blinded</td><td></td></tr> <tr> <td>Start Date</td><td></td></tr> <tr> <td>End Date</td><td></td></tr> <tr> <td>Indication (Code)</td><td></td></tr> <tr> <td>Reaction (Code)</td><td></td></tr> </tbody> </table>	Description	Name/Value	Drug Name		Blinded		Start Date		End Date		Indication (Code)		Reaction (Code)	
Description	Name/Value														
Drug Name															
Blinded															
Start Date															
End Date															
Indication (Code)															
Reaction (Code)															
11. Reaction	<p>Select "Reaction" from the tree menu</p> <div>  </div>														
11a.	Complete all mandatory "B.2" Data elements as applicable														

Description	Name/Value
Reaction Reported by Primary Source	
MedDRA llt (code)	
Highlighted Term ?	
Start Date	
End Date	
Duration	
Duration Unit	
Interval Administration-Reaction	
Interval Administration-Reaction Unit	
Interval Last Dose-Reaction	
Interval Last Dose-Reaction Unit	
Outcome	

B.2 Reaction reported by primary source – enter term as reported if not exact MedDRA term match.

B.2.i.1.b MedDRA llt (code) - Use lookup for MedDRA LLT to code the term.

Only enter the reactions reported in full accordance with the latest [MedDRA term selection points to consider document](#).

Typical symptoms associated with the reactions should only be entered in the narrative summary and not coded. Atypical symptoms can be coded if deemed necessary by the physician.

If only a series of reactions is listed which is indicative of a diagnosis, do not enter the presumed diagnosis and code all reactions.

If the symptoms are related to diagnosis, only enter the diagnosis in reaction section (B.2.i.1.b) and code it in MedDRA.

If only symptoms are provided in article, enter all the symptoms in reaction section (B.2.i.1.b) and code it with MedDRA.

Outcome (B.2.i.8):

Select 'outcome' from drop down menu:

	<div data-bbox="347 190 1197 728"> <div>Interval Last Dose-Reaction Unit</div> <div>Outcome</div> <div>Select option</div> <div>Press A - Z to find initial letter Press Enter to select, Escape to clear</div> <div>fatal (5)</div> <div>not recovered/not resolved (3)</div> <div>recovered/resolved (1)</div> <div>recovered/resolved with sequelae (4)</div> <div>recovering/resolving (2)</div> <div>unknown (6)</div> <div>Outcome of the reaction (B.2.i.8)</div> </div> <p>Where death is <u>unrelated</u> to the reported reaction, ensure the following data fields are in agreement</p> <p>B.1.9 Patient death section should be completed.</p> <p>B.2.i.8 Outcome – Fatal is NOT selected</p> <p>A.1.5.2 (Seriousness = yes) Results in Death? – Select ‘no’</p>																
12. Structured test	<p>Select “Test” (B.3) from the tree-view menu</p> <div data-bbox="351 1176 718 1377"> <div>Patient</div> <div> <div> <div>+</div> <div>Patient Medical History (1)</div> </div> <div> <div>+</div> <div>Patient Past Drug Therapy (1)</div> </div> <div> <div>+</div> <div>Reactions (1)</div> </div> <div> <div>+</div> <div>Tests (1)</div> </div> <div> <div>+</div> <div>Drug Information (1)</div> </div> </div> </div> <p>Enter the all the information in related fields, if reported in article.</p> <p>Use lookup for MedDRA LLT to code the terms under Indication and reaction fields.</p> <table border="1"> <thead> <tr> <th>Description</th><th>Name/Value</th></tr> </thead> <tbody> <tr> <td>Test Date</td><td></td></tr> <tr> <td>Test Name</td><td></td></tr> <tr> <td>Test Result</td><td></td></tr> <tr> <td>Test Unit</td><td></td></tr> <tr> <td>Normal Low Range</td><td></td></tr> <tr> <td>Normal High Range</td><td></td></tr> <tr> <td>More Information ?</td><td></td></tr> </tbody> </table> <p>Where necessary, use the duplicate functionality for test results repeated several times, ensuring the date and test results are changed appropriately.</p> <p>Use free text field for test information that does not code in MedDRA</p>	Description	Name/Value	Test Date		Test Name		Test Result		Test Unit		Normal Low Range		Normal High Range		More Information ?	
Description	Name/Value																
Test Date																	
Test Name																	
Test Result																	
Test Unit																	
Normal Low Range																	
Normal High Range																	
More Information ?																	
13. Drug Information	<p>Select “Drug Information” from the tree menu</p>																

