Catalog of AE Gaps

This page lists the gaps currently identified in FHIR R4 base resource and mapping to other standards. As a general note, AdverseEvent is not represented in either USCDI v1, v2, or draft v3.

FHIR R4 Adverse Event Resource (v4.0.1) – this version is the one our work references
FHIR R5 Adverse Event Resource (v4.6.0) – note: this is an older version of R5
FHIR R5 Adverse Event Resource (current build)

Patient Care Group Adverse Event Topic contains some background, to include primary use cases, and challenges

See comments on this page below for links to related Jira tickets

Update 6/1/22 – Team will be reviewing these gaps to determine how to represent them in a AdverseEvent profile for clinical research based on R5. Potential gaps/modifications for our R5 profile are highlighted in both tables below.

MedWatch Form 3500A Mapping (this form is for use by user-facilities, importers, distributors and manufacturers for MANDATORY reporting)

**Level set:** First pass (starting 3/17/22):

- Our primary reference source is FHIR R4 (v4.0.1). If there is a gap in R4, we’ll see if it is in R5 (v4.6.0) and make note of it.
- Our primary use case is clinical research trial AE reporting (e.g., not looking to identify AE by searching medical record)

**General notes:** What is architecture for supporting MedWatch form generation? This would help define how elements are populated. For example, Epic current integration is as a server and other systems query for data from Epic; Subscription model would be good architecture for AEs where systems that want AEs sent to them subscribe

<table>
<thead>
<tr>
<th>MedWatch Data Element</th>
<th>R4 (v4.0.1) FHIR Resource</th>
<th>FHIR Element</th>
<th>FHIRPath</th>
<th>FHIR Data Type</th>
<th>Value Set</th>
<th>Source of Data</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.1 patient identifier</td>
<td>ResearchSubject.where (individual=AdverseEvent.subject).identifier</td>
<td>Clinical Trial Management System (CTMS)</td>
<td>For clinical trials this is a subjectID that is sponsor assigned Data that is presented downstream is controlled by what is allowed to be shared - so if patient information is in the AE resource, if subject ID is what can be shared that is what will be exposed How to pass Patient resource with the Research Subject ID? Should we add ResearchSubject as option for AE.subject? There isn’t a gap, you can get the subjectID, but may not be efficient (depends on architecture/workflow) From FDA: patient identifier can be either the subject ID or their initials (we request for full name or social security number NOT to be on the identifier field)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.2 age or date of birth</td>
<td>Patient.birthDate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.4 weight</td>
<td>Observation.value[x]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.1 Type of report (adverse event or product problem)</td>
<td>N/A</td>
<td></td>
<td>for our use case, would be adverse event and not mapped to a specific element in AE resource Mike Hamidi This would need an extension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
B.2 Outcome attributed to AE

Check all that apply:
- Death with date of death
- Life-threatening
- Hospitalization (initial or prolonged)
- Other serious or important medical events
- Required intervention to prevent permanent impairment/damage
- Disability or permanent damage
- Congenital anomaly/birth defects

AdverseEvent.seriousness (but only allows 1 value)

this is not right in R4 and potentially not right in R5 - this needs more discussion by our group to determine how to handle this

R4 has an outcome required valueset resolved | recovering | ongoing | resolvedWithSequelae | fatal | unknown which is not what this form question is asking

This question on MedWatch is the criteria (or classification) for making it a serious AE. In R4, the values on this form are similar to the seriousness value set, however, in R5, seriousness changed and is an example valueset with values serious and non-serious.

Mike Hamidi: AdverseEvent.outcome Note: This is a CodeableConcept type and allows for any value set or coding system in R5. Need to confirm if the form is asking for the outcome or qualifiers relating to the seriousness of that AE.

B.3 Date of event

AdverseEvent.date

Note: AE R4 resource has 3 dates; make sure definition is clear

AE R5 resource replaced date with Occurrence which will cover start and end dates using Period

MedWatch instruction:
- Provide the actual or best estimate of the date of first onset of the adverse event. If day is unknown, month and year are acceptable. If day and month are unknown, year is acceptable.
- When a newborn baby is found to have a congenital anomaly, the event onset date is the date of birth of the child.
- When a fetus is aborted because of a congenital anomaly, or is miscarried, the event onset date is the date pregnancy is terminated.

B.4 Date of report

AdverseEvent.recordedDate

When it was recorded in the system

MedWatch instruction: For all mandatory reports filed for Medical Devices, Drugs and Biologics, including Human Cells, Tissues, and Cellular and Tissue-Based Products, enter the date the report is filled out.