	<ul style="list-style-type: none"> - Patient <ul style="list-style-type: none"> + Patient Medical History (1) + Patient Past Drug Therapy (1) + Reactions (1) + Tests (1) + Drug Information (1) <ul style="list-style-type: none"> - Drug Information <ul style="list-style-type: none"> + Drug Recurrences (1) + Drug Reaction Relatedness (1) + Active Substances (1) 																																																																										
13a.	<p>Complete all mandatory "B.4" Data elements as applicable</p> <table border="1"> <thead> <tr> <th>Description</th><th>Name/Value</th></tr> </thead> <tbody> <tr><td>Drug Role Characterisation</td><td></td></tr> <tr><td>Proprietary Medicinal Product Name</td><td></td></tr> <tr><td>Blinded</td><td></td></tr> <tr><td>Country of obtainment</td><td></td></tr> <tr><td>Batch/Lot Number</td><td></td></tr> <tr><td>Authorization/Application Number</td><td></td></tr> <tr><td>Authorisation Country</td><td></td></tr> <tr><td>MAH</td><td></td></tr> <tr><td>Dose</td><td></td></tr> <tr><td>Dose Unit</td><td></td></tr> <tr><td>Number of Separate Dosages</td><td></td></tr> <tr><td>Interval Number</td><td></td></tr> <tr><td>Definition of the Interval</td><td></td></tr> <tr><td>Cumulative Dosage to First Reaction</td><td></td></tr> <tr><td>Cumulative Dosage Unit to First Reaction</td><td></td></tr> <tr><td>Dosage Text</td><td></td></tr> <tr><td>Pharmaceutical Form</td><td></td></tr> <tr><td>Route of Administration</td><td></td></tr> <tr><td>Parent Route of Administration</td><td></td></tr> <tr><td>Gestation Period</td><td></td></tr> <tr><td>Gestation Period Unit</td><td></td></tr> <tr><td>Indication (Code)</td><td></td></tr> <tr><td>Date of Start of Drug</td><td></td></tr> <tr><td>Start Period</td><td></td></tr> <tr><td>Start Period Unit</td><td></td></tr> <tr><td>Last Period</td><td></td></tr> <tr><td>Last Period Unit</td><td></td></tr> <tr><td>Last Administration Date</td><td></td></tr> <tr><td>Treatment Duration</td><td></td></tr> <tr><td>Treatment Duration Unit</td><td></td></tr> <tr><td>Action Taken</td><td></td></tr> <tr><td>Reaction Recurred on Readministration</td><td></td></tr> <tr><td>Additional Information</td><td></td></tr> <tr><td></td><td>Drug Recurrences (1)</td></tr> <tr><td></td><td>Drug Reaction Relatedness (1)</td></tr> <tr><td></td><td>Active Substances (1)</td></tr> </tbody> </table>	Description	Name/Value	Drug Role Characterisation		Proprietary Medicinal Product Name		Blinded		Country of obtainment		Batch/Lot Number		Authorization/Application Number		Authorisation Country		MAH		Dose		Dose Unit		Number of Separate Dosages		Interval Number		Definition of the Interval		Cumulative Dosage to First Reaction		Cumulative Dosage Unit to First Reaction		Dosage Text		Pharmaceutical Form		Route of Administration		Parent Route of Administration		Gestation Period		Gestation Period Unit		Indication (Code)		Date of Start of Drug		Start Period		Start Period Unit		Last Period		Last Period Unit		Last Administration Date		Treatment Duration		Treatment Duration Unit		Action Taken		Reaction Recurred on Readministration		Additional Information			Drug Recurrences (1)		Drug Reaction Relatedness (1)		Active Substances (1)
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B.4.k.1 Drug role characterisation – Select from drop down menu, at least one drug should be characterised as (1) Suspect or (2) concomitant (3) or Interacting from drop down.

13a.

Complete all mandatory "B.4" Data elements as applicable

Description	Name/Value
Drug Role Characterisation	
Proprietary Medicinal Product Name	
Blinded	
Country of obtainment	
Batch/Lot Number	
Authorization/Application Number	
Authorisation Country	
MAH	
Dose	
Dose Unit	
Number of Separate Dosages	
Interval Number	
Definition of the Interval	
Cumulative Dosage to First Reaction	
Cumulative Dosage Unit to First Reaction	
Dosage Text	
Pharmaceutical Form	
Route of Administration	
Parent Route of Administration	
Gestation Period	
Gestation Period Unit	
Indication (Code)	
Date of Start of Drug	
Start Period	
Start Period Unit	
Last Period	
Last Period Unit	
Last Administration Date	
Treatment Duration	
Treatment Duration Unit	
Action Taken	
Reaction Recurred on Readministration	
Additional Information	
	Drug Recurrences (1)
	Drug Reaction Relatedness (1)
	Active Substances (1)

B.4.k.1 Drug role characterisation – Select from drop down menu, at least one drug should be characterised as (1) Suspect or (2) concomitant (3) or Interacting from drop down.

Description	Name/Value	
Drug Role Characterisation		Field is Mandatory
Proprietary Medicinal Product Name	Select option	
Blinded		
Country of origin		
Batch/Lot Number	Press A - Z to find initial letter Press Enter to select, Escape to clear	
Authorization/Application Number		
Authorisation Count	Concomitant (2)	
MA		
Dose	Interacting (3)	
Dose Unit		
Number of Separate Dosages	Suspect (1)	
Interval Number		

B.4.k.2.1 Proprietary medicinal product name field- Enter the proprietary medicinal product "brand" name if known.

B.4.k.2.2 Active substances (Subfolder of main tree) – Enter substance name in this mandatory field for every medicinal substance.

B.4.k.5 Structured Dosage Information: Enter the dosage information in related fields (e.g., 2 mg three times a day for five days)

B.4.k.5.1 dose (number) 2

B.4.k.5.2 dose (unit) mg

B.4.k.5.3 number of separate dosages 3

B.4.k.5.4 number of units in the interval 1

B.4.k.5.5 definition of the interval unit day. Select the option from drop down.

Select option

Press A - Z to find initial letter
Press Enter to select, Escape to clear

As Necessary (812)
Cyclical (811)
Days (804)
Hours (805)
Minutes (806)
Months (802)
Seconds (807)
Total (813)
Trimester (810)
Weeks (803)
Years (801)

B.4.k.7 Pharmaceutical Form – Where entered, this should conform to latest version of the [European Pharmacopoeia Dosage Forms List](#).

B.4.k.12b Date of start of drug – Where multiple date ranges exist, enter dates most significant to the date of the earliest reaction that is being reported.

B.4.k.14b Last administration date – Where multiple date ranges exist, enter date corresponding to the final administration date.

B.4.k.16 Action taken – Action taken with suspect drug as a result of the reaction.

Select the suitable option from drop down.

Select option

Press A - Z to find initial letter
Press Enter to select, Escape to clear

Dose increased (3)
Dose not changed (4)
Dose reduced (2)
Drug withdrawn (1)
Not applicable (6)
Unknown (5)

"Not applicable" should be used in circumstances such as if the patient died or the treatment had been completed prior to reaction/event.

B.4.k.17.1 Reaction recurred on re-administration? = Drug re-challenge

Select the option from drop down.

Reaction Recurred on Readmini. Additional Informatic

Select option

Press A - Z to find initial letter
Press Enter to select, Escape to clear

Yes (1)

No (2)

Unknown (3)

Did reaction recur on readministration ?

Unknown indicates that a re-challenge was done but it is not known if the event recurred. This segment should not be completed if it is unknown whether a re-challenge was done.