B.5 Describe event or problem

AdverseEvent.referencingDocument – event narrative

this is a reference to a Document resource

AdverseEvent.event – codeable concept

On a user interface, this is typically a text field

Will be helpful to understand how this form is used downstream to determine if/how coded - if this data is coming from EHR/RWD source, does it need both narrative and if available a code, or just the narrative?

From FDA: narrative is needed for internal assessment; can add the AE terms (english not code, internally use MedDRA) if they have it - would be captured in G-7

MedWatch instruction:

For an adverse event: Describe the event in detail using the reporter's own words, including a description of what happened and a summary of all relevant clinical information (medical status prior to the event; signs and/or symptoms; differential diagnosis for the event in question; clinical course; treatment; outcome, etc.). If available and if relevant, include synopses of any office visit notes or the hospital discharge summary.

To save time and space (and if permitted by the institution), attach copies of these records with any confidential information deleted. DO NOT identify any patient, physician, or institution by name. The initial reporter's identity should be provided in full in section E.

Information as to any environmental conditions that may have influenced the event should be included, particularly when (but not exclusive to) reporting about a device.

For HCT/Ps, provide information on the type of surgical procedure and anatomical site of implantation, and the date of onset of symptoms.

Results of relevant tests and laboratory data should be entered in block B6. (see instructions for B6).

Preexisting medical conditions and other relevant history belong in block B7.

B.6 Relevant tests /laboratory data and date (multiple line entry)

AdverseEvent.subjectMedicalHistory (Reference: Observation)

B.7 Other relevant history, including preexisting medical conditions (e.g., allergies, pregnancy, smoking and alcohol use, liver/kidney problems, etc)

AdverseEvent.subjectMedicalHistory (Reference: Condition | AllergyIntolerance | FamilyMemberHistory | Immunization | Procedure | Media | DocumentReference)
C.1 Name and Strength, NDC# or unique ID, Manufacturer/Compounder, Lot#  
SuspectEntity.instance (Reference: Medication, MedicationAdministration, MedicationStatement)  
Medication resources are changing; vendors use different resources.  
RS manufacturer is Medication.marketingAuthorizationHolder—>pointing to Organization.  
Unique ID might be an IND number (Medication.identifier).  
All suspected medications.  
See C.3—this item may need to be covered by MedicationAdministration or MedicationStatement, not Medication to capture additional information required on form.  
From MedWatch instructions:  
NDC # or Unique ID: The National Drug Code (NDC #) is a universal product identifier for human drugs. NDC is a three-segment number; zeros and dashes should be included as they appear on the original manufacturer’s product label and/or packaging. NDC numbers are particularly useful to the FDA in investigating drug product quality problems. Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) must have a Unique ID number to track the product. For reports involving HCT/Ps, this unique ID should be provided in this box.

C.2 List Medical Product or Treatment Given at the same time of the event and date  
all additional medications or products patient using at time of event but not suspected to be part of the event—free text  
this is not necessarily suspect entity, so would it go into medical history?  
medical history doesn’t include reference to Medication. 
GAP in R4—no place to put additional medications in current AE resource; Mike H. posed question in Zulip if you can extend a reference list in an IND ideally, we’d add Medication/MedicationAdministration/MedicationStatement to the AdverseEvent.subjectMedicalHistory in AE RS could go into supporting info.  
From MedWatch Instructions:  
C2: List Medical Products and Treatment Given at the Same time of the Event and Date List and provide therapy dates for any other medical products (drugs, biologics, including HCT/Ps, or medical devices, etc.) that a patient was using at the time of the event. Do not include products used to treat the event.

C.3 Dose, Frequency, Route Used  
SuspectEntity.instance (Reference: MedicationAdministration, MedicationStatement)  
these attributes are not in Medication, they are in MedicationAdministration.  
AE suspectEntity is one resource Reference, so won’t get all the medication details in one resource—will need to clearly specify which medication resource to use that will capture the elements in Part C of the form. Since Medication by itself, you don’t know if they actually took it; probably want to use MedicationAdministration/Statement (which point to the Medication) for the suspectEntity. 
Medication resources are complex; being addressed by others; R5 is modifying how they are handled.

C.4 Treatment Dates /Therapy Dates  
SuspectEntity.instance (Reference: MedicationAdministration, MedicationStatement)  
real-world practice determines which/how medication is reported—MedicationAdministration is typically inpatient.  
How is medication represented in a pharmacy system? In an inpatient system, what is actually dispensed?  
MedicationRequest-->MedicationDispense-->MedicationAdministration / MedicationUsage / MedicationStatement...all anchored to Medication. How it gets designed an EHR can vary?  
use case specific: 100% adherence/in-person administration, infusion?  
MedicationAdministration  
Is the detailed medication information (e.g., lot) stored in an EHR?