B.4.k.18 Drug reaction relatedness –

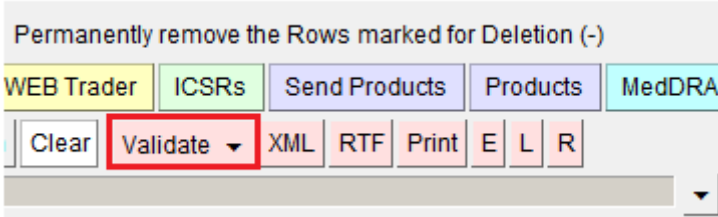
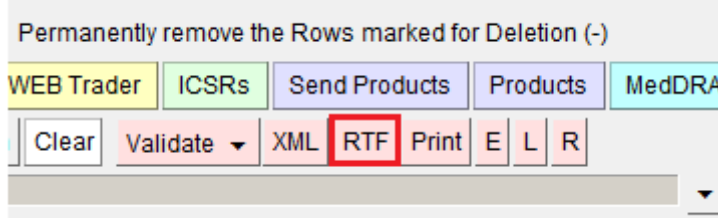
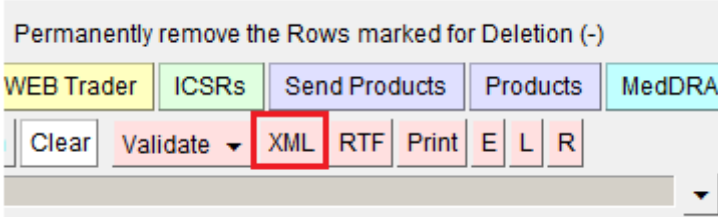
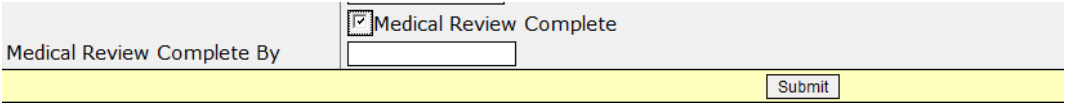
In most cases, you would not need to enter drug-reaction relatedness. If you do, enter records for the reporter, for each reported reaction taking into account the following criteria for relatedness assessments.

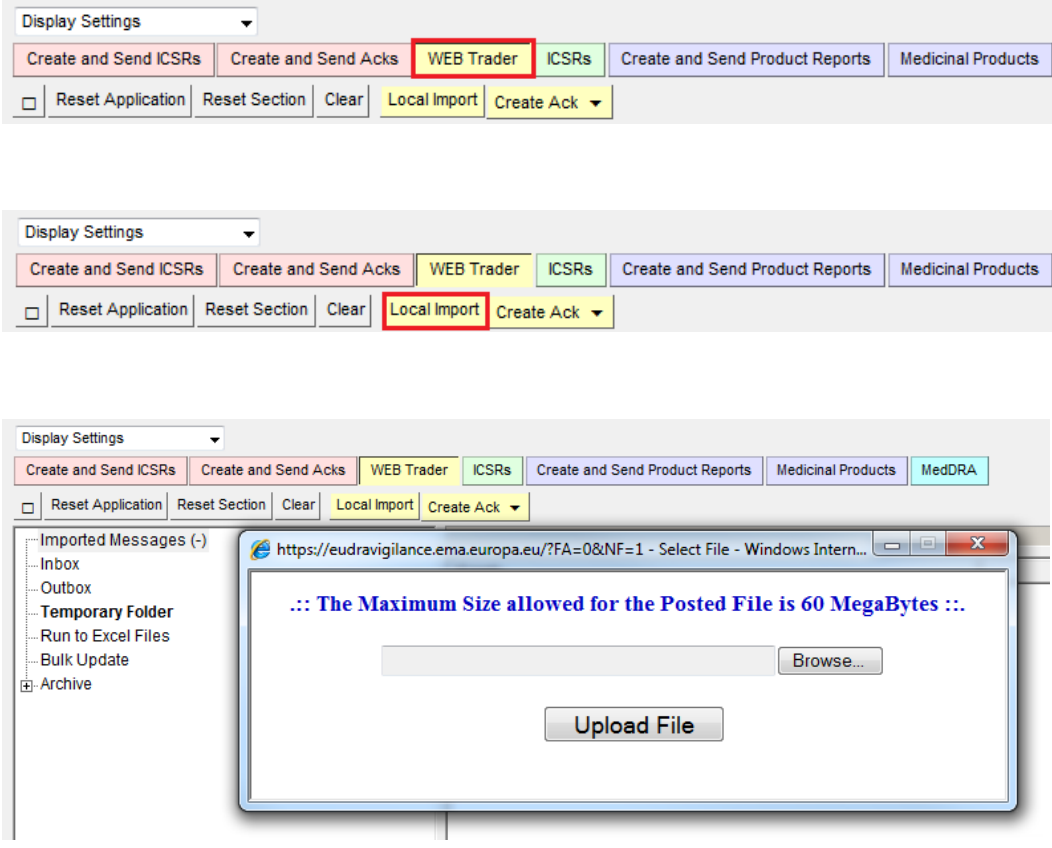
- For spontaneous cases with assumed causality, there is no need to provide a drug-reaction relatedness, except where specifically stated by the author(s) in the literature article
- For cases where not all reactions are related to all drugs (e.g. 2 drugs, 2 reactions, drug 1 associated with both, drug 2 only associated with the 1st reaction), provide all relevant relatedness sections as stated by the author(s) in the literature article
- For cases from non-interventional studies: always provide relatedness (even if not provided by the primary author)

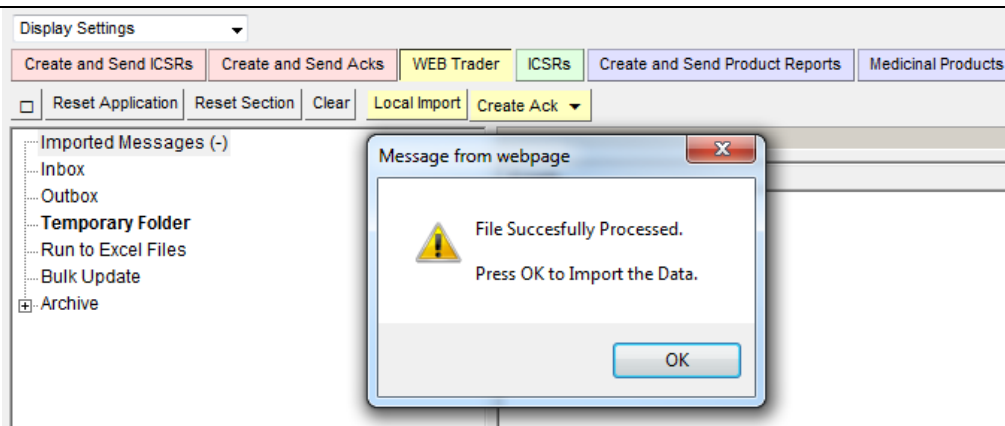
Description	Name/Value
Reaction (Code)	
Source of Assessment	
Method of Assessment	
Result	

B.4.k.18.4 Result – For all MLM Initial cases, the minimum is 'possible'

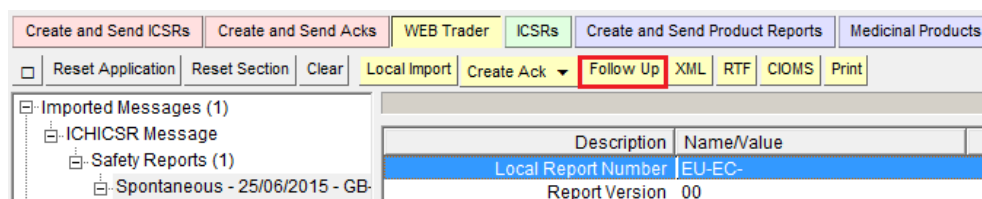
14. Summary Select 'Summary' from the tree-view menu