C.5 Diagnosis for Use  
SuspectEntity.instance (Reference: MedicationAdministration, MedicationStatement)  

C.6 Product Type (OTC, Compounded, Generic, Biosimilar)  
some of this would come from the NDC, not necessarily a “checkbox” on a form—can be figured out from RxNorm code.  
RxNAV https://mor.nlm.nih.gov/RxNav/  
Is this captured for a clinical trial drug?  
This field isn’t represented in any FHIR R4 medication resources.  
How important is this information for MedWatch? FDA wants it if available.  
Is there any effort going on to record NDC in EHR?

C.7 Expiration Date  
SuspectEntity.instance (Reference: MedicationAdministration, MedicationStatement)
C.8 Event Abated After Use Stopped or Dose Reduced? (yes, no, doesn't apply)

Gap: create an extension to model this question for direct input

What is the action? Related to the treatment - correlation to medication not AE – start and stop of treatment and reason is in medication resource
Is this an assessment after the fact? Or is it part of the event assessment?
R5 AE has mitigating action (not in R4) - reference medicationAdministration
AE points to a Condition, which also has Condition.abatement[ ]
Can this be answered by the RWD source or does it require inference based on other information? (Patient reported is putting it into a document reference)
C8 can also be fulfilled by Questionnaire.item.enableWhen.answer[ ]
MedWatch instructions:
C8: Event Abated After Use Stopped or Dose Reduced In addition to checking the appropriate box, provide supporting lab tests and dates, if available, in block B6

C.9 Event Reappeared After Reintroduction? (yes, no, doesn't apply)

To discuss further - from 4/28/22 discussion leading towards fact that this might not be answerable at time of event; If reoccurrence, would be recorded as another AE.
5/12/2022: Not recorded as new AE - update to previous AE - record on same record; could depend on the sponsor on how they want it reported
To infer this from data, would need date and time
Consider making this a discrete element as extension; maybe add unknown as an option; test it out with use case

Section D: Suspect Medical Device
SuspectEntity.Reference(Device)

Don't go deeper on this section - the AE on a device will use this resource

Section E: Initial Reporter
Recorder.Reference()
SuspectEntity.Causality.author

This is where definitions are important - there is difference between who recorded the event and who attests/signs off on it
Again, don't go to deep at this time

Extensions in R4 compared to R5

<table>
<thead>
<tr>
<th>Data Element</th>
<th>R4 Gap</th>
<th>Current Extensions / IGs</th>
<th>R5 Status</th>
<th>Next Step</th>
</tr>
</thead>
</table>
| Event End Date | Not present | - EPIC: https://fhir.epic.com/Specifications?api=982
- adverse-event-resolved-date
- CTCAE IG: https://build.fhir.org/ig/standardhealth/fsh-ae
/StructureDefinition-adverse-event-resolved-date.html
- ICSR IG includes the extension (icsr-ext-eventenddate) to capture the end date | Addressed with https://build.fhir.org/adverseevent-definitions.html#AdverseEvent occurrence_x using Period.end | Not a gap, can model resolved date as occurrence to match R5 |
| Expectedness | Not present | - EPIC: https://fhir.epic.com/Specifications?api=982
- adverse-event-expected
- CTCAE IG: https://build.fhir.org/ig/standardhealth/fsh-ae
/StructureDefinition-adverse-event-expected.html | Added to R5 ballot: [FHIR-36007 - Adverse Event - add expectedInResearchStudy APPLIED] | In context of clinical trial, is AE expected; if not used outside of clinical trials, should it go in base resource?
This may be used in registries
Included on Medwatch form which is for post market surveillance
Bring this to Patient Care for addition to R5 |
| Study Attribution | ResearchStudy not allowed in https://www.hl7.org/fhir/adverseevent-definitions. html#AdverseEvent. suspectEntity.instance | None | Added to R5 ballot: [FHIR-36008 - Adverse Event.suspectEntity. instance support reference to ResearchStudy APPLIED] | ResearchStudy is relevant for downstream workflows
Need correlation back to researchstudy, but this is not explicit in current resource – allowing ResearchStudy as SuspectEntity can also capture the relatedness; also if no other information (e.g., medication) is available, can specifically tie AE to the study.
Bring this to Patient Care for addition to R5 |
### Grade/Severity
- Epic uses severity for the grade, not an extension.