	<table border="1"> <thead> <tr> <th>Description</th><th>Name/Value</th></tr> </thead> <tbody> <tr> <td>Case Narrative</td><td></td></tr> <tr> <td>Reporter Comment</td><td></td></tr> <tr> <td>Diagnosis (Code)</td><td></td></tr> <tr> <td>Sender's Comment</td><td></td></tr> </tbody> </table> <p>B.5.1 Case narrative – Copy and paste MLM ICSR narrative into this section. Character limit is 20,000. Use the Annex 2, as a template and complete in MS Word, including performing spell check, before copying and pasting. Avoid entering special characters</p>	Description	Name/Value	Case Narrative		Reporter Comment		Diagnosis (Code)		Sender's Comment	
Description	Name/Value										
Case Narrative											
Reporter Comment											
Diagnosis (Code)											
Sender's Comment											
15. Validate	<p>Select 'Validate' to ensure that the entered data fields meet the validation criteria within the EVWEB tool.</p>  <p>Select 'ISCR' from the drop-down menu.</p> <p>If an error is identified, correct the issue in the appropriate data entry screens.</p>										
16. Generate RTF											
17. Generate XML											
18. Medical Review	<p>The Physician accesses the RTF and reviews against the source information saved in DMTT (literature or follow-up information), and requests updates to the case as necessary.</p> <p>Confirm medical review in the DMTT by ticking the medical review box and enter initials.</p>  <p>Once medical review is complete in DMTT. Update case status to 'processed' and submit in DMTT.</p>										

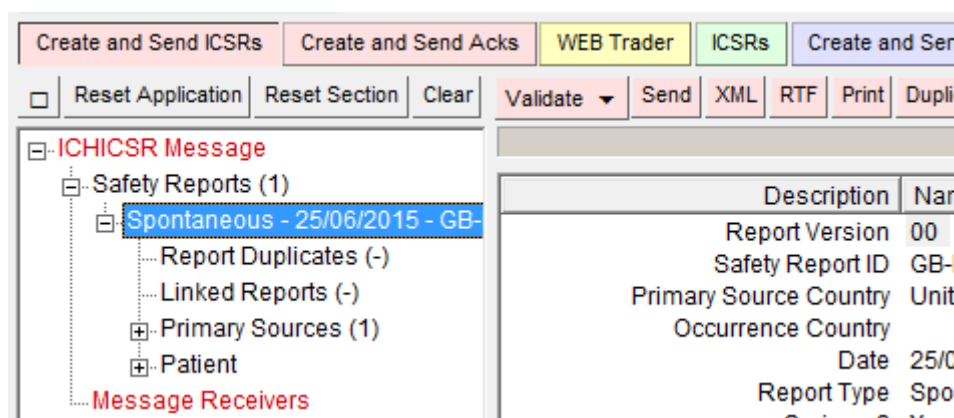
	<div> <div>Case Serious?</div> <div>Yes</div> </div> <div> <div>Suspect or Interacting</div> <div></div> </div> <div> <div>Case Status:</div> <div>Processed</div> </div> <div> <input type="checkbox"/> Follow-up required </div>
19. Message No.	<p>The "Message Number" is a unique tracking number assigned to the ICSR message by the report generating database, or where manual, the responsible MLM analyst, prior to submission of an ICSR.</p> <p>For manually assigned message numbers, the following format is followed:</p> <p>Format = DMTT ID (version number in brackets)</p> <p>Note. No two ICSRs (or versions of an ICSR) should have the same message number.</p>
20. Submit ICSRs	 <p>The screenshots illustrate the process of submitting ICSRs via the EudraVigilance interface. The first screenshot shows the 'WEB Trader' button highlighted. The second screenshot shows the 'Local Import' button highlighted. The third screenshot shows a file upload dialog box with the message 'The Maximum Size allowed for the Posted File is 60 MegaBytes' and an 'Upload File' button.</p>



Once the Xml is uploaded in web trader, select the follow-up.

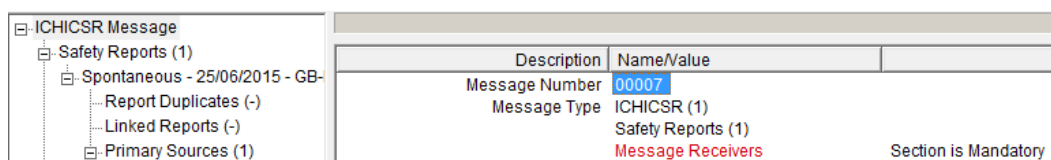


ICSR would shift in to create and sent ICSRs Section to amend if require.