Not addressed. "severity" field no longer present, no alternative place for grade - removed in

#### FHIR-22995 - Adverse Event.severity - confusing
Severity is now addressed in resulting Condition (mild, moderate, severe).

leave severity, but have a different value set than mild/moderate/severe - unlikely that Patient Care will put severity back into R5

FDA doesn't use CTCAE
does severity really need to be on the AE? PC decided it belongs on condition

Worth mentioning to PC there are use cases for severity, but no need to discuss adding it back in - it can be addressed as an extension - be sure to document the extension in the IG well as to its meaning and use.

### Grade / Severity History
- Not present

#### FHIR-22977 - Adverse Event.severity - confusing
Not addressed

EPIC: https://fhir.epic.com/Specifications?api=982
- adverse-event-severity-history
- adverse-event-severity
- adverse-event-severity-start-date

### Event Narrative / Comments
- Not present

#### FHIR-23023 - Addition of value set entries for AdverseEvent.seriousness
RESOLVED - NO CHANGE
(Additional value set entries for AdverseEvent.seriousness)

R5 cardinality is still 0..1
R5 value set is serious or non-serious
R5 changes outcome to be related to the seriousness criteria with cardinality is 0..*

Discussion: There is still a need to have an outcome of the AE which is different than seriousness_criteria (hospitalized, life threatening, defect, ...)

Outcome as defined in R4 was more appropriate (resolved, recovering, ongoing, ...)

Seriousness criteria is different than outcome of the AE, if only used by research, better as an extension than in the base resource

### Seriousness
- Exists as a boolean (i.e., non-serious and serious)
  - Only allows for one choice and there could be more than one thing that happens
  - It is almost like an outcome, but there is an outcome in AE that has different values
  - In most clinical studies, if serious then go onto indicate the outcome
  - AE outcome attribute is different than seriousness
  - What is expected on other side?
  - Is this detail about seriousness only used for clinical research?
  - For research, need to link outcome of AE to factors of seriousness

#### FHIR-23032 - Suggested values for AdverseEvent.outcome
APPLIED
(Suggested values for AdverseEvent.outcome)

R4 `(Additional value set entries for AdverseEvent.seriousness)`

Seriousness is now addressed in resulting Condition (mild, moderate, severe)

Could use occurrence.period? or occurrence.timing (duration is subset of timing)

#### ICSR IG
- Includes an extension (icsr-ext-eventseriousness) to allow specificity of seriousness via ValueSet (http://hl7.org/fhir/us/icsr-ae-reporting/ValueSet-ICSRSeriousness.html)
- CTCAE IG includes an extension "seriousness outcome" (https://build.fhir.org/ig/standardhealth/fsh-ae/StructureDefinition-adverse-event-seriousness-outcome-value-set.html) for this extension is similar to that of the ICSR IG.

Epic only uses serious and non-serious and Advarra only pulls in serious events

#### FHIR-23022 - Suggested values for AdverseEvent.outcome
APPLIED
(Suggested values for AdverseEvent.outcome)

RESOLVED - NO CHANGE
(Additional value set entries for AdverseEvent.seriousness)

Outcome as defined in R4 was more appropriate (resolved, recovering, ongoing, ...)

Seriousness criteria is different than outcome of the AE, if only used by research, better as an extension than in the base resource

### Event Duration
- Not present

#### ICSR IG
- Includes an extension (icsr-ext-eventduration) to capture the duration of an AE

Need to evaluate the definition of occurrence[s]

### Participant
- Not present

#### FHIR-23023 - Addition of value set entries for AdverseEvent.participant
RESOLVED - NO CHANGE
(Additional value set entries for AdverseEvent.participant)

Addressed with https://hl7.org/fhir/2021may/adverseevent-definitions.html

Participant function-value-set.html to support the need to indicate an "approver" or "authenticator" of the adverse event (beyond just the recorder).

Value set is an example and does not include an authenticator function
- contributor and recorder no longer present, they would be represented, if needed, using the participant element

ICSR IG includes an extension (icsr-ext-eventParticipant) with a value set adding authenticator (https://build.fhir.org/ig/standardhealth/fsh-ae/ValueSet-icsr-ext-eventParticipant) to support the need to indicate an “approver” or “authenticator” of the adverse event (beyond just the recorder).

Epic uses severity for the grade, not an extension - CTCAE IG: https://build.fhir.org/ig/standardhealth/fsh-ae/StructureDefinition-ctcae-grade.html with a value set: https://build.fhir.org/ig/standardhealth/fsh-ae/ValueSet-ctcae-grade-value-set.html