The Message number (M.1.4) would be the number as allocated by DMTT and Message type (M.1.1) would be ICHICSR for all literature case.

Ensure the transmission date is entered.



Select the Message Receivers> Message Receivers> Regulatory Authority.

Select all relevant NCAs (EV plus NCA where necessary) to which the case has to be sent and validate.

Prior to sending the case, select Validate and select ICHICSR. If the validation step does not report any error, the case is ready to be submitted to the selected NCAs.

The screenshot shows the 'ICHICSR Message' window. On the left is a tree view with categories like 'Safety Reports (1)', 'Spontaneous - 25/06/2015 - GB-MLMSERVICE-20...', 'Linked Reports (-)', 'Primary Sources (1)', 'Patient', 'Patient Medical History (-)', 'Patient Past Drug Therapy (-)', 'Reactions (1)', 'Tests (-)', 'Drug Information (1)', 'Summary', and 'Message Receivers'. The 'Message Receivers' section is expanded, showing 'United Kingdom - Eudravigilance' and 'Germany - Federal Institute for Drugs and Medical...'. On the right is a table with columns: Num, Name, Country, ID, and Type. The table lists various regulatory authorities, with '1726 Eudravigilance' and '1727 Eudravigilance Web Trader' highlighted in blue.

Num	Name	Country	ID	Type
<input type="checkbox"/> 0247	Federal Agency for Medicines an...	Belgium	AFIGP	Regulatory Authorit
<input checked="" type="checkbox"/> 0806	Federal Institute for Drugs and M...	Germany	BFARM	Regulatory Authorit
<input type="checkbox"/> 1492	Danish Medicines Agency Clinic...	Denmark	DKMACTM	Regulatory Authorit
<input type="checkbox"/> 1493	Danish Health and Medicines Au...	Denmark	DKMAEUDRA	Regulatory Authorit
<input type="checkbox"/> 1514	DIVISION DE LA PHARMACIE M...	Luxembourg	DPM	Regulatory Authorit
<input type="checkbox"/> 1702	European Commission XEVMP...	Belgium	EUCOMPROD	Regulatory Authorit
<input type="checkbox"/> 1718	EUDRAVIGILANCE	United Kingdom	EVCTMPROD	Regulatory Authorit
<input checked="" type="checkbox"/> 1726	Eudravigilance	United Kingdom	EVHUMAN	Regulatory Authorit
<input type="checkbox"/> 1727	Eudravigilance Web Trader	United Kingdom	EVHUMANWT	Regulatory Authorit
<input type="checkbox"/> 1858	Finnish Medicines Agency	Finland	FINAM	Regulatory Authorit
<input type="checkbox"/> 1859	Finnish Medicines Agency	Finland	FINAMW	Regulatory Authorit

Save a copy of the XML in the case folder on the shared drive and select send.

A pop-up opens with the NCAs that have been selected. Click OK and a webpage dialog box opens. Click OK and a summary of the case as well as the authorities the case was sent to appear.

The screenshot shows the same 'ICHICSR Message' window as before, but with a 'Message from webpage' dialog box open in the foreground. The dialog box has a question mark icon and the text: 'Message Receivers: Eudravigilance, Federal Institute for Drugs and Medical Devices. OK to Send?'. There are 'OK' and 'Cancel' buttons at the bottom.

Save a text copy of the screen that appears showing the intended recipients in share drive.

21. Acknowledgements in WEB Trader

The acknowledgements should be checked every business day for cases submitted.

Access the DMTT and run query for ICSR submission for case submitted, ack not received.

To retrieve message acknowledgements in EVWEB, navigate to the menu and select 'ICSRs'

Navigate to 'Queries' and click on '+'

Click on '+' on MLM Reports and click on Conditions and select the appropriate filter Case Safety Report (matches)

The screenshot shows the ICHCSR system interface. At the top, there is a 'Display Settings' dropdown and a row of buttons: 'Create and Send ICSRs', 'Create and Send Acks', 'WEB Trader', 'ICSRs' (highlighted with a red box), 'Create and Send Product Reports', 'Medicinal Products', and 'MedDRA'. Below these are buttons for 'Reset Application', 'Reset Section', 'Clear', 'E', 'R', 'Run' (highlighted with a black box), and 'Run to Excel'. On the left, a tree view shows 'Safety Reports (-)', 'ICHCSR Messages (-)', 'Queries', 'Case Tracking List', 'All Reports', 'MLM Reports', 'Fields', 'Conditions (AND)' (highlighted with a blue box), 'Results', 'Reports with Warnings', 'Reports with Errors', 'ICHCSR Messages', and 'Statistics'. On the right, a table lists search criteria with checkboxes:

Description	Name/Value
Reporting Type	<input type="checkbox"/>
Local Report Number (Matches)	<input type="checkbox"/>
Blinded Suggestion	<input type="checkbox"/>
Blinded	<input type="checkbox"/>
Blinded (Manual Recode Status)	<input type="checkbox"/>
Message Receive date	<input type="checkbox"/>
Message Receive date (From)	<input type="checkbox"/>
Message Receive date (Up to)	<input type="checkbox"/>
Transmission date	<input type="checkbox"/>
Transmission date (From)	<input type="checkbox"/>
Transmission date (Up to)	<input type="checkbox"/>
Primary Source Country	<input type="checkbox"/>
Occurrence Country	<input type="checkbox"/>
Reporter Country	<input type="checkbox"/>
Study Name (Matches)	<input type="checkbox"/>
Study Number (Matches)	<input type="checkbox"/>
Study Type	<input type="checkbox"/>
Medicinal product (Matches)	<input type="checkbox"/>
Active substance (Matches)	<input type="checkbox"/>
Drug characterization	<input type="checkbox"/>
Product Scientific Name (Matches)	<input type="checkbox"/>
Drug Indication (code)	<input type="checkbox"/>

Run the search to retrieve the case and load.

Click Safety Report ack to see the ack(s) retrieved for this case.

This screenshot shows a portion of the ICHCSR system interface. It includes the 'Display Settings' dropdown and buttons for 'Create and Send ICSRs', 'Create and Send Acks', 'WEB Trader' (highlighted with a red box), and 'ICSRs'. Below these are buttons for 'Reset Application', 'Reset Section', and 'Clear'.

21c.

An acknowledgment is received for each message recipient (EV and relevant NCAs).

Review each acknowledgment and save on the Share drive in each case file.

Access DMTT and update that acknowledgement received.

If a 02 Ack is received, revert back to the ICSR to ascertain the root cause. Correct the case and resubmit. If the reason for 02 is not apparent, escalate to the EMA MLM coordinators for resolution immediately.

Annex 1: Spanish INE codes.



Copia de
Tabla_CCAA_codigo.

Annex 2: Case Narrative Template

"This case was detected in the medical literature by the EMA MLM Service from (insert article reference in Vancouver style) on (insert date of search or receipt of FTA if appropriate).

This spontaneous case was reported in the medical literature by a <physician> from <enter Country> and concerns a <enter age/ gender if available> patient who experienced a (serious) adverse reaction of <enter reaction terms> associated with <enter suspect active substance(s)>

The patient's medical and drug history included <xx>. (Delete if not known / reported)

On <insert DD MMM YYYY/ or an unknown date>, the patient began treatment with <active substance> (batch number and expiration date, if available) at a dose of <XX / frequency> for <indication>.

On (insert date DDMMMYYYY or unknown), the patient experienced <Preferred terms>. This reaction was considered serious due to <insert qualifying criteria>

The patient received treatment with [all available details of treatment (delete if not stated)

The outcome of the adverse events was <recovered/not recovered/ recovering/ unknown>

<If follow-up or FTA has been requested> Follow-up has been requested

Annex 3: Reporting Matrix, EEA NCA requiring cases sent directly to NCAs



NCAs list.pdf